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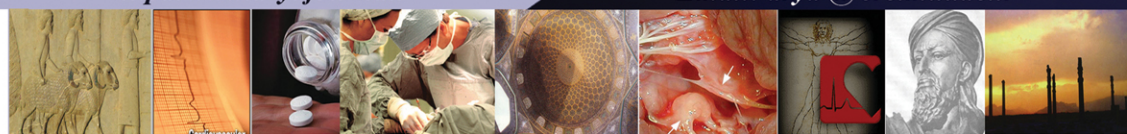

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2. Bonow RO, Mann DL, Zipes DP, Libby P. Braunwald's Heart Disease E-Book: A Textbook of Cardiovascular Medicine. 7th ed. Philadelphia, PA: Elsevier Health Sciences; 2007. p. 1976, 1981, 1982.

3. Gaston M. The psychological care of patients following a myocardial infarction [Online]. 2003; Available from: URL: http://www.nursingtimes.net/the-psychologicalcare-of-patients-following-a-myocardialinfarction/199464.article/

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The effect of patients' time of arrival at the hospital on the rate of Thrombolytic therapy

Toba Kazemi[(1)], Gholam-Reza Sharifzadeh[(2)], Samaneh Neikhonjy[(3)]

Letter to Editor

Date of submission: 8 Aug 2012, ***Date of acceptance:*** 14 Oct 2012

The honorable editor-in-chief of the Journal of ARYA

We read with interest the article of Dr. Maleki that has recently been published.[1] We conducted a similar study in Birjand Vali-e-Asr Hospital in 2009-2010. This study was done on 125 patients with STEMI with a mean age of 59.2 ± 11.9 years. In this study, 65.6% of patients underwent thrombolytic therapy. This showed a crucial increase compared to the previous study in Birjand in 2003 that showed 17.3% of patients underwent thrombolytic therapy.[2] Mean door to needle time was 74.8 ± 42.7 minutes (median 60 minutes). Thrombolytic therapy showed no difference for difference in sex (69.4% in males, and 51.9% in females, P = 0.08). However, in working staff (86.7% in employees, and 51.2% in farmers/workers, P = 0.003), in highly educated individuals (92.3% at university level, and 45.5% illiterate, P < 0.001), and in citizens (73.2% in urban, and 51.2% in rural citizens, P = 0.01) there was a higher percentage of thrombolytic therapy. The main reason for this difference between them is earlier arrival to the hospital since the onset of symptoms. The arrival time in the city's residents was 166.7 ± 179.6 minutes, but for villagers it was 221.6 ± 112 minutes (P = 0.001). Furthermore, the rate of thrombolytic therapy during the night was not significantly different compared to the rest of the day (73% during morning, 62.9% during afternoon, and 62.3% during night, P = 0.52). The patient's arrival time to the hospital at night was not different compared to the rest of the day (166.9 ± 174.7 minutes in the morning shift, and 148.2 ± 85.2 minutes during the night shift, P = 0.63). Visiting patients during the night shift was similar to other shifts; visit by intern was 12.3 ± 9.1 minutes during the morning shift, and 14.1 ± 9.3 minutes during the night shift (P = 0.73). The rate of thrombolytic therapy in our study was similar to the study by Dr. Maleki;[1] however, door to needle time was longer. In our hospital (Birjand Vali-e-Asr Hospital), due to lack of residents, it is necessary that patients should certainly be visited by a cardiologist (on call) before starting thrombolytic therapy and the cardiologist should himself/herself be present at the patient's bedsides.

It is necessary that public awareness be increased through educational programs on television, and local journals. Providing telemedicine facilities, through which a patient's ECG is observed by a cardiologist at home, is one of the necessities.

Conflict of Interests

Authors have no conflict of interests.

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1. Maleki A, Shariari A, Sadeghi M, Rashidi N, Alyari F, Forughi S, et al. Evaluation of fibrinolytic medical therapy for patients with acute myocardial infarction. ARYA Atheroscler 2012; 8(1): 46-9.
2. Kazemy T, Sharifzadeh GR. Changes in risk factors, medical care and rate of acute myocardial infarction in Birjand (1994-2003). ARYA Atheroscler 2006; 1(4): 271-4.

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Obesity and risk of hypercholesterolemia in Iranian northern adults

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Original Article

Abstract

BACKGROUND: The main aim of this study was to evaluate the association between serum cholesterol level and body mass index (BMI) in northern Iran.

METHODS: This was a cross-sectional study carried out on the 1995 subjects (997 males and 998 females) aged 25-65 years that were selected using multistage cluster sampling method. Plasma cholesterol was measured in the morning after a 12-hour fasting and was determined by auto-analyzer. Hypercholesterolemia (HC) was defined by a total plasma cholesterol level over 200 mg/dl. Weight and height were measured and BMI 25-29.9 kg/m² and ≥ 30 kg/m² was classified overweight and obesity, respectively.

RESULTS: Mean of age was 44.2 ± 11.5 years (44.3 ± 11.5 in men and 44.1 ± 11.2 in women) and plasma total cholesterol level was 203.1 ± 41.8 mg/dl. The HC was detected in 49.1% with higher rate in women (57.0%) than men (44.7%). In men at age 25-35 years, the odds ratio was 3.42 (1.60-7.29) in obese group and 1.90 (1.03-3.50) in overweight group compared to normal weight. In women, at age 35-45 years, the risk of HC in obese group was 3.01 (1.58-5.73) and in overweight group it was 2.06 (1.58-5.73), while in men aged 35-45 years the relative risk was 4.03 (2.22-7.34) in overweight and 3.58 (1.77-7.25) in obese group. In women after age 45 years, higher BMI was not a risk factor for HC.

CONCLUSION: There was a positive association between BMI and serum cholesterol level. In early middle age, obese individuals were at risk of HC more than overweight subjects. In men, after age 35 years, the risk of HC increased in overweight group while in women there was no statistically significant association between BMI and HC.

Keywords: Serum Cholesterol Level, Adult, Body Mass Index, Gender, Iran

Date of submission: 23 Jul 2012, ***Date of acceptance:*** 23 Oct 2012

Introduction

In middle-age, serum cholesterol level is well known as a risk factor for cardiovascular disease (CVD).[1] World Health Organization (WHO) reported that the prevalence of hypercholesterolemia (total cholesterol ≥ 6.5 mmol/l or taking lipid-lowering drugs) is varied across populations from 3% to 53% in men, and from 4% to 40% in women.[2] Some factors such as life style, diet, smoking, BMI (Body Mass Index), gender, physical activity and age are associated with plasma cholesterol level.[2-5]

The relationship between BMI and risk of CVD is well established in some studies[6-8] whereas the negative correlation was shown between serum cholesterol level and height in others.[9,10] BMI is positively associated with serum cholesterol level in middle-age men in Helsingborg, Sweden and the changing in cholesterol levels over the six-year follow-up was significantly related to the changing in BMI and WHR.[11] Alterations in lipid and lipoprotein concentrations and changing the CVD risk factors was seen in some studies.[12-15] In Framingham study,[16] the mortality and morbidity due to CVD was estimated by determining of plasma cholesterol levels in young and adult people. The risk of CVD death among subjects with high serum cholesterol was approximately 5-fold more than of those individuals having low serum cholesterol level and 10% decline of serum cholesterol decreased 30% in mortality rate due to it.[17]

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Golestan province is in the north of Iran (south east of Caspian Sea). Of 1.6 million people in this area, 66.4% are 15-64 years old. 43.9% and 56.1% people live in urban and rural areas, respectively. Agriculture is the main job in rural area and different ethnic groups such as Fars (native), Turkman and Sisstani live in this region.[18] The aim of this study was to evaluate the association between serum cholesterol level and BMI in men and women among 25-65 years old people in northern Iran.

Materials and Methods

We established a cross-sectional study with a sample of 1995 cases (997 men and 998 women with equal age) of urban and rural area, aged 25-65 years living in 11 districts in Golestan, Iran, situated at the south east of Caspian Sea. With assumption of 25% obesity rate,[3] a confidence level of 95% and a maximum marginal error about 0.02, the sample size was calculated 1800 subjects. For more efficiency the sample size was raised to 1995 subjects. We conducted a multistage cluster sampling techniques by 100 clusters with equal size of 20 subjects. In the first stage, the clusters were chosen randomly using systematic sampling technique based on postal code in urban areas and family health number in Primary Health Centers in rural areas. In the second stage, we randomly selected 20 subjects in each cluster. All family members in blocks (a complex of building) who were 25-65 years old were included in our study. Weight was measured with light clothing and without shoes and height was measured standing up with head, back and buttock on the vertical land of the height-gauge.

BMI was calculated as weight (kg) / height $(m)^2$ and World Health Organization classification was applied. BMI of 25.0-29.9 kg/m^2 was classified as overweight, BMI of 30.0 to 39.9 kg/m^2 was classified as obese and BMI equal to or greater than 40 kg/m^2 was classified as pathologic obese.[19]

For measuring of serum cholesterol level, blood sample was taken in the morning after 12 hours fasting. Serum cholesterol was measured by commercial kits (Pars Azmoon, Karaj, Iran) using auto-Analyzer. Plasma hypercholesterolemia (HC) was defined by a total plasma cholesterol level over 200 mg/dl.[20]

Quantitative and qualitative data are presented as mean ± standard deviation and frequently (%), respectively. SPSS software (version 16.0; SPSS Inc., Chicago, IL., USA) was used for the statistical analysis. Pearson's correlation coefficient was employed to determine correlation between BMI and serum cholesterol level. ANOVA and post-hoc Tukey's test were used to compare the means. Logistic regression analysis was applied to estimate the odds ratio (OR) of HC risk according to the BMI ranges. P-value under 0.05 was considered as statistically significant. This study approved by Ethical Research Committee and consent was received from all participants. Pregnant women, those on cholesterol lowering drugs and those who were unwilling to participate in this study were excluded from the study.

Results

The characteristics of subjects are presented in table 1. Mean of age and serum cholesterol level were 44.2 ± 11.3 years (44.3 ± 11.5 in men and 44.1 ± 11.2 in women) and 203.1 ± 41.8 mg/dl (196.7 ± 39.5 in men and 209.4 ± 42.9 women), respectively. The obesity and overweight were seen in 29.5% and 33.9%, respectively. HC was detected in 49.1% of population and was more in women (57.0%) than men (44.7%).

The serum cholesterol levels and BMI in age and sex groups are presented in table 2. The serum cholesterol level tended to increase with BMI and ANOVA test showed significant differences in all age groups ($P < 0.001$) in both genders. In men, the post-hoc Tukey test done for pair-waise comparison between three BMI ranges revealed a statistically significant differences in the mean cholesterol between normal and overweight as weel as between normal and obese people in all age groups ($P < 0.05$). There was no statistically signiifcant differences in the mean cholesterol between overweight and obese groups. In women, the post-hoc Tukey test showed a significant difference in the mean cholesterol based on overweight in all age groups and in the whole population, except in 45-55 years age groups ($P < 0.05$). This test was significant between normal weight and obese in all age groups and in total ($P < 0.05$). However, this relationship was not seen between overweight and obese people in all age groups and in total population.

The odds ratio was estimated for HC based on BMI and age by logistic regrision. Normal weight (BMI < 25 kg/m^2) was considered as reference. In men, the results of logistic regresion analysis showed that the risk of HC before age 35 years in obese group was more than overweight. At age 25-35 years, the risk of HC was 3.42 (1.60-7.29) in obese group and in overweight it was 1.90

(1.03-3.50) compared to normal subjects [Odds ratio (95% Confidence Interval)]. In contrary, in over 35 years, the relative risk of HC in overweight men [4.03 (2.22-7.34)] was more than obese men [3.587 (1.77-7.25)].

In women, the relative risk of HC among those aged under 45 years, in obese was more than overweight. Hence, the odds ratio at age 25-35, in obese was 4.05(2.07-7.90) and in overweight was 3.71(1.91-7.18). In 35-45 year age group in obese, the risk was 3.01(1.58-5.73) and in overweight was 2.06(1.58-5.73).

In women, the odds ratio of HC in obese was 2.75(2.00-3.77) and in overweight was 2.11(1.52-2.94). After age 45, the odds ratio for HC was not significant.

Table 1. The characteristics of subjects with respect to gender (N = 1995)

	Men	Women	Total	P
	Mean ± SD	Mean ± SD	Mean ± SD	
N (%)	997 (50)	998 (50)		
Age (year)	44.3 ± 11.5	44.1 ± 11.2	44.2 ± 11.3	0.700
Serum cholesterol (mg/dl)	196.7 ± 39.5	209.4 ± 42.9	203.1 ± 41.8	0.001
Body mass index (Kg/m2)	26.0 ± 4.8	28.7 ± 6.3	27.3 ± 5.8	0.001

*Numbers represent mean ± standard deviation;
SD: Standard deviation

Table 2. Serum cholesterol level and body mass index based on age and gender

Age group (Year)		No	Body mass index status	Cholesterol mg/dl Mean ± SD	P*	OR (CI 95%)	P§
25-35	Men	119	Normal	178.6 ± 33.2	0.001	(1)	-
		84	Overweight	188.9 ± 38.3		1.90(1.03-3.50)	0.040
		39	Obese	202.6 ± 33.8		3.42(1.60-7.29)	0.001
	Women	106	Normal	177.5 ± 32.8	0.001	(1)	-
		71	Overweight	202.1 ± 42.3		3.71(1.91-7.18)	0.001
		68	Obese	204.3 ± 33.1		4.05(2.07-7.90)	0.001
35-45	Men	114	Normal	185.9 ± 43.8	0.001	(1)	-
		85	Overweight	208.2 ± 36.6		4.03(2.22-7.34)	0.001
		48	Obese	211.5 ± 41.6		3.58(1.77-7.25)	0.001
	Women	62	Normal	184.9 ± 38.3	0.001	(1)	-
		71	Overweight	206.5 ± 37.6		2.06(1.58-5.73)	0.041
		114	Obese	213.2 ± 36.9		3.01(1.58-5.73)	0.001
45-55	Men	91	Normal	189.4 ± 37.3	0.002	(1)	-
		92	Overweight	208.5 ± 35.3		2.37(1.31-4.30)	0.004
		64	Obese	207.5 ± 35.2		1.93(1.01-3.69)	0.047
	Women	52	Normal	204.1 ± 34.7	0.001	(1)	-
		65	Overweight	208.3 ± 37.6		0.98(0.47-2.05)	0.967
		123	Obese	218.4 ± 43.4		1.64(0.84-3.19)	0.142
55-65	Men	111	Normal	187.4 ± 39.6	0.001	(1)	-
		95	Overweight	213.2 ± 42.3		2.92(1.65-5.16)	0.001
		39	Obese	209.5 ± 25.9		2.73(1.28-5.79)	0.009
	Women	66	Normal	217.8 ± 44.8	0.001	(1)	-
		96	Overweight	233.3 ± 48.1		1.48(0.73-2.97)	0.270
		83	Obese	235.0 ± 41.6		1.81(0.86-3.81)	0.117
Total	Men	438	Normal	185.0 ± 38.6	0.001	(1)	-
		356	Overweight	205.1 ± 39.2		2.78(2.08-3.72)	0.001
		191	Obese	207.8 ± 34.8		2.82(1.99-4.01)	0.001
	Women	286	Normal	193.2 ± 40.6	0.001	(1)	-
		304	Overweight	214.3 ± 44.0		2.11(1.52-2.94)	0.001
		388	Obese	217.9 ± 40.6		2.75(2.00-3.77)	0.001

* ANOVA § Logistic regression

Discussion

The association between hypercholesterolemia and BMI in men and women was not the same. In early middle-age the risk of HC in obese people was more than overweight people while in older age this relation was increased in overweight men without significant differences in women.

The association between serum cholesterol levels and BMI based on age and gender was reported in other studies. Serum cholesterol level increased with age.[21] BMI and waist circumference were positively associated with total serum cholesterol and non-HDL cholesterol level and inversely associated with HDL cholesterol.[11] Alteration in serum cholesterol levels was related to lifestyle factors in some areas.[22,23]

In pubertal children, total serum cholesterol level was negatively associated with height.[24] In Gostynski et al. study, the prevalence of hypercholesterolemia increased with age and compared with women, it was significantly increased more in men at age 24-46 years.[25] The association between hypercholesterolemia and BMI became significantly weaker in high age groups while it was not significant in female aged 50-64 years. A study in white Americans[26] revealed that changing in BMI from 21.1 to 30.0 kg/m^2 were associated with a higher total serum cholesterol level up to 23 mg/dl. Relationship between BMI and serum cholesterol level was not significant at menopause age.[21] The relationship between dyslipidemia and BMI, waist circumference and age was seen in Turkish adult men.[27]

Similar to mentioned studies, we found the obesity and overweight as the risk factors for HC that was steeper in early middle-age while in women was weaker than men. The insignificant association between BMI and serum cholesterol level in menopause women was shown in other studies.[21,25] Moreover, different ethnic groups live in northern Iran and inherent factors may influence changing of serum cholesterol level. The variation of serum cholesterol level among ethnic groups should be considered in future studies. Due to the changes in life style in Iran as a developing country in nutrition transition phase,[28] we recommend to establish an educational planning to control obesity and HC especially in early middle-age. Food behavior, weight gain control and serum cholesterol treatment was not assessed and they were limitations of our study.

Conclusion

HC is a major health problem in the Iranian northern adults and BMI is a risk factor for it. In early middle-age, obese subjects more than overweighed subjects were in the risk of HC, while in men, this pattern altered after age 35 years. In women, obesity and overweight was not a risk factor for HC in older middle-age.

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Conflict of Interests

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Correlation between seizure in children and prolonged QT interval

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Original Article

Abstract

BACKGROUND: Long QT is a cardiac electrical disorder. One of the symptoms of long QT caused by fatal ventricular arrhythmia is seizure. In some studies it was indicated that up to 35% of seizures induced by long QT may be misdiagnosed as other causes of seizure.

METHODS: In a case-control study, patients experiencing primary seizure with unknown etiology and referring for clinical diagnosis were selected as the case group. The control group consisted of patients hospitalized for other reasons except seizure. Corrected QT Interval (QTc) was measured for each patient on an electrocardiogram, and the two groups were compared. Long QT was defined as a QT more than 0.46 seconds.

RESULTS: Among 508 subjects who were recruited in this study 254 children were in the case group and 254 were in the control group. There were 66 children experiencing seizure and long QT in the case group. In the control group, 48 children with long QT were observed; the difference was statistically significant (P = 0.02). Syncope and sudden death were not significantly different between the two groups.

CONCLUSION: The present study showed that children with unknown causes of seizure have more frequently long QTc, which implies the possibility of an arrhythmic origin of some seizures. Therefore, it is advised to get an electrocardiography for patients with unknown causes of seizure.

Keywords: Seizure, Children, Long QTc

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Introduction

Long QTc is one of the cardiac electrical disorders caused by prolonged ventricular re-polarization which can be acquired either by drugs, such as anti-arrhythmia or three-ring drugs, or appears congenitally.

A normal QTc is less than 0.44 seconds. When QTc is equal to or more than 0.46 seconds, it is considered as long QT Syndrome.[1] Long QT syndrome (LQTS) occurs in about 1 in 2500 of the general population.[2] The clinical symptoms of long QT differ from the classical symptoms of absolutely long QT to sub-clinical forms which have long borderline QT. It was indicated that long QT and fatal ventricular arrhythmias were the cause of the seizures, and have been controlled by suitable treatment.[3]

Other studies conducted at the Neurology Department of The University of California indicated that long QT may emerge as seizure or epilepsy convulsion, but by early diagnosis sudden death can be avoided.[4,5] If an EKG is taken, this Syndrome can easily be diagnosed and be taken care of.[6]

Investigations carried out in the year 2010 showed that one of the most important complaints in LQTS was syncope and seizure. Research on 1059 patients with syncope or seizure showed that a large number of patients suffering from this complain that "they have been under treatment with beta-blocker for a long time due to wrong diagnosis".

Patients who suffer from convulsions complain that "The treatment with beta blocker has been longer, caused more errors, and has a higher percentage of exposure to deadly disorders and fatal heart attack than other treatments".[7]

In some studies, misdiagnosis between Long QT, and arrhythmia caused by neurological seizure has shown to be up to 35%. Therefore, initial EKG has been recommended.[8] In one study, the possibility of misdiagnosis has been determined to be 20-30%.[9]

A twenty one year old woman was diagnosed

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with ventricular tachycardia after experiencing seizures with high fever. By taking her EKG it was found that signs of Brugada during fever were observed in the patient.[10] Therefore, in order to prevent an incorrect diagnosis and delay in making the correct diagnosis, EKG recording should be performed for every patient presenting with a seizure, considered to be of epileptic origin, not only at the beginning of the disease but also when fits occur in spite of antiepileptic treatment.[11]

A recent study showed that sudden loss of consciousness can be caused by syncope or epileptic seizure, which therefore requires a diagnostic work-up including cardiological and neurological examinations. Cardiac channelopathies such as LQTS may be associated with seizures, suggesting a possible link between cardiac and cerebral channelopathy.[12]

On the whole, in all the studies mentioned above patients experiencing seizure referring to the emergency room are diagnosed with febrile seizure and hospitalized. For this reason, a study that determines LQTS among these patients was conducted. The prevalence of long QT among patients with febrile seizures was studied. In addition, the need for performing EKG as a screening test was examined.

Materials and Methods

All those patients who had experienced seizure without any specific cause, and all those patients without any history of seizures referring to Amirkabir Hospital of Arak, Iran, were included in the case and control groups, respectively. The need to attain both an accurate examination and EKG to diagnose the cause of their complaints was clarified for patients. The patients were also assured that their information would remain confidential.

Sample size was estimated to be 254 subjects for each group. The aim of the present study was to determine the association of long QT of hospitalized children aged 1-12 years with epilepsy. The primary examinations showed neither any evidence of secondary causes, such as hypoxia and hypocalcaemia, nor any signs of known neurological injuries. Moreover, no evidence of secondary causes was found in clinical examinations. Patients in the case group were also included in the study seeing that many cases of seizures lead to fever; additionally, cases of seizures with cardiac etiology may emerge following a fever. Hence, seizure patients who had a fever were also included in the case group. Patients of the control group consisted of children aged 1-12 years hospitalized due to reasons other than seizure.

A questionnaire collecting information about patient's age, gender, family history of seizure, family history of heart disease, family history of sudden death, family history of syncope of children, type of delivery, drugs prescribed for the children, and also drugs used by the mothers during breast feeding was completed in both case and control groups.

A twelve lead EKG was taken for patients of both groups. The QT and RR were measured and calculated using the QTc Bazett Formula by a cardiologist. The SPSS software was used for statistical analysis using the chi-square test and logistic regression for data analysis.

Results

508 subjects were recruited in this study; 254 children were in the case group and the same number of children were in the control group. In each group 142 were male (55.9%) and 112 were female (44.1%). There was no statistically significant difference between gender and QTc interval. The gender distribution and different levels of QT is presented in table 1.

Table 1. Frequency distribution of different QTc levels of males and females

Group			Female	Male	Total
Case	QT Interval	< 0.044	74	101	175
		0.44-0.46	6	7	13
		0.46 <	30	36	66
Control	QT Interval	< 0.044	79	100	179
		0.44-0.46	10	17	27
		0.46 <	20	28	48

In the case group, 175 children (34.4%) had a QTc level of 0.44 seconds or less. 64 children (12.6%) had a QTc level of 0.44-0.46 seconds. 66 children (13%) had a QTc level of more than 0.46 seconds. Regarding the control group, 178 children (35%) had a QTc level of 0.44 seconds or less. 71 children (14%) had a QTc level of 0.44-0.46 seconds. 48 children (9.4%) had a QTc level of more than 0.46 seconds. The difference in prolonged QT between case and control groups (13% vs. 9.4%) was statistically significant (P = 0.02). Three children in the case group and two in the control group had a previous history of syncope according to their parents, but this was not statistically significant.

There were two cases of sudden death among the family of the patients in the case group, but there was no record of this among the immediate family of the control group, the difference was not statistically significant.

Discussion

No significant difference was observed between men and women in terms of QTc in previous studies. In a study conducted on 328 families, higher rates of syncope and cardiac arrest were seen among probands (first family members who had long QT), which were mostly young females.[13]

In a study in 1998 on clinical presentation related to gender of proband patients, 70% of the patients were females, but it was presented earlier in men.[14] The main difference between the present study and the studies previously stated was that they were conducted on patients having long QT, whereas the present study was conducted on patients experiencing seizure. In addition, more males were included in the present study.

In a study on 287 patients in seven different countries, it was revealed that long QT emerged in 9% of cases by cardiac arrest, 26% by syncope, and 10% by seizure.[15] This shows that long QTc probably leads to seizure. Another study conducted on patients with long QTc indicated that 50% of the patients had no symptoms; as a result, any young patient admitted to hospital with seizure uncontrolled by medication should be evaluated for long QTc.[16] Another study noted that the LQTS in young patients can easily be mistaken for seizure.[17]

Overall, these studies show that one of the symptoms of long QT is seizure and many of these cases are discovered incidentally; hence, it seems necessary to take a test for long QTc on cases admitted for seizure. The present study confirms that the seizure group had a longer QT than the control group. Therefore, it seems helpful to take an EKG for young patients being admitted for seizure.

The present study showed no significant statistical difference in syncope and sudden death between case and control groups. On the other hand, the previous studies were carried out on patients with long QTc, consequently numerous syncope and deaths were observed.

It should be noted that there were some limitations, such as fever among the patients of the case group, which was discussed earlier in the method section. Another limitation was the lack of extensive analysis, such as CT-scan to rule out secondary causes of seizures. In conclusion, findings of the present study imply that an EKG should be taken on young patients experiencing seizures with unidentified causes.

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Conflict of Interests

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The incidence of in-hospital atrial fibrillation after coronary artery bypass grafting using ventricular and atrial pacing

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Original Article

Abstract

BACKGROUND: Atrial fibrillation (AF) after coronary artery bypass graft (CABG) surgery is a common problem. In this study, we sought to evaluate the safety and tolerance of continuous atrial pacing after CABG. We hypothesized that a strategy of temporary atrial pacing after CABG would reduce the incidence of postoperative AF.

METHODS: During 2012, CABG candidates over 18 years of age at Sina Hospital (Isfahan, Iran) were recruited. Before surgery, the participants were randomly assigned to two groups of ventricular pacing and left atrial ventricular pacing (atrial pacing). The primary end point of the study was the initial occurrence of AF or atrial flutter with a ventricular rate greater than 100 beats per minute for 10 consecutive minutes or completion of the 48-hour monitoring period.

RESULTS: We evaluated 64 consecutive CABG candidates with sinus rhythm. They were allocated to two groups of ventricular pacing and atrial ventricular pacing (n = 32 in each group). Three patients in the ventricular pacing group (10%) and six in the atrial ventricular pacing group (22%) had sustained AF during the first 48 hours after CABG (P = 0.18 according to Fisher's exact test).

CONCLUSION: Continuous atrial pacing in the postoperative setting is safe and well-tolerated. In this study, we found that temporary atrial pacing increased the frequency of postoperative AF. Since the difference between the two groups was not significant, larger studies are required to determine the exact relation between pacing method and AF.

Keywords: Atrial Fibrillation, Coronary Artery Bypass Graft, Atrial Pacing

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Introduction

Atrial fibrillation (AF) after coronary artery bypass graft (CABG) surgery is a common problem.[1] It is associated with longer intensive care unit (ICU) and hospital stay and increased costs of postoperative care.[2] On the other hand, treatment with electrical cardioversion, antiarrhythmic and anticoagulant drugs adds significant morbidity and cost.[1,3] Prophylactic pharmacological treatment has also been disappointing. Although a recent trial found a significant reduction in postoperative AF after treatment with amiodarone, the incidence of AF in the treatment group was still 25% and concerns about potential morbidity exist.[4] Atrial-based pacing has become an attractive non-pharmacological therapy for the prevention of AF.[5]

Patients undergoing CABG surgery have temporary atrial and ventricular pacing wires implanted at the time of surgery. Since the incidence of AF is high among these patients, they may provide a model to examine the impact of prophylactic atrial pacing. Such a technique would also be of extreme clinical value in reducing the cost and morbidity associated with postoperative AF. In this study, we sought to evaluate the safety and tolerance of continuous atrial pacing after CABG. We hypothesized that a strategy of temporary atrial pacing after CABG would reduce the incidence of postoperative AF.

Materials and Methods

During 2012, CABG candidates over 18 years of age

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at Sina Hospital (Isfahan, Iran) were recruited. All patients had to be in sinus rhythm before surgery and on no antiarrhythmic medications. Before surgery, the participants were randomly assigned to two groups of ventricular pacing and left atrial ventricular pacing (atrial pacing). The subjects were followed for 48 hours after the operation.

Patients were excluded if they had a known history of AF or atrial flutter requiring antiarrhythmic medications, had renal or hepatic dysfunction (serum creatinine > 3mg/dl, liver enzyme tests > 3 × normalU/L), or were unable to give informed consent. In addition, patients in whom epicardial pacing wires could not be placed during surgery, or patients who developed postoperative ventricular arrhythmias requiring therapy with oral or intravenous antiarrhythmic agents other than intravenous lidocaine were excluded. Patients who required temporary pacing immediately after surgery due to hemodynamic compromise remained in the study. Baseline characteristics and history of arrhythmia were ascertained from direct patient interviews and review of their medical records.

All patients had one set of ventricular pacing wires (Model #6500, Medtronic Inc., Minneapolis, Minnesota, USA) implanted at the conclusion of surgery. Half of the patients also had atrial wires implanted in the standard location attached to the posterior surface of the left atrium between the right superior and inferior pulmonic veins. The ventricular wires were attached to the right ventricular apex in the standard fashion.

Patients in the ventricular group were paced using the single-chamber pacing mode at a backup rate of 50 pulses per minute (ppm) in the surgical ICU. Patients in the atrial group were paced with a temporary external dual-chamber pacemaker (Model #5346, Medtronic Inc., Minneapolis, Minnesota, USA) using the atrioventricular (AV) universal (DDD) mode at a lower rate limit of 100 ppm with an AV delay of 220 ms to establish continuous atrial pacing at rest. Pacemaker settings included an upper-rate limit of 140 ppm, a post ventricular atrial refractory period of 175 ms, atrial sensitivity of 0.5 mV, ventricular sensitivity of 2 mV and maximum atrial and ventricular pacing output of 20 mA. Pacing was continued for 48 hours or until the first sustained episode of AF (> 10 minutes).

After the operation, physicians were instructed to continue beta-adrenergic blocking agents in all patients who had received preoperative beta-blocker therapy. Preoperative beta-blockers were administered through the morning of surgery. Oral metoprolol (25 mg twice daily) was also started postoperatively as soon as all intravenous inotropes were discontinued. The dose was titrated upward at the discretion of the attending surgeon. Patients not on preoperative beta-blockers received these agents in the postoperative period if no contraindications were found.

Patients were continuously monitored during the study period with a telemetry system. Pacing and sensing thresholds for both atrial and ventricular leads were checked after arrival at the ICU and daily thereafter to ensure the capture. The underlying heart rhythm and rate were documented daily. When considered stable, patients were transferred from the ICU to monitored beds in the general hospital ward where pacing was discontinued.

The primary end point of the study was the initial occurrence of AF or atrial flutter with a ventricular rate greater than 100 beats per minute for 10 consecutive minutes or completion of the 48-hour monitoring period. An investigator reviewed the hospital chart and full telemetry at least once daily to monitor the cardiac rhythm and establish the time of onset of AF.

Data analysis

All values were expressed as mean ± standard deviation (SD). Baseline characteristics of the study groups were compared using Student's t-test or analysis of variance for continuous variables and chi-square test for discrete variables. Other tests including Mann-Whitney, Fisher's exact, and Mantel-Haenszel tests were applied for analysis of data. All analyses were performed with SPSS for Windows 20.0 (SPSS Inc., Chicago, IL, USA).

Results

We evaluated 64 consecutive CABG candidates with sinus rhythm. They were assigned to two groups of ventricular pacing and atrial ventricular pacing. (n = 32 in each group). The mean age of the participants was 57.86 ± 10.16 years. Independent t-test did not show significant differences in age, LVEF, Hb level, O_2 saturation, and Cr level between the two groups (Table 1). Moreover, the two groups matched well in terms of gender distribution (P = 0.08 in chi-square test and P = 0.86 in Mantel-Haenszel test).

Chi-square test did not suggest the two groups to be significantly different in terms of risk factors such as presence of hypertension, pulmonary disease, history of smoking, and diabetes (Table 2).

None of the patients in either group reported documented lung disease.

Mann-Whitney test showed that the two groups were matched in regard to angina level (according to the Canadian Cardiovascular Society classification)[6] and level of dyspnea (according to New York Heart Association classification)[6] (Table 3). Three patients in the ventricular pacing group (10%) and six in the atrial ventricular pacing group (22%) had sustained AF during the first 48 hours after CABG (P = 0.18 according to Fisher's exact test).

Discussion

Echocardiography recordings during the first 48 hours after CABG showed that AF occurred in 10% of patients with ventricular pacemakers and 22% of those with atrial ventricular pacemakers.

The pathogenesis of post-CABG AF has been proposed to be multifactorial with abnormal atrial conduction and lack of uniformity of atrial repolarization as main elements. It can have different triggers including premature contractions, pericarditis, electrolyte disorders, cardiopulmonary bypass and cardioplegia.[7,8]

The limited efficacy of conventional agents has led to searches for non-pharmacological modalities for the prevention of postoperative AF. About a decade ago, Coumel[9] and Attuel et al.[10] were among the first to report the potential of pacing in prevention of AF. They described the use of single-site atrial overdrive pacing to prevent AF or flutter in a selected group of patients with vagally mediated AF or flutter.[9,10] Further studies by Murgatroyd et al. utilized a unique pacing algorithm for the suppression of atrial premature depolarizations.[11] This technique resulted in a significant reduction in episodes of AF. The mechanism by which atrial

Table 1. Description of quantitative variables

Variable	Atrial ventricular pacing			Ventricular pacing			P
	Minimum	Maximum	Mean ± SD	Minimum	Maximum	Mean ± SD	
Age	36.00	75.00	57.85 ± 9.82	28.00	78.00	57.87 ± 10.63	0.99
Creatinine	2.00	0.70	1.01 ± 0.28	3.00	0.70	1.03 ± 0.44	0.81
Oxygen saturation	95.00	99.70	98.40 ± 0.60	94.00	100.00	98.24 ± 0.96	0.48
Left ventricular ejection fraction	20.00	65.00	51.66 ± 11.00	60.00	25.00	49.80 ± 10.70	0.92
Hemoglobin	12.00	16.00	13.19 ± 2.60	9.90	15.30	13.16 ± 1.20	0.95

Table 2. Description of qualitative variabes

		Atrial pacing group (%)	Atrial ventricular pacing group (%)	P
Gender	Male	88.9	70.0	0.08
	Female	11.1	30.0	
Hypertension	No	59.3	53.3	0.23
	Not known	3.7	3.3	
	Treated	37.0	43.3	
Smoking history	Never	77.8	79.3	0.83
	Ex-smoker	11.1	6.9	
	Smoker	11.1	13.8	
Diabetes	No	63.0	70.0	0.57
	On diet	3.7	0	
	On oral agent	33.3	26.7	
	On insulin + oral agent	0	3.3	

Values are expressed as percentages.

Table 3. Description od Angina and Dyspnea in Atrial And Ventricular Pacing groups

		Atrial ventricular pacing group (%)	Ventricular pacing group (%)	P
Angina*	1	3.7	6.7	0.44
	2	85.2	86.7	
	3	7.4	6.7	
	4	3.7	0	
Dyspnea**	1	7.4	6.7	0.91
	2	92.6	93.3	
	3	0	0	
	4	0	0	

* Canadian Cardiovascular Society classification ** New York Heart Association classification

overdrive pacing reduces the occurrence of AF is unclear. However, suppression of atrial premature depolarizations and a reduction in the dispersion of refractoriness have been proposed.[12,13]

Most evidence suggests that AF is a reentrant rhythm consisting of multiple wandering wavelets of electrical activity.[14,15] It is often initiated by atrial premature beats (APB) encountering areas of slow conduction and unidirectional block.[16] There are many reasons why one might expect atrial pacing to be effective in preventing AF. Increasing atrial rate suppresses the APB which may initiate AF. A prospective randomized trial found that AF recurrences are reduced in patients receiving right atrial pacing compared to those receiving ventricular pacing.[17] Papageorgiou et al. found that the posterior triangle of Koch is a critical area of slow conduction and that coronary sinus (i.e. left atrial) pacing prevented the induction of AF by high right atrial APB.[18]

In our study, three patients in the ventricular pacing group (10%) vs. six in the atrial ventricular pacing group (22%) had sustained AF during the first 48 hours after CABG. Although the frequency of AF was higher in the atrial paced group, the difference was not significant. Another study suggested that temporary pacing may paradoxically induce AF in some patients if inappropriate sensing leads to pacing during atrial repolarization.[19] While the findings of some studies about the absence of a significant reduction in recurrence of AF using atrial pacing were similar to our observations,[5] other researchers have reported favorable effects of right atrial pacing in reducing post-CABG AF.[19]

Pacing was well tolerated in all patients and did not increase hospital stay. There were no complications related to the placement of left atrial pacing wires at the conclusion of surgery.

Among the strengths of our study was eliminating the effects of risk factors associated with frequency of AF. In other words, age, sex, LVEF, Cr level, pulmonary disease, diabetes mellitus, hypertension, anemia, and hypoxia were completely adjusted in the two groups.

Conclusion

Continuous atrial pacing in the postoperative setting is safe and well tolerated. In this study, we found that temporary atrial pacing increased the frequency of postoperative AF. Since the difference between the two groups was not significant, larger studies are required to determine the exact relation between pacing method and AF.

Conflict of Interests

Authors have no conflict of interests.

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Relationship between left ventricular ejection fraction and depression following myocardial infarction: an original article

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Original Article

Abstract

BACKGROUND: The aim of this study was to examine the association between left ventricular ejection fraction (LVEF) and incidence of depression following the myocardial infarction (MI).

METHODS: In a prospective study, 176 patients aged 32-84 years with the mean age of 56 years (SD = 10.05) with a definitive diagnosis of myocardial infarction and admitted to one of the coronary care units (CCU) of Isfahan during April to August 2006 were selected through consecutive sampling method. The demographic and medical characteristics were collected by their medical record and also the results of the LVEF assessment of the patients were obtained through echocardiography or angiography following the myocardial infarction. Thereafter, the patients were given Beck Depression Inventory for the primary care (BDI-PC) in three months after myocardial infarction. The collected data were analyzed during the hospitalization and follow-up periods using logistic regression method.

RESULTS: The findings indicated that left ventricular dysfunction identified by the Left ventricular ejection fraction index was significantly correlated with depression three months after the myocardial infarction ($P < 0.01$). In addition, the exploratory model (which only includes LVEF variable) had the predictive validity of 64.8% with 55.7% sensitivity and 72.1% specificity.

CONCLUSION: Left ventricular dysfunction is associated with increased risk of depression following the myocardial infarction.

Keywords: Depression, Myocardial Infarction (MI), Left Ventricular Ejection Fraction (LVEF)

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Introduction

Incidence of depression symptoms following myocardial infarction (MI) is a very common psychological problem among patients with MI. This psychological problem has negative impacts on the prognosis of cardiac disease.[1] Many researchers believe that regardless of cardiac disease intensity, depression is associated with its negative prognosis. In addition, the question of whether or not characteristics of MI intensity such as left ventricular ejection fraction (LVEF) are associated with the incidence of depression has been raised by some researchers.[1]

Although the number of conducted articles regarding the effects of depression following MI and its etiology is increasing, many studies have not given attention to indicators such as LVEF as MI intensity.

Lesperance et al. in a study regarding major depression before and after MI as well as risk factors of depression after MI including LVEF and history of MI, found no relationship between the required variable and depression.[2] Moreover, while Frasure-Smith et al.[3] showed a significant correlation between LVEF (which has been defined as a two-level variable higher than 35% and lower than 35%) and depression scores in Beck Depression Inventory (BDI), Carney et al showed no significant correlation between LVEF and depression.[4] It seems that Carney et al. had created some limitations in their analysis by controlling the

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social isolation; because social isolation and depression are often manifested together in cardiac patients.[5]

van Melle et al. confirmed lower age, low LVEF and high depression level during admission as variables predicting depression following the MI.[1] van Melle et al. in a separate analysis of the data of their study reviewed the relationship of LVEF and incidence of depression in MI patients and found that the LVEF level has a significant inverse correlation with the depression score of patients in BDI three months after MI.[6] These researchers demonstrated that by controlling the demographic variables, risk factors of cardiovascular diseases, comorbidities and depression score during hospitalization, there is still a significant correlation between LVEF level and depression intensity.

Spijkerman et al. also reported a high risk of depression following MI in Netherland. They also evaluated a wide range of psychological, cardiovascular, physical and demographical risk factors as predictors of depression variables following MI and concluded that history of depressive disorder, being female, low LVEF and hospitalization duration can be considered as independent predictive variables for depression symptoms following MI.[7] Certain studies did not report any significant relationship between LVEF and depression; however, they showed a higher tendency toward depression in patients with lower LVEF.[1] Carney et al.[5] analyzed LVEF as a continuous variable and found no correlation between LVEF in depressed and non-depressed patients.

The present study was also conducted in line with this objective aiming to determine the potential correlation between left ventricular dysfunction and incidence of depression following MI.

Materials and Methods

This was a prospective study. The study subjects were 176 MI patients aged 32 to 84 years (Mean age = 56 ± 10.05 years) with a definitive diagnosis of MI who had been admitted to one of the hospitals of Isfahan equipped with a Cardiac Care Unit (CCU) during April to August 2006. The majority of the subjects were males (84%), married (89%) and of low-moderate socioeconomic class (87%). 123 of them had no previous history of MI. 48.3% of the patients have been admitted with diagnosis of anterior MI and 51.7% with non-anterior MI.

The patients were selected through consecutive sampling method and by considering the inclusion and exclusion criteria. The inclusion criteria were the following:

A) Two out of three diagnostic criteria were taken into account: 1. Chest pain caused by low blood supply to heart muscle (typical ischemia) which takes at least 20 minutes, 2. Presence of pathologic changes indicative of ischemia/infarction in ECG waves, 3. Increase in cardiac enzymes; B) Patient's consent for participation in the study.

The exclusion criteria were the following:

A) Secondary MI for bypass surgery or angioplasty, B) Presence of another serious physical disease that reduces life expectancy, C) Presence of major psychiatric disorders in the patient, D) Treated with antidepressants and E) Impossibility of follow-up with the patient after their discharge.

The following tools were used to collect data:

Echocardiography: LVEF is an appropriate clinical indicator of the functionality or dysfunctionality of the left ventricular systolic which can be determined by echocardiography and its result will absolutely be identified. This indicator is shown by the following formula:

$$LVEF = \frac{\text{End diastolic volume} - \text{End systolic volume}}{\text{End diastolic volume}} \times 100$$

In most conducted studies in this regard, this index is used as a categorical variable (e.g. for the two low and normal levels).[1,8]

Demographic and medical information Questionnaire: Demographic and medical data of the patients were collected through a questionnaire designed to do so. Their medical information was gathered from their records.

Beck Depression Inventory for Primary Care (BDI-PC): It has been designed by Beck et al by removing the physical symptoms from the original questionnaire for application in medical centers as a screening tool aiming to decrease the likelihood of reaching false estimates of depression among physical patients.[9] Previous studies indicated a preference for this tool compared with anxiety and depression index in hospitals.[10,11] This is a 7-item inventory, in which each item indicated a depression symptom. The items of this inventory are in accordance with the Diagnostic and Statistical Manual of Mental Disorder 4th edition (DSM-IV) for the diagnosis of clinical depression.[12] Intensity of each symptom in each item has been stated in four phrases. Phrases of each item scored from zero to three. Zero in each item indicates lack of that symptom and 1 to 3 indicate the existence and amount of that symptom. The highest score in this

inventory is 21.

Beck et al.[9] and Steer et al.[13] reported this inventory for screening depression in physical patients with high sensitivity and efficiency. Cronbach's alpha obtained an internal consistency of 0.88 for this inventory in an Iranian population (n = 176) in the present study. Furthermore, reliability of this inventory showed correlation coefficient of 0.74 through test re-test method with a three-week interval (n = 62) in cardiac patients. Construct validity of this inventory, in comparison with the depression subscale of the Iranian version of hospital depression and anxiety scale, in 140 patients obtained 0.87.[14] Moreover, through an organized clinical interview based on DSM-IV in the mentioned sample, the cut-off point is five which was obtained with sensitivity of 0.84, and specificity of 0.97 and the maximum clinical efficiency for screening clinical depression obtained 0.91 (including major depressive disorder and minor depression).

The present study was designed using logistic regression in order to determine the medical risk factors i.e. depression following MI. First, during the hospitalization time, the required data were collected from the study subjects enrolled in the study and LVEF was assessed as an appropriate clinical indicator from left ventricular function using echocardiography or angiography by a cardiologist in a short time after myocardial infarction. The depression of the patients was evaluated three months after the MI through Beck Depression Inventory for Primary Care. In order to complete this scale, the patients were asked to read the choices of every item carefully and choose the correct one by considering their status during the past two weeks.

In follow-up stage (3 months after discharge), by the help of patients' score in BDI-PC and based on cut-off point five, depressed patients were separated from non-depressed patients. Thereafter, the collected data were analyzed during hospitalization and follow-up stages in both depressed and non-depressed groups using stepwise logistic regression test.

Results

Out of 176 MI patients, 79 patients (44.9%) suffered from depression three months after discharge. Table 1 shows depressed and non-depressed patients three months after discharge in terms of demographic and medical variables during hospitalization (base line) using univariate analysi.

Table 1. Results of univariate analysis of the relationship of each possible predicting variable in base line and incidence of depression three months after discharge

Demographic and medical variables	The group of depressed patients three months after discharge (n = 79)	The group of non-depressed patients three months after discharge (n = 79)	Odds Ratio	Confidence Interval 95%	Significant level
Mean age	54.37	57.16	0.97	(0.42-1.00)	N.S.
Sex					
Male	35.20%	48.90%	2.14	(0.94-4.95)	N.S.
Female	9.70%	6.30%			
Marital status					
Married	38.10%	50.60%	1.99	(0.77-5.15)	N.S.
Single	6.80%	4.50%			
Socioeconomic class					
Low	27.30%	24.40%			0.05
Average	14.80%	20.50%	0.55	(0.35-0.86)	0.05
High	2.80%	10.20%			N.S.
History of MI					
Yes	17.00%	13.10%	1.97	(1.03-3.81)	0.05
No	27.80%	42.00%			
LVEF 40%	25.00%	15.30%	3.26	(1.74-6.11)	0.001
Family history of cardiac disease	22.16%	30.68%	0.78	(0.43-1.41)	N.S.
Hypertension	13.00%	17.61%	0.87	(0.46-1.67)	N.S.
Smoking	25.00%	25.56%	1.45	(0.80-2.64)	N.S.
Diabetes	14.00%	14.00%	1.33	(0.69-2.58)	N.S.
Hyperlipidemia	18.20%	25.00%	0.82	(0.45-1.50)	N.S.
Logarithm of maximum creatine phosphokinase	0.05	0.05	1.06	(0.59-1.90)	N.S.

As indicated in table 1, in univariate analysis most of the depressed patients were in low-moderate socioeconomic class ($P < 0.05$) and had a history of MI (17% vs. 13%; $P < 0.05$). In addition, the results of univariate analysis showed that most of the patients who have been depressed during the three months after discharge had lower LVEF 40% (25% vs. 15.3%; $P < 0.001$).

Hypothetical predictive variables including demographic and medical variables listed in table 1 had been assessed shortly after myocardial infarction. Data analysis related to these variables in logistic regression showed that left ventricular function lower than 40% could predict depression following MI ($P < 0.01$; $\beta = 1.18$; OR = 3.259; CI 95% = 1.739-6.106). These findings showed that among the variables assumed to predict depression following MI, LVEF had a significant contribution.

This study showed that exploratory model (which only includes LVEF variable) had a predictive validity 64.77% with 55.7% sensitivity and 72.2% specificity. This model correctly predicted 55.7% of depressed and 72.2% non-depressed patients. Given that this model had a degree of freedom of less than one, it was impossible to use Hosmer-Lemeshow test in determining its goodness of fit.

Discussion

In this study, demographic and medical variables were taken into account during hospitalization in predicting depression following required MI. The results showed that left ventricular dysfunction represented by LVEF had a significant contribution to analyzing the model including the mentioned variables in predicting depression three months after myocardial infarction. Nevertheless, it is generally accepted that depression by itself is associated with poor prognosis in cardiac disease; however, some researchers believe this relationship as a reflection of cardiac disease intensity.[15,16] The results of the present study showed that low LVEF is correlated with incidence of depression in patients following the myocardial infarction. Although, it seems that the number of studies conducted on depression following MI is increasing;[1] LVEF has not been evaluated in most of these studies and in most cases, the degree of depression was assessed immediately after MI.

The results of the present study were not in accordance with the study of Carney et al.[5] which found no correlation between LVEF and depression but they were in accordance with the results of Frasure-Smith et al. who found a significant correlation between LVEF and depression scores in BDI.[3] Lesperance et al. also found no correlation between LVEF and depression.[2] However, it seems that there were two major issues in the study of Lesperance et al; first, in their study, the cut-off point 35% was considered as low LVEF; while it seems that a cutoff point of 40% is an appropriate and logical point for dividing the LVEF data.[2] The second issue was a small study sample. It is obvious that by considering a low cut-off point, many patients with really low LVEF will be excluded from the range of low LVEF and this issue in a small sample size results in the effect of low LVEF is not provided with the opportunity of emerging in the predictive model.

The results of the present study were in accordance with the studies of van Melle et al.[1], van Melle et al.[6]and Spijkerman et al.[7] Perhaps, these three studies were more psychologically reliable studies in this regard. In the first study, the cut-off point of low LVEF was considered as 30% and in the second study, it was considered as 40%. Nevertheless, given to the appropriate sample size in both studies, the difference in cutoff point did not prevent the emergence of the LVEF effect in predicting depression following MI. van Melle et al.[1] in a separate analysis on data of their own study reviewed the correlation of LVEF with depression in MI patients. Results of this study also confirmed the obtained findings from the above mentioned analyses. The mentioned researchers in their study showed that the LVEF level had a significant correlation with the depression score in BDI three months after MI and the lower the LVEF level was, the higher the depression score after three months.

In other studies,[17-19] there was also no significant correlation between LVEF and depression; however, most of these studies showed a tendency toward a higher degree of depression in patients with low LVEF. Therefore, perhaps lack of a significant relationship has resulted from type II error i.e. low sample size.

In most of the conducted studies, LVEF index is used as a categorical variable (e.g. low level and normal level).[1,7] van Melle et al.[6] who reviewed the correlation between LVEF and the incidence of depression following MI more than others emphasized that they prefer to use this variable as a categorical variable due to some reasons. First, it is impossible to use a similar method in all medical centers for evaluating LVEF as a continuous variable; hence, LVEF is assessed by various

methods such as echocardiography and angiography. Therefore, the difference in the assessment method can cause difference in continuous sizes. Second, although the mentioned tools are used to determine this index, clinical judgment based on individual's observation can also determine the percentage of LVEF. Hence, it seems that its classification has less error.[6]

Generally, given to the findings of the present study and previous studies it can be said that there is a correlation between LVEF and depression following MI. It is worth mentioning that the circumstance of the relationship between poor left ventricular function and incidence of depression in MI patients is important. In terms of possible mechanisms among left ventricular dysfunction and depression there are two considered ways; 1. Psychological way: in revising the conducted studies about heart failure, this correlation can be due to low quality of life resulting from overall poor physical conditions,[18] increased rate of hospitalizations and inappropriate social functioning[20] and increased unemployment.[21] All these factors can lead to depression due to stress. 2. Biological way: on the other hand, the correlation between left ventricular dysfunction and depression can be due to biological adaptability, which merges with left ventricular dysfunction.[22] The correlation between brain and heart has been reported very much in medicine; e.g. patients with subarachnoid haemorrhage may show severe changes of echocardiography and even refer with new (recurrent) left ventricular dysfunction and some symptoms from myocardial injury.[23] There were some similar findings in MI patients[24] and in those with severe emotional stress.[25]

Perhaps, it can be said that an increased level of cytokines in heart failure such as interleukin 1 (IL-1), IL-6 and tumor necrosis factor-alpha have a mediating role in the incidence of depression.[6] However, it is also possible for depression to lead to LVEF.

In reviewing the conducted studies regarding the objective of this study, the finding that left ventricular dysfunction is correlated with an increased risk of depression following MI is a new achievement and has only been obtained in two other recently implemented studies. This finding can illustrate the necessity of reviewing the role of nervous-hormonal system function or increased inflammatory cytokines associated with left ventricular dysfunction. Perhaps these processes have a major role in incidence of depression following MI. Moreover, the achievement that low LVEF can predict depression is a reasonable logic for further more accurate studies about the effect of LVEF in the prognostic role of depression.

Due to time limitation in selection criteria of the study subjects, the sample size was small. Therefore, generalization of the results should be done with caution. Lack of accurate information about consumed drugs and their dosage during the three months after incidence of myocardial infarction confined the definite conclusion of the results in the present study. In order to generalize the findings, it is suggested that the sample size be increased in further studies, similar method of assessment of LVEF be used, the role of cardiac medications in exacerbation and incidence of depression symptoms in MI patients be evaluated and also the role of cardiac diseases risk factor such as diabetes mellitus, hypertension and hyperlipidemia in incidence of depression following MI be considered.

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Conflict of Interests

Authors have no conflict of interests.

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Effects of streptokinase on reflow in rescue percutaneous coronary intervention

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Original Article

Abstract

BACKGROUND: Primary percutaneous coronary intervention (PPCI) is the preferred treatment method for ST elevation myocardial infarction (STEMI). However, the required equipments are not available in all hospitals. Thus, due to shortage of time, some patients receive thrombolysis therapy first. Patients with chest pain and/or persistent ST segment elevation will then undergo rescue percutaneous coronary intervention (PCI). The present study evaluated and compared the frequency of no-reflow phenomenon and 24-hour complications after PCI among patients who underwent PPCI or rescue PCI.

METHODS: This cross-sectional study assessed no-reflow phenomenon, 24-hour complications, and thrombolysis in myocardial infarction (TIMI) flow in patients admitted to Chamran Hospital (Isfahan, Iran) with a diagnosis of STEMI during March-September, 2011. Subjects underwent PPCI if they had received eptifibatide. Rescue PCI was performed if patients had chest pain and/or persistent ST segment elevation despite receiving streptokinase (SK). Demographic characteristics, history of diseases, medicine, angiography findings, PCI type, and complications during the first 24 hours following PCI were collected. Data was then analyzed by Student's t-test, chi-square test, and logistic regression analysis.

RESULTS: A total number of 143 individuals, including 67 PPCI cases (46.9%) and 76 cases of rescue PCI (53.1%), were evaluated. The mean age of the participants was 58.92 ± 11.16 years old. Females constituted 18.2% (n = 26) of the whole population. No-reflow phenomenon was observed in 51 subjects (37.1%). Although 9 patients (6.3%) died during the first 24 hours after PCI, neither the crude nor the model adjusted for age and gender revealed significant relations between rescue PCI and death or no-reflow phenomenon. Rescue PCI and no-reflow phenomenon were not significantly correlated even after adjustments for age, gender, history of diabetes, hypertension, hyperlipidemia, coronary artery disease, smoking, platelets number, myocardial infarction level, the extent of stenosis, and the involved artery.

CONCLUSION: According to the present study, although SK is more effective than eptifibatide in resolution of thrombosis and clots, rescue PCI did not differ from PPCI in terms of the incidence of no-reflow phenomenon or short-term complications.

Keywords: Primary Percutaneous Coronary Intervention, Rescue Percutaneous Coronary Intervention, No-Reflow Phenomenon

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Introduction

Primary percutaneous coronary intervention (PPCI) is suggested for treating ST elevation myocardial infarction (STEMI).[1] Rescue percutaneous coronary intervention (PCI) is also recommended in patients under fibrinolysis without electrocardiographic (ECG) improvements.[2] Reductions in short-term and 30-day mortality after PPCI have been found by a number of meta-analyses.[3-5]

An important factor in determining the success of reperfusion therapy (RT) is the comparison of thrombolysis in myocardial infarction (TIMI) flow

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before and after treatment. TIMI flow is of high value in prognosis of patients.[6,7] This semi-quantitative scale divides patients into three categories among which the best prognosis belongs to the TIMI3. Compared to other two groups, patients with TIMI3 present better local and general improvements in left ventricular perfusion and performance, enzyme level reductions, and overall morbidity and mortality.[8]

RT is considered as successful if no-reflow phenomenon does not occur. Kloner et al. defined no-reflow as reduced coronary reperfusion without any arterial obstruction, dissection, or spasm in angiography.[9] However, the prevalence of no-reflow phenomenon has been reported as high as 20% in PPCI.[10]

Although PPCI is the preferred treatment for patients with STEMI, its successful implementation depends on available facilities and circumstances. An appropriate hospital, availability of an angioplasty department with an experienced cardiologist, as well as accessibility to the equipments and the staff at any time are among the most important factors affecting the success of the treatment. Thus, absence of any of the above-mentioned factors would make PPCI problematic.[11] In such cases, patients do not have much time and are often suggested to undergo intravascular thrombolysis. If the patient does not respond to the treatment, PCI would also be applied. This procedure is called rescue PCI.[2]

On the other hand, some studies have indicated that even a successful PCI cannot guarantee the perfusion in all parts of myocardium. In fact, the existing thromboemboli may interfere with perfusion and even lead to clotting in capillaries.[12,13] Therefore, some researchers have recommended facilitated PCI which consists of thrombolytic treatment prior to PCI. However, contrastive results have been reported for this treatment method, i.e. although some studies indicated PCI after thrombolytic treatment to have negative outcomes, others considered it as efficient.[11]

The high incidence of coronary artery disease (CAD) in Iran[14] has increased the need to implement PPCI. However, absence of necessary facilities for PPCI in villages and small towns makes thrombolytic treatment the first choice management in many cases. Streptokinase (SK) is more effective than eptifibatide in resolution of thrombosis and risk of bleeding. The present study compared the prevalence of complications among patients who received SK prior to PCI (Rescue PCI) and those who received eptifibatide during PPCI.

Materials and Methods

In a cross-sectional study, the short-term complications, incidence of no-reflow phenomenon, and TIMI flow grades were assessed in patients who underwent PPCI in Chamran Hospital (Isfahan, Iran) during March-September, 2011. Using census sampling method, all hospitalized patients who had undergone PPCI due to a diagnosis of STEMI and consented to participate were included. A sample size of 140 patients was calculated based on the ratio comparison formula and considering the incidence of no-reflow among individuals who receive eptifibatide (6%[15]) and SK (21.8%[16]).

In the beginning, the subjects were explained about the study procedure and informed consents were obtained. Then, a questionnaire containing demographic data (age and gender), history of diseases (diabetes mellitus, stroke, hypertension, CAD, and hyperlipidemia), smoking, medicines [aspirin, heparin, Plavix, eptifibatide, adenosine, adrenaline, beta-blockers, SK, and angiotensin-converting enzyme (ACE) inhibitors], and MI level was completed.

SK was prescribed if the patient had not received thrombolysis treatment with SK, the symptoms had started less than 12 hours before, and the angiography ward was not ready. However, patients were not prescribed with SK if they had cardiogenic shock or were categorized in class 3 or 4 of heart failure.

In case the angiography ward was ready, the subjects underwent angiography and were then prepared for PPCI. In order to perform angiography, Seldinger method was applied by 6 French catheter. The results of angiography including the involved artery and the position and extent of stenosis were recorded for each patient.

After receiving a 70 IU/kg dose of stat heparin, PCI was applied using Seldinger method by a 7 French catheter. In patients who did not receive SK, 10 mg eptifibatide was injected into the coronary artery candidate for PCI immediately after catheter insertion. The interventionist selected the stent based on the involved artery and plaque length and diameter. The size of catheter balloon was determined by a skilled operator who simultaneously viewed a cineangiogram. Ballooning and stenting were applied according to the involved artery and the extent of obstruction. Angiography was performed after PCI to assess TIMI and no-reflow phenomenon and the results were recorded

for all patients.

Patients were transferred to coronary care unit (CCU) after PCI. Individuals who had received eptifibatide during PCI were kept under treatment with 75 mg eptifibatide infusions by a micro-set for about 18 hours.

In addition, all patients received 600 mg clopidogrel and 325 mg aspirin stat prior to PCI. They were also prescribed with 325 mg aspirin and 75-150 mg clopidogrel daily following PCI. Any observed complications, including death, reinfarction, bleeding, arrhythmia, and repeated PCI, during or 24 hours after PCI were recorded.

In order to analyze the collected data, descriptive statistics (frequency and mean) was applied. PPCI and rescue PCI groups (that had received eptifibatide and SK, respectively) were compared in terms of complications, incidence of no-reflow phenomenon, and TIMI flow using chi-square test. The effects of SK on any of the complications were determined by logistic regression. After evaluating the crude relations, the effects of age, gender, medicines, MI levels, and history of diseases on no reflow phenomenon were adjusted by multivariate logistic regression. Moreover, the model was adjusted based on sex and age (by multivariate logistic regression) to assess the effects of rescue PCI on 24-hour death. P values less than 0.05 were considered statistically significant. All analyses were performed in SPSS for Windows 19.0 (SPSS Inc., Chicago, IL, USA).

Results

A total number of 143 individuals with a mean age of 58.92 ± 11.16 years old were studied. Females constituted 18.2% (n = 26) of the whole population. PPCI and rescue PCI were performed for 67 (46.9%) and 76 (53.1%) subjects, respectively. No-reflow phenomenon was observed in 51 cases (37.1%). During the first 24 hours after PCI, 9 individuals died and arrhythmia, allergy, reinfarction, and bleeding occurred in 6 (4.02%), 1 (0.7%), 1 (0.7%), and 0 (0%) participants, respectively.

Table 1. The demographic characteristics and history of diseases in the rescue and facilitated percutaneous coronary intervention (PCI) groups

	Primary PCI (n = 67)	Rescue PCI (n = 76)	P
Age	57.01 ± 11.49	60.61 ± 10.66	0.055
Sex (female)	15 (22.4)	11 (14.5)	0.221
Diabetes	45 (68.2)	54 (72.0)	0.621
Hypertension	41 (63.1)	50 (66.7)	0.657
Previous CAD	55 (83.3)	64 (85.3)	0.744
Smoking	45 (68.2)	49 (65.3)	0.720
Hyperlipidemia	42 (64.6)	45 (60.0)	0.574
SBP	121.89 ± 20.38	121.99 ± 22.60	0.980
DBP	73.28 ± 13.37	78.20 ± 21.43	0.115
RBC	4.55 ± 0.43	4.52 ± 10.72	< 0.001
HCT	42.68 ± 3.53	41.02 ± 0.60	0.726
Platelet	2198356 ± 51062	193460 ± 48415	< 0.001
LVEF	38.76 ± 11.00	40.77 ± 9.47	0.259
Anterior MI	40 (59.7)	40 (52.6)	0.395
Inferior MI	16 (23.9)	22 (28.9)	0.494
Posterior MI	0	0	
RV MI	0	0	
Lateral MI	2 (3.0)	0 (0)	0.218
Posterior-inferior MI	2 (3.0)	8 (10.5)	0.106
Anterolateral MI	7 (10.4)	5 (6.6)	0.405
Aspirin	66 (98.5)	76 (100)	0.469
Plavix	66 (98.5)	76 (100)	0.469
Heparin	64 (95.5)	75 (98.7)	0.341
Beta-blocker	60 (89.6)	71 (93.4)	0.405
Statin	66 (98.5)	73 (96.1)	0.623
ACE	59 (88.1)	70 (92.1)	0.417
TNG	21 (31.3)	31 (40.8)	0.425

CAD: Coronary artery disease; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; RBC: Red blood cell count; HCT: Hematocrit; LVEF: Left ventricular ejection fraction; MI: Myocardial infarction; RV: Right ventricular; ACE: Angiotensin-converting enzyme; TNG: Nitroglycerin
Data is presented as mean ± SD or number (%)

Table 2. Angiographic and percutaneous coronary intervention (PCI)-related data in rescue and facilitated PCI groups

	Primary PCI (n = 67)	Rescue PCI (n = 76)	P
Stenosis			
Cut-off	30 (44.8)	46 (60.5)	0.600
90-99	28 (41.8)	23 (30.3)	0.151
70-90	9 (13.4)	8 (10.5)	0.592
LAD stent number			
0	1 (2.0)	0 (0)	
1	43 (86.0)	30 (68.2)	< 0.001
2	5 (10.0)	13 (29.5)	
3	1 (2.0)	1 (2.3)	
RCA stent number			
0			
1	14 (93.3)	23 (85.2)	0.639
2	1 (6.7)	4 (14.8)	
3	0	0	
LCX stent	1	3	0.165
Complications			
CVA	0 (0.0)	0 (0.0)	1.000
Death	5 (7.5)	4 (5.3)	0.734
Arrhythmia	3 (4.5)	3 (3.9)	1.000
Bleeding	0 (0.0)	0 (0.0)	
Reinfarction	1 (1.5)	0 (0.0)	0.469
No-reflow phenomenon	23 (34.3)	30 (39.5)	0.525
TIMI flow			
1	8 (11.9)	5 (6.6)	0.266
2	12 (17.9)	21 (27.6)	0.169
3	43 (64.2)	45 (59.2)	0.542

LAD: Left anterior descending artery; RCA: Right coronary artery; LCX: Left circumflex artery; CVA: Cardiovascular arrest; TIMI: Thrombolysis in myocardial infarction
Data is presented as number (%)

Table 3. Odds ratio of streptokinase for no-reflow phenomenon and 24-hour death

	Odds ratio	95% confidence interval	P
No-reflow phenomenon			
Crude model	1.240	0.630-2.469	0.525
Model 2	1.200	0.595-2.428	0.607
Model 3	0.925	0.409-2.093	0.852
24-hour mortality			
Crude model	0.689	0.177-2.678	0.591
Model 2	0.846	0.202-3.542	0.891

Crude model: The effects of streptokinase or eptifibatide on dependent variables
Model 2: Adjusted based on age and sex
Model 3: Adjusted based on age, sex, history of diabetes, hypertension, hyperlipidemia, coronary artery disease, smoking, platelets, myocardial infarction level, vascular involvement (cutoff: 90-99 and 70-99) and the involved artery

Table 1 summarizes the demographic data, history of diseases, medicines intake, medical tests, MI type, and left ventricular ejection fraction (LVEF) of subjects in the PPCI and rescue PCI groups. As it is seen, the two groups were only significantly different in terms of red blood cell count (RBC) and platelets.

The two groups were not significantly different in vascular involvements. However, a significant difference in the number of left anterior descending artery (LAD) stents was observed, i.e. 31.8% of the cases in the rescue PCI group had more than 2 stents. The incidences of no-reflow phenomenon or complications were not significantly different between the two groups (Table 2).

Table 3 presents the effects of PCI type on

no-reflow phenomenon and mortality. In order to evaluate the effects of SK, 3 models of crude, adjusted for age and sex, and adjusted for age, sex, history of diabetes, hypertension, hyperlipidemia, CAD, smoking, platelets, MI level, vascular involvement (cutoff: 90-99 and 70-99), and the involved artery were used. The effects of PCI type on mortality were assessed in the crude model and the model adjusted for age and sex. Due to small sample size, adjustment for other factors did not result in an appropriate model for mortality. As Table 3 shows, PCI type did not affect no-reflow phenomenon and 24-hour death in either crude or adjusted models.

Discussion

In this study, the two groups were not significantly different in terms of 24-hour mortality and complications or no-reflow phenomenon. The frequency of no-reflow phenomenon among the PPCI group was 34.3%. Palomo Villada et al. found no-reflow phenomenon to occur in 21.8% of 32 cases of rescue PCI.[16] However, their mortality rate was much higher than ours (18.7% vs. 7.5%) which might have been the result of higher ages of their participants.

Steg et al. followed 362 patients with STEMI for 10 years. They reported the in-hospital death rate among the 91 individuals who underwent PCI after angiography as 5.5%. In addition, 1.6% of the same patients experienced intracerebral hemorrhage and 2.8% suffered from bleeding in other organs.[17] In our study, however, despite the higher in-hospital death rate, brain damage and bleeding were not observed probably due to not using heparin after PCI.

In a study on 109 patients with STEMI who underwent rescue PCI after unsuccessful thrombolysis, Balachandran et al. reported the in-hospital death rate as 9%.[18] Perez-Berbel et al. evaluated 361 similar patients and observed no-reflow phenomenon in 73 individuals (20.2%). Moreover, 33 subjects (10.4%) died throughout their study.[19] Interestingly, Perez-Berbel et al. used abciximab, a glycoprotein (GP) IIb/IIIa inhibitor, during the PCI procedure[19] which makes their groups comparable to ours.

In a multi-country, double-blind, placebo-controlled clinical trial, Ellis et al. compared the efficacy of reteplase plus abciximab (combination-facilitated PCI) with abciximab-facilitated PCI and PPCI in patients whose ischemic signs initiated at most 6 hours before and who qualified for undergoing fibrinolysis or PCI. A total number of 2452 patients were randomized into three groups of PPCI (n = 806), abciximab-facilitated PCI (n = 818) and combination-facilitated PCI (n = 828). Mortality rates in the three mentioned groups were not significantly different (4.5%, 5.5%, and 5.2%, respectively).[20] The mortality rate among the patients treated by facilitated PCI with eptifibatide was 5.3% in the present study. In contrast to Ellis et al., we performed either rescue PCI on patients who had received SK followed by PCI or PPCI on individuals who had received eptifibatide.[20] Furthermore, in our cross-sectional study, no placebo group was included and the interventionist decided to conduct PCI according to the conditions of the patients.

Another clinical trial was conducted by Kanakakis et al. to measure the effects of facilitated PCI on patients with STEMI. Patients were included if STEMI symptoms had started not more than 6 hours earlier. They were then randomly allocated to two groups of facilitated PCI with tenecteplase or PPCI (control group). The mortality in the two groups was not significantly different (6% vs. 3.5%).[21]

Likewise, in a randomized clinical trial, Le May et al. divided 400 patients with STEMI into two groups of PCI with eptifibatide or PPCI and evaluated death and major complications during a 30-day period following PCI. Although bleeding was increased in the first group, they did not report any significant differences in the outcomes between the two groups.[22] However, the present study could not make such a comparison since it did not assess the long-term outcomes. In addition, PCI was not performed without eptifibatide or SK to compare the efficacy of the two medicines.

Vienna STEMI Registry was a study to investigate STEMI treatment in five hospitals in Vienna. It included 1053 individuals. PPCI with eptifibatide and abciximab was conducted on 631 patients. However, 281 cases first underwent thrombolysis with tenecteplase (TT). They were then transferred to hospitals equipped with angioplasty wards where PCI was performed. The remaining 141 individuals did not receive PCI at all. The total in-hospital death rate and the rates in the PPCI and TT groups were not significantly different (9.5%, 8.1%, and 8.2%, respectively). However, in the no reperfusion group, 18.4% of the subjects died.[23]

Although the present study could not determine factors related with no-reflow phenomenon among the two groups of rescue PCI and PPCI with

eptifibatide, various studies have shown the phenomenon to have negative effects on clinical outcomes of patients with STEMI. Resnic et al. reported an odds ratio (OR) of 3.6 when the effects of no-reflow phenomenon on mortality and MI was concerned among 4264 patients who had experienced PCI ($P < 0.001$).[24] Similarly, Morishima et al. followed 120 patients with STEMI who had undergone PCI for five years. No-reflow phenomenon occurred in 25% of the subjects. They suggested the phenomenon to be an independent risk factor for cardiac arrest [OR: 5.25; 95% confidence interval (CI): 1.79-7.69].[25] No-reflow phenomenon was also considered as an independent risk factor for death during the first year after PCI [hazard ratio (HR): 3.35; 95% CI: 1.97-5.69] by Ndrepepa et al. who observed the complication in 9.5% of the studied patients with STEMI.[9] Therefore, identification and prevention of contributing factors to no-reflow phenomenon might lead to reduced complications and mortality following PCI.

The present study could not evaluate effective factors on death since it aimed to determine in-hospital complications and thus followed the patients for a short period. According to the obtained results, however, the mortality rates, in either the primary or rescue PCI groups, did not seem different from the studies in other countries. It can therefore be concluded that thrombolytic therapy and RT for patients with STEMI in Iran follow standards similar to other countries and cause the same short-term complications.

Ethical considerations imposed a limitation on the present study. In fact, we could not perform a double-blind randomized clinical trial. In addition, due to the short follow-up period, long-term complications of the two methods could not have been compared with previous researches. Another limitation was the absence of a control group for making appropriate comparisons. A clinical trial model with completely aware and consented patients is suggested for better evaluation of the outcomes. Moreover, long-term follow-up may find the best treatment method applicable by the interventionists in the country.

Overall, the present study suggested thrombolytic therapy (when angioplasty is not accessible) not to significantly differ from PCI with eptifibatide in terms of no-reflow phenomenon and short-term complications. Thrombolytic therapy is thus recommended in all hospitals lacking an angioplasty ward. However, the patient must be quickly transferred to a fully equipped hospital for PCI afterwards.

Conflict of Interests

Authors have no conflict of interests.

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Improvement of dietary oil consumption following a community trial in a developing country: The role of translational research in health promotion

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Original Article

Abstract

BACKGROUND: This study aimed to determine the effects of the interventions of Isfahan Healthy Heart Program (IHHP) on the type of oil consumed at the population level. It also tried to assess how this strategy has been effective as a health policy.

METHODS: The IHHP, a six-year community intervention program (2001-07), aimed at health promotion through the modification of cardiovascular disease risk factors. It was performed in Isfahan and Najafabad counties (intervention area) and Arak county (reference area), all in central Iran. This study targeted the whole population of over 2,000,000 in the intervention area. The findings of annual independent sample surveys were compared with the reference area. Dietary interventions were performed as educational, environmental, and/or legislative strategies.

RESULTS: From 2001 to 2007, the mean of changes for hydrogenated oil consumption was -3.2 and -3.6, and for liquid oil it was 3.6 and 2.8 times per week in the intervention and reference areas, respectively ($P < 0.001$). According to Commerce office record, the increase in liquid oil distribution during 2000-2007 was significantly higher in Isfahan than Arak (34% vs. 25%).

CONCLUSION: The effects of the simple, comprehensive, and integrated action-oriented interventions of our program could influence policy making and its results at the community level. It can be adopted by other developing countries.

Keywords: Oil Consumption, Hydrogenated Oil, Liquid Oil, Community Trial

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Introduction

The prevalence of noncommunicable diseases (NCDs) has been rapidly increasing worldwide. Their related mortality has been estimated to increase by 15% globally between 2010 and 2020 (to 44 million deaths).[1] Cardiovascular diseases (CVDs) are currently considered as major NCDs causing mortality and morbidity in most countries. They are a great concern in low- and middle-income countries which will face an epidemic of NCDs in the near future. Population-based interventions might reduce the burden of NCDs and their risk factors.[2]

Healthy lifestyle habits are recommended both in health and disease conditions to prevent further diseases. Healthy nutrition for improvement of lipid profile is an integral part of all interventions to prevent or reduce CVD risk at individual or population levels.[2] The quality of the fat consumed in each population is one of the most important nutritional elements that affects cardiovascular

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health. Unlike other dietary fats, trans fatty acids are not essential and have potential health hazards. Most of the trans fat is artificially created in a process known as hydrogenation. Trans fats from partially hydrogenated oils are more harmful than naturally occurring oils.[3] Besides their health hazards to the cardiovascular system and malignancies, there is evidence to suggest that consumption of trans fats can trigger insulin resistance and boost the risk of developing type 2 diabetes. Trans fats not only increase total and low density lipoprotein (LDL) cholesterols, triglycerides, and saturated fatty acids, but also decrease high density lipoprotein (HDL) cholesterol levels.[4,5] Large cross-population studies have shown a strong correlation between trans fat intake and mortality.[6-8]

High prevalence of NCDs, particularly CVDs,[9] and their risk factors[10] have been well documented in Iran. Implementation of public health policies for lifestyle modification is hence necessary. In 2003, about 89% of the Iranian population consumed hydrogenated oils while trans fatty acids constituted 59.1% and 51.2% of available hydrogenated oils and margarines, respectively.[11]

Efforts to reduce trans fatty acid consumption have been performed in several countries. In the 1990s for instance, trans fatty acid content of retail foods was decreased in the Netherlands through interventions in food industries.[3] In the US, mandatory disclosure of trans fat content on food labels led to the reduction of trans fat content of foods by production industries. The improvement was mostly based on population knowledge about the hazards of this type of fatty acids.[12]

In response to the increased burden of NCDs in Iran,[13] the Isfahan Healthy Heart Program (IHHP) was implemented as a comprehensive community-based demonstration program with reference area. The IHHP aimed to integrate programs and policies that effectively impact the major determinants of NCDs, mainly through lifestyle change.[14,15] One of the main strategies of this program targeted improvement in oil production and consumption.

Here, we report the main effects of this six-year interventional program on the type of oil consumed by the population living in interventional areas in comparison to the reference population. We also evaluate how this strategy of the program has been translated to a health policy.

Materials and Methods

Design and sampling

The IHHP aimed to improve the knowledge, attitude, and practice of the population, health professionals, and CVD patients in order to reduce the risk factors of NCDs that share the same risk behaviors.[14-16]

The IHHP was conducted in the central part of Iran, in two neighboring counties (Isfahan and Najafabad) as the intervention area and one county (Arak) as the control area. According to the national census in 2000, the population was 1895856, 275084, and 668531 in Isfahan, Najafabad and Arak, respectively. Multistage cluster random sampling was used to select eligible individuals from urban and rural areas. Residents older than 19 years of age in these counties were included while pregnant women and mentally retarded subjects were excluded. Written informed consent was obtained from all participants after full explanation of the study. The program was designed in three phases: baseline survey, intervention, and post-intervention phase.

The baseline survey was performed in 2001 in both the intervention and reference areas. It included a total of 12514 participants. The intervention was started in 2002 in Isfahan and Najafabad and lasted until 2006. Annual surveys on independent samples were conducted in both the intervention and reference areas. In baseline and final survey, sampling was performed according to age and sex distribution. Sampling method of Countrywide Integrated Noncommunicable Disease Intervention (CINDI) was used in other annual surveys in both the intervention and reference areas.[14] While routine national health activities continued in the intervention and reference areas, the IHHP interventions aimed at improving four major lifestyle behaviors including tobacco control, healthy diet, physical activity, and stress management. In 2007, a final survey was performed on independent random samples from the two communities. Overall 9570 individuals were studied in the post-intervention survey.

A questionnaire including sociodemographic characteristics and other health-related issues was completed for the participants by trained health professionals.

Dietary assessment

An open-ended food frequency questionnaire (FFQ) was used to assess dietary behavior. This 48-item qualitative questionnaire was adapted from the CINDI program questionnaire.[17] The Persian version of the questionnaire had shown good reliability (r = 0.8) and validity in a previous study.[18] For the present study, the two questions related to

consumption of hydrogenated and non-hydrogenated oils were used. The participants were asked "How many times per week do you consume hydrogenated oil?" and "How many times per week do you consume liquid oil?". The mean number of times these types of oils were consumed in a week was calculated. Additional nutritional status of the intervention vs. reference area were compared in a randomly selected subsample of 1000 adults aging ≥ 19 years old from urban populations in each of the intervention and reference areas. The obtained data was included in the cross-sectional survey. A 24-hour dietary recall questionnaire was used to study the nutritional habits in the subsample. Nutrients contents of the questionnaire were computed by the Iranian Food Consumption Program (IFCP) designed by Isfahan Cardiovascular Research Center (ICRC),[17] based on the Iranian Food Composition Table.[18] Trained nutritionists assisted in fulfillment and rechecking as well as data entry of the assembled dietary questionnaire.

Intervention strategies

Based on the findings from the baseline survey, intervention strategies were designed by considering available human and economic resources. Interventions were conducted through 10 interventional projects with various target groups including youth, women, children and adolescents, worksite staff, health professionals, health volunteers and non-governmental organizations, individuals with CVD risk factors, CVD patients and their family members.[15]

Nutritional interventions were performed through a project entitled "Healthy Food for Healthy Community" (HFHC). This project aimed to improve the knowledge, attitude, and practice of the society regarding healthy nutrition, to increase the availability of healthy nutrition, and to improve the quality of food production and distribution. Details of nutritional interventions have been described previously.[16,19] Only strategies and activities related to hydrogenated/liquid oil consumption are presented here.

Training involved the target groups of all IHHP interventional projects regarding the hazards of hydrogenated oil. It encouraged reduced consumption of fat and substitution of hydrogenated oils with liquid oils. Training sessions were held for owners and staff of restaurants, pizzerias and confectionaries and kitchens of factories, universities, garrisons, and hospitals. Training was supported by formal instructions for serving healthy food choices and healthy cooking in restaurants and fast food shops through reducing oil consumption and using liquid oil. In order to make improvement in oil consumption, collaborations were made with Isfahan Provincial Health Center and food unions to implement approved instructions aimed at reducing the amount of fat and oils in cooking, substituting hydrogenated oil with non-hydrogenated oil, and using modified deep frying oils for frying. Similar instructions were implemented in universities and worksites including offices and factories that served foods.

A monitoring checklist of healthy food choices was designed by ICRC and was integrated into ongoing health system supervising activities to ensure the implementation of the IHHP interventions. Accommodations were made with food industries to produce healthy foods with reduced oil and without hydrogenated oil in order to sustain an initially established partnership between the academic field, industry, and other health-related sectors. This partnership was later transferred and registered as a non-governmental organization named "Food Industry and Healthy Community Association". Its members were from food industries, faculty members specialized in nutrition, medicine, and public health, and other stakeholders such as Provincial Commerce Office, the Food and Drug Supervision Office, Standard and Industrial Research Institution, and researchers and collaborators of HFHC. The association aimed at facilitating the cooperation between food industries and scientific institutes toward manufacturing healthy food products. Moreover, it offered new and healthy formulations for food products and provided facilities to encourage food industries to produce healthy products. The intervention covered products such as oil, margarines, beverages, canned fish, soymilk, sweets, candies, cakes, pies, biscuits, and low-fat dairy products.

At the beginning of the IHHP interventions in 2001, subsidized dietary oil distributed by the Ministry of Commerce was mainly in the form of hydrogenated oil. Therefore, users of liquid oil had to pay some extra money for receiving liquid oil. Collaborations were made with the provincial Commerce Office to substitute hydrogenated oil with liquid oil in 2003. The proposal was reflected to the Nutrition Improvement Department in the Ministry of Health and then to the Ministry of Commerce, responsible for provision and distribution of oil throughout the country. It was later implemented at the national level. Moreover, extensive requested letters were sent to Isfahan

Provincial Commerce Office to increase liquid oil subsidiaries in Isfahan and Najafabad. Correspondences were made with this office to substitute production of hydrogenated oil with liquid oil by the only oil production factory in Isfahan which was approved by Ministry of Commerce. Food industries were asked to add information about trans fatty acids and saturated fat content of oils to the labels on their food products and the community was informed to read these labels.

Statistical analysis

Univariate analysis of variance (ANOVA) was used to compare the mean consumption of hydrogenated and liquid oil per week in intervention and control areas in annual surveys. T-test was used to compare the mean values of weekly consumption of hydrogenated or liquid oil in pre- and post-intervention phases. General linear model was used to compare the trend and the mean changes of hydrogenated oil and liquid oil consumption in intervention and reference areas. SPSS for Windows 15.00 (SPSS Inc., Chicago, Il, USA) was used to analyze the data. P values of less than 0.05 were considered as significant.

Results

Table 1 shows the characteristics of the study population. The baseline survey included a total of 12514 subjects. The annual surveys included 5891, 4793, and 6083 subjects from 2002 to 2004, respectively. Because of financial limitations, the fourth annual evaluation (in 2005) could not be conducted in the reference area and just included 3010 individuals in the intervention area. The final survey in 2007 included 9572 participants. Additional nutritional status was assessed in 1749 and 1632 urban individuals in 2001 and 2007, respectively.

Figure 1 shows the trend of hydrogenated oil consumption in the reference and intervention areas. Throughout the study, the mean frequency of weekly hydrogenated oil consumption was significantly lower in the intervention area than in the reference area. The mean frequency of hydrogenated oil consumption decreased in both reference and intervention areas from 2001 to 2007 but with a greater slope in the intervention area. The mean weekly consumption of liquid oil was significantly higher in the intervention area. In fact, it increased in both areas but with a higher slope in the intervention area ($P < 0.001$) (Figure 2). The mean changes in weekly consumption of hydrogenated oil were -3.2 and -3.6 times in the intervention and reference areas, respectively. During 2001-2007, the mean increase of liquid oil consumption was 3.6 and 2.8 times per week in the intervention and reference areas, respectively ($P < 0.001$).

Table 1. Characteristics of the study population in the reference and intervention areas from 2001 to 2007

		Baseline survey (2001)	First evaluation (2002)	Second evaluation (2003)	Third evaluation (2004)	Forth evaluation (2005)	Fifth evaluation (2006)
Residency							
Urban	Intervention	4873	2438	1950	2402	2652	3897
	Control	4220	1932	1556	2119		2795
Rural	Intervention	1302	556	450	613	360	822
	Control	2119	965	837	962		2058
Sex							
Male	Intervention	3006	1482	1186	1479	1453	2320
	Control	3117	1416	1183	1492		2458
female	Intervention	3169	1512	1214	1534	1558	2399
	Control	3222	1481	1210	1578		2395
Education (years)							
0-5	Intervention	2738	1316	1040	1649	1454	1641
	Control	3659	1717	1203	1768		2658
6-12	Intervention	2704	1220	1041	1071	1185	2130
	Control	2112	973	927	1001		1862
> 12	Intervention	626	417	299	288	372	931
	Control	451	198	257	301		333
Age (years)*							
	Intervention	6.80 ± 4.36	6.43 ± 4.74	5.69±4.48	3.76 ± 4.36	3.97 ± 4.63	3.04 ± 4.45
	Control	10.63 ± 4.61	10.15 ± 4.93	8.90±4.68	8.62 ± 5.08	-	7.38 ± 5.36

* Mean ± SD

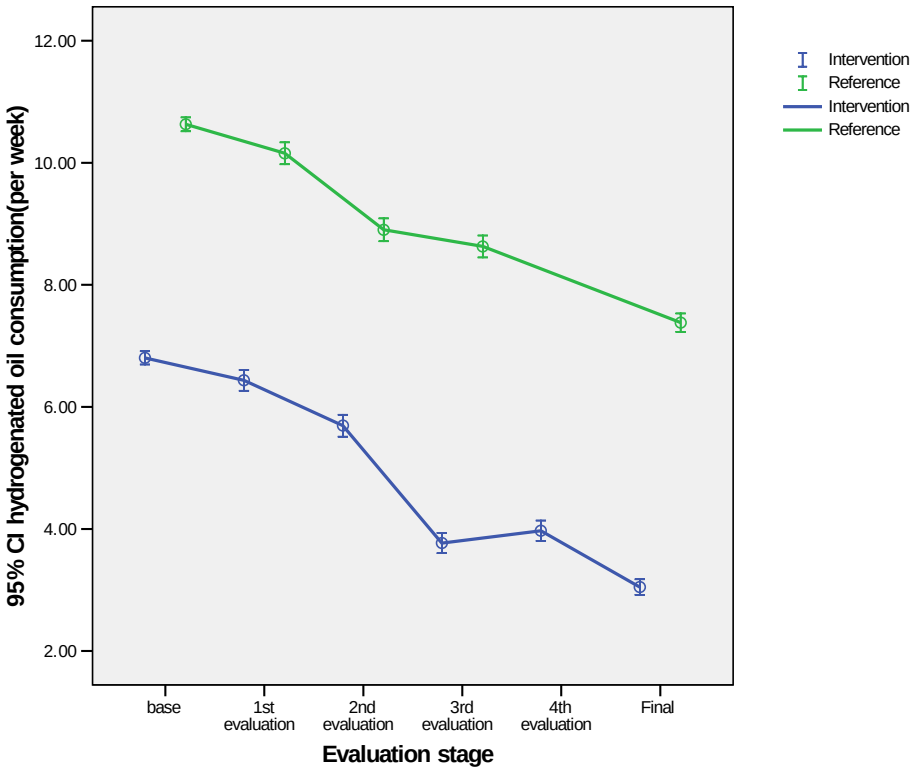

Figure 1. Trend of hydrogenated oil consumption in the intervention and reference areas

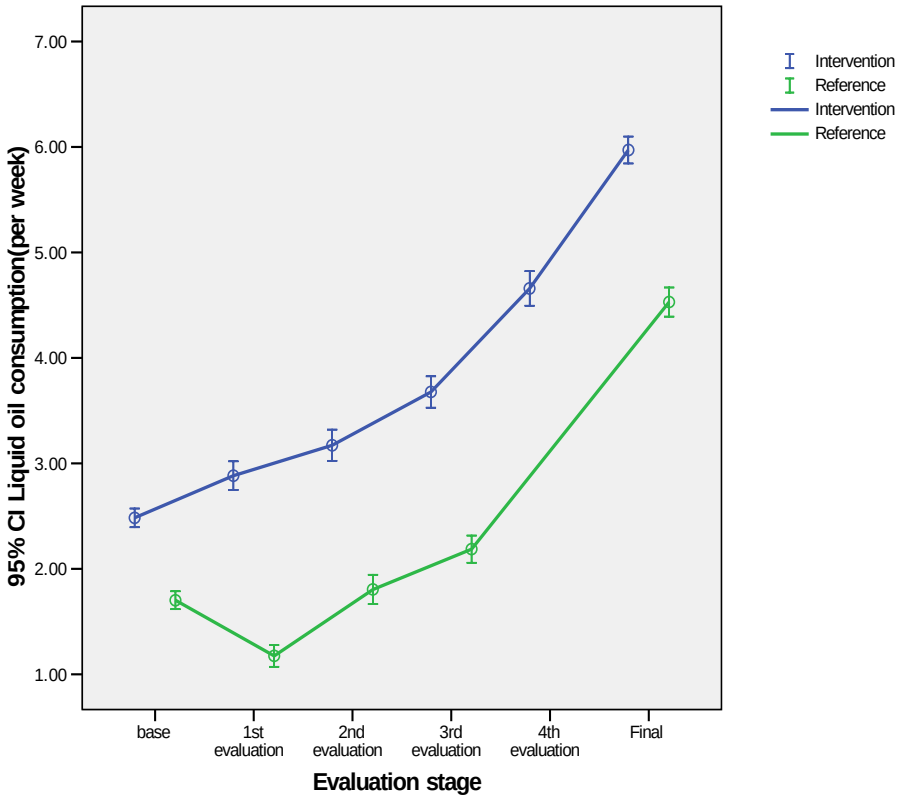

Figure 2. Trend of liquid oil consumption in the intervention and reference areas

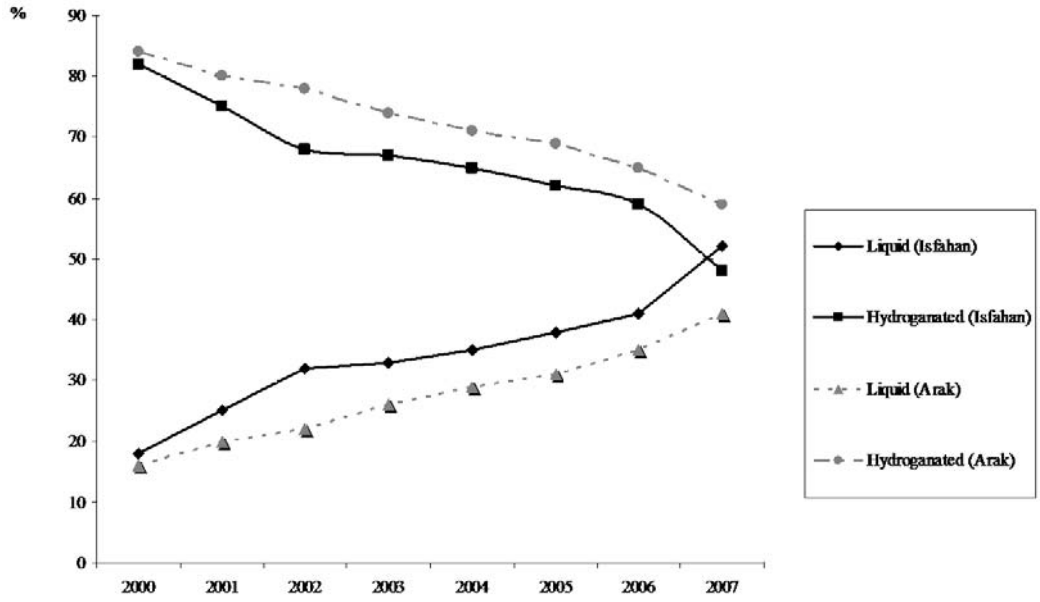

Figure 3. Trend of hydrogenated and liquid oil distribution in intervention and reference area based on Commerce office records

Table 2. The mean changes in dietary fat and oils intake in subsamples of the intervention and reference areas in 2001-07

Oils	Intervention Area			Reference Area			P
	2001	2007	P	2001	2007	P	
Hydrogenated oil (g/day)	15.2 ± 4.3	7.4 ± 3.8	0.005	18.3 ± 4.2	13.4 ± 3.7	0.020	0.030
Liquid oil (g/day)	9.6 ± 3.7	16.7 ± 4.9	0.006	10.5 ± 3.8	12.7 ± 3.9	0.100	0.008

Values are expressed as mean ± SD.

Based on the Commerce Office records, from 2000 to 2007, the distribution of hydrogenated oil was higher in the reference area. On the other hand, distribution of liquid oil was higher in the intervention area. Trend of hydrogenated oil distribution showed a descending slope in both intervention and control areas. Distribution of liquid oil had a rising trend in both areas with a higher slope in the intervention area ($P < 0.05$, Figure 3).

Liquid oil production increased from 21.5% in 2004 to 56.5% in 2008. Canola oil comprised the greatest share of produced oils. At the end of the intervention, restaurants and food shops increased usage of frying oil to 100%. Restaurants used liquid oil for cooking all foods except rice (15% hydrogenated oil).

Table 2 shows changes of hydrogenated and liquid oils intake in intervention vs. reference areas based on 24-hour recall in 2001-2007. The trend of hydrogenated oil consumption showed significant reduction and liquid oil showed a significant enhancement in intervention area ($P = 0.03$ and $P = 0.008$, respectively).

Discussion

To the best of our knowledge, this interventional study was the first of its kind not only in Iran, but also in the east Mediterranean region. It could successfully decrease the consumption of hydrogenated oil and substitute it with liquid oil. Increasing liquid oil distribution in intervention acea has become circulated as a health policy by the Commerce Office. According to independent reports of Commerce Office, the implementation of this policy showed consistent changes in the type of distributed oil. It was confirmed at population level based on the results of IHHP surveys. The hazardous effects of high fat intake have been known for more than five decades. It is well-documented that limiting dietary fat reduces cardiovascular mortality.[7] Further studies revealed that diets lower in trans fat and higher in unsaturated fat may particularly decrease the risk of cardiovascular death even among individuals with previous cardiovascular events.[6] All scientific evidence in this field has improved knowledge on the role of diet on health. In addition, better

understanding of dietary elements at molecular level has directed scientific recommendations to focus on diets low in saturated fat. The Global Strategy on Diet, Physical Activity and Health (DPAS) considers diet and physical activity as two main risk factors of NCDs. It hence recommends lower daily fat intake and a shift from saturated fat toward unsaturated fat with the final goal of eliminating trans fatty acids from diet.[20] Latest dietary recommendations advise reduction of trans fatty content of foods to less than 1%.[21]

Various strategies have been implemented in different countries to reduce total, saturated, and trans fat intake. Based on scientific evidence,[22] government support,[23] legislation, ratifying regulations for food industries,[12] enhancement of public knowledge,[24] and using technology in production of new and healthier formulations for fats and oils[3,25] are among these strategies. The IHHP benefited from a variety of action plans and strategies to implement healthy nutrition in the intervention area. It in fact tried to increase public knowledge, improve public attitudes and behaviors, develop new regulations and enforce the existing ones based on collaboration with food industries, and increase the production and distribution of healthier types of oils.

Using an FFQ and a 24-hour recall questionnaire, we observed reduced hydrogenated fat consumption and increased liquid oil consumption after six years of intervention at the community level. This reflects improved public consumption pattern that can be explained in part by enhanced knowledge and practice. The IHHP strategy to improve people's knowledge can also be observed in other dietary habits of the population such as improvements in fat and meat consumption indices reported in a previous study.[16] Although as a reflection of the national policies in increasing the production of liquid oils, favorable changes were also documented in the reference area of our study, the considerably higher levels of improvement in the intervention area are an evidence for the success of the project's interventions.

The role of public knowledge in the amount and type of consumed fat can be proved by reduced consumption of fat and oils in the American diet between 1989 and 1996. The American population seemed to effectively reduce foods classified in the 'oil and fat' category. However, the amount of fat within other food categories, especially meat, was increased.[3] Consumers' awareness on healthy and unhealthy food items will also affect the food industries that seek consumer satisfaction to keep their sale and reputation.[26,27]

The IHHP enhanced labeling of food products, in particular oils and trans fat content, by encouraging oil production companies to add the level of industrial trans fatty acids on their labels and educating and encouraging people to read labels on food products. In the beginning of IHHP, an evaluation was done to assess the awareness, use and understanding of these labels by the consumers. Only 7% reported that they read the labels regularly, mainly because labels are too complicated and reading them needs longer time. Furthermore, 95% of participants stated that they did not understand the labels. Together with the food producers and based on the consumers' suggestions, IHHP started an initiative to simplify the labels, so that contents only refer to total energy, total fat, saturated fat and trans fatty acids, sugar and salt and to place the labels by the production date to increase consumers attention.[28] The effects on consumers' choice and sensitivity to quality of products might have indirectly reduced the rate of hydrogenated oil consumption. A similar experience was observed in the US where mandatory labeling of industrial trans fat content of food products was enacted in 2006. Primary recommendations had been made in 1994 (about 12 years earlier). Later, the regulations were extended to ban the use of industrial trans fats in restaurants. The chain of improvement, which started from federal regulations in food industry, developed rapidly to other parts of food production industry and supply and even enhanced related research in the field for providing more qualified oils.[12] In 2006, about 96% of packaged foods in the US had nutrition labeling with 12% providing data about the amount of tans fats.[26]

The present report from our study is mainly devoted to reporting one of the outcomes of the IHHP. Educational and intersectoral collaboration between scientific and executive manager of the study influence the policy of a public sector responsible for distributing oil in the community level. This strategy improved the availability of a healthier type of oil. As supported by the World Health Organization's latest scientific update in 2004, modification of public nutritional habits requires the collaboration of many stakeholders in public and private sectors.[22] The completing part, that is the population demand, was affected through various activities aimed at improving people's knowledge about the health hazards of hydrogenated oil and the necessity of substituting it

with liquid oil.

Previous studies have advised the discrimination of percentage versus total fat intake when interpreting trends of dietary components.[24] Therefore, the observed improvement in the trend of hydrogenated and liquid oil intake in Iranian population cannot be counted as a real improvement in oil consumption unless the findings of a previous study from the IHHP data are considered. This study showed an improvement in the kind of oil consumption in the intervention area.[16] In the setting of reduced total fat intake, relative improvement in type of oil is interpreted as a positive change in dietary habits. This seems a possible result of activities and policies that have been implemented in the IHHP. Moreover, reports of Commerce Office, which provides a major source of oil consumption in the community, adds to the validity of our findings. The political will and community request besides our extensive contacts and follow-up with the Office of Nutrition Improvement in the Ministry of Health resulted in a recent legislation that mandates the production of oils with trans fatty acid content less than 15%. An external evaluation by a team of experts from National Institute for Health and Welfare of Finland in 2009 confirmed the benefits of nutritional interventions.[28]

However, as a limitation of our study, improved knowledge of the population might have made them say they had consumed liquid oil than hydrogenated oil. We did not assess intake of other sources of hydrogenated oil. Hence, the findings cannot be generalized unless we know total caloric intake and percentage of all dietary nutrients from the beginning to the end of this intervention.

Conclusion

Community-based interventions can improve healthy lifestyle in the population through establishing partnership between stakeholders, population, and industries. This is practiced through enhancing public knowledge based on scientific findings that sensitize people to shop healthier products. Healthy recommendations help industries keep their credit by elevating the quality of their products. Involving stakeholders and policy makers in such community trials assures the implementation of recommendations. The leading role of research centers can enhance the acceptance of the recommended improvements among authorities and the society. The effects of simple, comprehensive, and integrated action-oriented interventions of our program are evidences on how research can influence policy decisions at community level.

Conflict of Interests

Authors have no conflict of interests.

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Primary percutaneous coronary intervention in the Isfahan province, Iran; A situation analysis and needs assessment

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Original Article

Abstract

BACKGROUND: Primary percutaneous coronary intervention (PPCI) is considered as a choice of treatment in ST-elevation myocardial infarction (STEMI). PPCI has been performed in the Isfahan Province for several years. This study was performed to describe the situation, and determine in-hospital and early (30 days) clinical outcomes of the patients in order to provide sufficient evidence to evaluate and modify this treatment modality if necessary.

METHODS: All patients, who underwent PPCI for STEMI from July to December 2011 at Chamran and Saadi Hospitals (PPCI centers in the Isfahan Province), were included in this case series study. Premedication, angioplasty procedure, and post-procedural treatment were performed using standard protocols or techniques. All discharged patients were followed for 30 days by phone. Endpoints consisted of clinical success rate, and in-hospital and 30 day major adverse cardiac events (MACEs) (death, reinfarction, stroke, and target vessel revascularization).

RESULTS: 93 patients (83 (89.2%) at Chamran Hospital and 10 (10.8%) patients at Saadi Hospital) had PPCI. Mean Age of the patients was 59.60 ± 11.10 and M/F ratio was 3.89. From the 181 involved vessels (involved vessels/patient ratio = 1.97 ± 0.70), the treatment of 105 lesions (lesions/patient ratio = 1.13 ± 0.368) was attempted. The clinical success rate was 72%. Pain-to-door and door-to-balloon times were, respectively, 255.1 ± 221.4 and 148.9 ± 168.5 min. The reason for failure was impaired flow (n = 17 (18.3%)), failure to cross with a guidewire (n = 2 (2.2%)), suboptimal angiographic results (n = 2 (2.2%)), and death in one patient. The in-hospital and 30 days MACE rates were, respectively, 8.6% and 3.2%.

CONCLUSION: Low success rate in our series could be due to prolonged pain-to-door and door-to-balloon times and lack of an established, definite protocol to regularly perform PPCI in a timely fashion. We should resolve these problems and improve our techniques in order to prevent and treat slow/no-reflow phenomenon.

Keywords: Acute Coronary Syndrome, Myocardial Infarction, Percutaneous Transluminal Coronary Angioplasty, Cardiogenic Shock, No-Reflow Phenomenon

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Introduction

ST-elevation myocardial infarction (STEMI) is a dangerous manifestation of coronary artery disease (CAD) and continues to be a significant public health problem in industrialized and developing countries.[1,2]

The cornerstone of treatment of these patients is the rapid and effective restoration of blood flow with fibrinolytic therapy, and/or primary percutaneous coronary intervention (PPCI).[3] PPCI

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has been shown to be the superior strategy resulting in a markedly lower occurrence of short-term major adverse cardiac events (MACEs).[4-9]

Impaired or ceased flow in the absence of anatomical obstruction may occur after PPCIN; this can influence the prognosis negatively.[10,11] this event known as angiographic slow/no-reflow phenomenon is recognized angiographically in 5-20% of patients undergoing PPCI for acute myocardial infarction (AMI).[10,12,13]

A major disadvantage of PPCI is related to the availability of facility and an experienced team; PPCI is the treatment of choice for reperfusion therapy of STEMI whenever available and feasible.[14,15] Its golden time is within 90 min of admission to the hospital (door-to-balloon time 90 min) especially when thrombolytic therapy has failed (known as rescue PCI).[2,4,16]

In the Isfahan Province, PPCI has been performed since 2006. It was performed in Chamran Hospital for the first time, and has recently been performed in Saadi Hospital. However, after 6 years of experience of PPCI we could not find any study describing the situation, problems, and clinical outcomes of PPCI in Isfahan. Therefore, the objective of this study is to describe the situation and determine in-hospital and early (after discharge until 30 days) clinical outcomes of the patients who underwent primary or rescue PCI in the Isfahan Province. This study was done in order to provide sufficient evidence to evaluate and modify our system if necessary.

Materials and Methods

All patients who underwent primary or rescue PCI for the STEMI from July to December 2011 in the Isfahan Province (at Chamran and Saadi Hospitals) were included in this case series study.

All patients received orally 325 mg of chewable aspirin, and 600 mg of Plavix in the emergency room. After coronary angiography if the anatomy was eligible for PCI additional heparin (100 units/kg) was administered intravenously, and angioplasty procedure was performed using standard techniques.[2,16] However, strategic planning of the procedure and device selection were dependent on the operator's discretion.

After the angioplasty, patients received 325 mg of aspirin daily, beta-blockers, and angiotensin-converting enzyme inhibitors if not contraindicated. All patients (DES or BMS) received 75 mg of Plavix daily for the first month, and were suggested to continue using it for 12 months under the supervision of their physician.

Lesion types were noted according to the American College of Cardiology/American Heart Association's (ACC/AHA) lesion characteristics classification.[16]

All Patients who were discharged alive from hospitals were eligible to be followed by a phone survey for 30 days.

Definitions: Myocardial infarction (MI) was defined as Ischemic symptoms accompanied by at least one of the following criteria: positive cardiac enzymes, electrocardiographic changes (pathologic Q wave or new ST changes), and new cardiac motion abnormality on echocardiographic or radionuclide imaging.

Coronary blood flow after PPCI is graded on a scale of 0 through 3 depending on flow characteristics. Thrombolysis In myocardial infarction (TIMI) 0 is defined as no contrast flow beyond the site of occlusion (no perfusion), TIMI 1 as contrast flow beyond the site of occlusion but failing to opacify the entire artery (penetration with minimal perfusion), TIMI 2 is defined as contrast flow beyond the site of occlusion and opacification of the entire artery but at a rate slower than normal (partial reperfusion), and TIMI 3, known as normal flow, as opacification of the entire artery at a normal rate. No-reflow is traditionally defined as TIMI grade 0 or 1, and slow flow is defined as TIMI grade 2 in this scheme.[13]

Angiographic success was defined as post-procedure TIMI flow grade 3 and a residual stenosis of less than 20%.[2] The procedure was considered as successful if it was angiographically successful in all attempted lesions.

Clinical success was defined as a successful procedure in the absence of in-hospital major adverse cardiac events (MACEs: death, reinfarction, stroke and target vessel revascularization (TVR)) during hospitalization.[2,16] Reinfarction after PCI was defined as recurrent symptoms of ischemia with new electrocardiographic changes, and/or a rise in cardiac troponin more than twice the normal limits. Early MACEs were defined as the occurrence of mentioned events during the first 30 days after STEMI. TVR was defined as ischemia-driven repeat percutaneous intervention, or bypass surgery of the target vessel. Target lesion revascularization (TLR) was defined as ischemia-driven repeat percutaneous intervention, or bypass surgery for the target lesion. Other adverse events in this study included arrhythmia, congestive cardiac failure, allergy, access site complications, and bleeding.

The left ventricular ejection fraction was determined using either echocardiography, or contrast ventriculography during the procedure.

Data Collection and Management: The data were collected by specific data collection forms. Data entry was done using the forms designed in EPI Info™ 3.3.2 (Center for Disease Control and Prevention; Atlanta, GA). Moreover, data were analyzed using the Statistical Package for Social Sciences (SPSS) for Windows 15.0 (SPSS Inc., Chicago, IL, USA).

All the continuous data were expressed as mean ± SD or range (min-max) and categorical data were expressed as number, and percentages. After descriptive analyses, categorical variables were compared using the chi-square test (or Fisher's exact test if required), and continuous variables by using student's t-test or Mann-Whitney test. P values of less than 0.05 were considered as statistically significant.

Results

From July to December 2011, 83 (89.2%) patients at Chamran Hospital and 10 (10.8%) patients at Saadi Hospital (93 patients in total) underwent PPCI. Table 1 describes baseline characteristics of the patients at the time of reaching the hospital. Mean age of the patients was 59.60 ± 11.10, and M/F ratio was 3.89.

Table 2 reveals angiographic success, lesion characteristics, and treatment strategies of the patients. The interventionalists attempted to treat 105 lesions (lesions/patient ratio = 1.13 ± 0.368) of the 181 involved vessels (involved vessels/patient ratio = 1.97 ± 0.70) in our patients. In total 116 stents (62 BMS and 54 DES) were deployed in 98 lesions, and 4 lesions were treated only by balloon angioplasty. 3 lesions remained inaccessible during the PPCI.

83 of 105 lesions were treated successfully (angiographic success rate = 79.0%).

Procedural details are described in table 3. Pain-to-door (time from onset of symptoms to hospital admission and door-to-balloon time were 255.1 ± 221.4 and 148.9 ± 168.5 min, respectively. Their medians were 255.1 and 148.8 min, respectively.

Pain-to-door time was significantly different in primary and rescue PCI (207.9 ± 203.9 min vs. 396.3 ± 217.3 min, P < 0.001), but the door-to-balloon time was not (137.1 ± 150.9 min vs. 184.7 ± 217.3 min, P = 0.359).

Thrombectomy was used in 23 (24.7%) patients, and stents were deployed in lesions of 87 (93.5%) patients.

Table 1. Baseline characteristics of patients

Age	
Mean (years)	59.60 ± 11.10
Range (years)	33-86
Age ≥ 65 years	34 (36.6)
Gender, M/F ratio	74/19
MI location	
Anterior	58 (63)
Inferior	32 (34.8)
Other	2 (2.2)
Killip class	
1	72 (77.4)
2	12 (12.9)
3	4 (4.3)
Ischemic time (pain-to-door time)	
Mean (minutes)	255.1 ± 221.4
Range (minutes)	16-720
< 2 hr	29 (31.2)
≤ 2 hr - < 4 hr	21 (22.6)
≤ 4hr - < 6 hr	6 (6.5)
≤6hr - < 12 hr	30 (32.3)
Missed	7 (7.5)
Unconsciousness at admission	4 (4.3)
Cardiogenic shock at admission	9 (9.7)
Renal insufficiency(Cr > 1.5)	12 (12.9)
Smoker *	28 (30.1)
Diabetes mellitus	19 (20.4)
Hypertension†	24 (25.8)
Hyperlipidemia‡	18 (19.4)
Previous stroke	1 (1.1)
Previous CAD	25 (26.9)
EF	
Mean (%)	36.02 ± 11.58
Range (%)	15-60
Low EF (< 40%)	40 (43.0)

Categorical variables are expressed as n (%) and continuous variables are expressed as Mean ± SD or range (Min-Max).
M/F: Male/Female; MI: Myocardial infarction; SBP: Systolic blood pressure; CAD: Coronary artery disease; EF: Ejection fraction
*Smoker: a person who has smoked at least 1 cigarette (or cigar, pipe) in the last month.
†Hypertension: Systolic blood pressure > 140 mmHg; diastolic blood pressure > 90 mmHg; or taking hypertensive drugs
‡Hyperlipidemia: LDL cholesterol ≥ 130 mg/dl; triglycerides ≥150 mg/dl; and HDL ≤ 40 mg/dl; or on treatment of hyperlipidemia

Table 2. Basic angiographic success, lesion characteristics, and treatment strategies*

Attempted lesions	105 (100)
Left main	1 (1.0)
LAD	58 (55.2)
D1	5 (4.8)
LCX	9 (8.6)
OM1	4 (3.8)
RCA	25 (23.8)
PDA	2 (1.9)
Ramus	1 (1.0)
Lesion characteristics	
Mean preprocedural stenosis,%	96.19 ± 7.44
Total occlusion	61 (59.9)
Proximal location	44 (41.9)
Small vessels (RVD < 3mm)	23 (21.9)
Long (>10, < 20 mm)	52 (49.5)
Diffuse (≥ 20 mm)	49 (46.7)
Treatment strategy	
Predilation balloon	74 (70.5)
Stenting	98 (93.3)
Postdilation balloon	11 (10.5)
Thrombectomy	25 (23.8)
TIMI grade after procedure	
0–1	9 (8.6)
2	10 (9.5)
3	84 (80.0)
Angiographic success	83 (79.0)

Categorical variables are expressed as n (%) and continuous variables are expressed as mean ± SD.
LAD: Left anterior descending; D1: Diagonal1; LCX: Left circumflex artery; OM1: Obtuse marginal; RCA: Right coronary artery; PDA: Posterior descending artery; BMS: Bare metal stents; DES: Drug-eluting stents; BMS+DES: Combined DES and BMS stenting in a lesion, TIMI: Thrombolysis in myocardial infarction
*Lesion-based Analysis

The procedure failed due to impaired flow (n = 17 (18.3%)), failure to cross with a guide wire (n = 2 (2.2%)), suboptimal angiographic results (n = 2 (2.2%)), and death during procedure in one patient (procedural success rate = 76.3%). As mentioned above, impaired flow was the most frequent cause of failure. Slow flow (TIMI less than 3) was detected in 8 (47.1%) and no-reflow in 9 (52.9%) cases all of whom had been treated by stenting (BMS 9 (52.9%), DES 6 (35.3%), and combined stents 2 (11.8%)). This phenomenon was treated by intracoronary (IC) Integrilin in 12 cases (70.6%), IC epinephrine in 8 cases (47.1%), IC adenosine in 6 cases (35.3%), IABP in 3 cases (17.6%), and Nitrate in 3 cases (17.6%) in this series.

8 (8.6%) patients had MACEs during hospitalization which included 5 (5.4%) cases of in-hospital death (Figure 1). Of the five patients who died, 3 (60.0%) had cardiogenic shock, 3 (60%) had impaired flow. In-hospital mortality was significantly higher in the shock group (33.3% vs. 2.5%, P < 0.001), and in the older patients (over 65 years of age: 11.8% vs. 1.7%, P < 0.05). Successful PCI decreased in-hospital mortality significantly (33.3% vs 3.4%, P < 0.05) in our series.

PPCI was clinically successful in 67 (72.0%) patients. The response rate in the follow-up was 100%, and 3 other patients developed MACEs in this period (Figure 1). In total 11 (11.8%) patients had MACEs (combined MACEs) in our study. The rate of MACEs was significantly higher in the patients with impaired flow (29.4% vs. 7.0%, P = 0.009).

All of the PPCI failures and MACEs occurred in Chamran Hospital, but due to the small sample size at Saadi Hospital we could not compare clinical outcomes of the patients in these hospitals.

Table 3. Procedural details* and complications of primary percutaneous coronary interventions

SVD	24 (25.8)
Multivessel PCI‖	11 (11.8)
Primary	69 (74.2)
Rescue	24 (25.8)
Door-to-balloon time	
Mean (min)	148.9 ± 168.5
Range (min)	24-900
IABP	6 (6.5)
Arrhythmia	27 (29.0)
Procedure	
Plain old balloon angioplasty (POBA)	3 (4.3)
Guide wire cross failure	2 (2.2)
Cardiogenic shock, only IABP / discontinue procedure for CPR	1 (1.1)
Use of stent	87 (93.5)
Only BMS	42 (48.3)
Only DES	34 (39.1)
BMS+DES	11 (12.6)
Stent/patient ratio	1.31 ± 0.64
Procedural acute adverse events	
Impaired flow	17 (18.3)
Access site complications	7 (7.5)
Congestive cardiac failure	13 (14)
Bleeding	1 (1.1)
Procedural success rate	71 (76.3)

Categorical variables are expressed as n (%) and continuous variables are expressed as mean ± SD.
SVD: Single vessel disease; PCI: Percutaneous coronary intervention; IABP: Intra-aortic balloon pump; PVC: Premature ventricular contraction; VF: Ventricular fibrillation; VT: Ventricular Tachycardia; CPR: Cardiopulmonary resuscitation; LAD: Left anterior descending; LCX: Left circumflex artery; RCA: Right coronary artery
*Patient Based Analysis
‖Multivessel PCI: PCI on more than one lesion in one stage

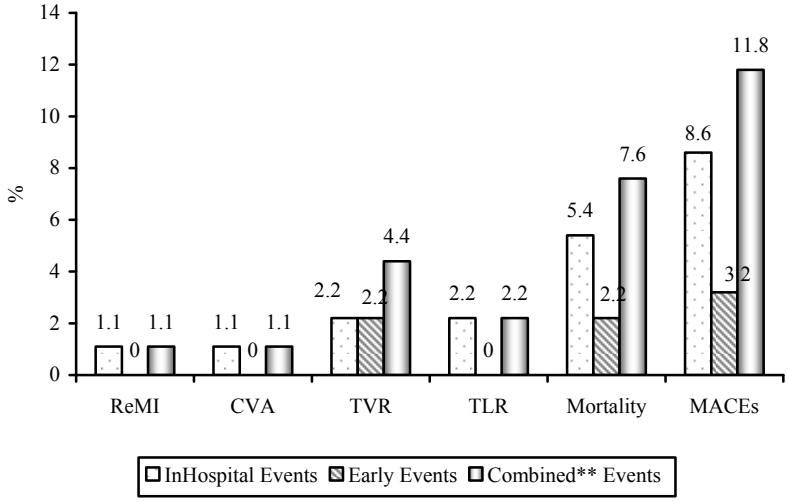

Figure 1. In-hospital and early* clinical outcome of the patients
*Early clinical outcome: after discharge until 30 days; **Combined: In-hospital and early clinical outcome
MACE: Major adverse cardiac events; ReMI: Repeated myocardial infarction; CVA: Cerebrovascular accident; TVR: Target vessel revascularization; TLR: Target lesion revascularization

Discussion

PPCI is considered to be a superior strategy in treatment of STEMI.[14,15] This procedure has been carried out for our patients since 2006, but, to our knowledge it has not yet been evaluated in any research project.

Our study revealed that procedural success rate was 76.3%, in-hospital MACEs was 8.6%, and combined MACEs was 11.8%. Alidoosti et al. described their experience of 83 primary angioplasty in STEMI based on their single center registry at Tehran Heart Center during a period of 2 years (2003-2005).[17] Their reported procedural success rate was 95%, both in-hospital MACEs and mortality were 8.4%, and MACEs after 9 months was 12%.[17] The results of our study are in accordance with that of the study by Alidoosti et al. regarding in-hospital MACEs, but are different in terms of success rates and in-hospital mortality. In comparison with other studies, although we reported lower success rates our patients' early clinical outcomes were in accordance with international data.[10,11,17] For instance, the in-hospital mortality, which was 5 (5.4%) cases, in our series of patients is comparable to international data, which showed in-hospital mortality of 5.2% in the second national registry of Myocardial infarction (NRMI2).[18]

In our study 9 patients had cardiogenic shock; 3 (33.3%) of them died, which is again in agreement with international data, which showed higher mortality in patients with cardiogenic shock (i.e. 32% in NRMI 2, 46.4% in shock registry, and 59.1% in American College of Cardiology-National Cardiovascular Data Registry (ACCNCDR).[18-20]

Poor angiographic and procedural results in our series were related to the most frequent cause of failure, which was impaired flow (18.3%). Although, the mechanisms of slow-flow and no-reflow phenomenon have been debated extensively, it has been proposed that obstruction of the myocardial microcirculation is a result of distal embolization or vasospasm.[12] Moreover, it was revealed that the degree of impaired flow is associated with the duration of the preceding myocardial ischemia, infarct size, procedural variables, and patient characteristics.[10]

Our study revealed that pain-to-door and door-to-balloon times had an extremely wide range of almost 12, and 14.5 hours, respectively. These wide ranges, which were observed both in primary and rescue PCI, demonstrated that PPCI was not performed in a timely fashion.

In Tehran, 88% of the patients arrived at the hospital in the first 6 hours.[17] 46% of our patients arrived during this time. This shows that our patients request medical help later. We think that this is a multifactorial issue (cultural, socioeconomic, political, and educational), which could be improved by intersectoral and cross-sectoral collaboration, and the contribution of all authorities of the province.

Door-to-balloon time is exclusively related to health management, and it is an important

determinant of the quality of care. The door-to-balloon time recommended by the American College of Cardiology (ACC)/American Heart Association (AHA) guidelines is 90 minutes.[2] However, achieving this time is only possible in an ideal world scenario. In developing countries financial constraints, insurance coverage problems, and delay in decision making due to lack of knowledge are the major obstacles in following door-to-balloon time recommendations. In Pakistan the median door-to-balloon time was reported to be 115 minutes with 40% of patients having PCI performed at or over 90 minutes.[3] In China the median door-to-balloon time was 132 min, and only 22% of patients had PCI performed in less than 90 minutes.[21] In Germany this time, from admission to start of PPCI, was 86 ± 42.[22] In Tehran door-to-balloon time was not reported.[17] Solving the Insurance problems, facilitating the process of admittance, discharge, and transfer, providing well-established protocols and an expert team, and informing the community could improve this Index.

Conclusion

The low success rate in our series could be due to prolonged pain-to-door time; community education is necessary to decrease this type of delay.

Long door-to-balloon time could be due to lack of a definite protocol to regularly perform PPCI in a timely fashion. We should define the duty and role of different components of the process of patient admission, transfer, and treatment to reduce door-to-balloon time.

Finally, we should improve our technique, especially to prevent and treat slow/no-reflow phenomena, in order to reach a better outcome after PPCI.

Conflict of Interests

Authors have no conflict of interests.

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Social norms of cigarette and hookah smokers in Iranian universities

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Original Article

Abstract

BACKGROUND: First experiences of tobacco use usually occur in adolescence. The recognition of social norms leading to youth smoking is hence necessary. We tried to assess the social norms among Iranian young cigarette and hookah smokers.

METHODS: This cross-sectional study was conducted on 451 girls and 361 boys aging 20-25 years old who entered Isfahan and Kashan Universities (Iran) in 2007. Demographic factors (age, gender, and age at smoking onset) cigarette and hookah smoking status, having a smoking father or smoking friends and four related social norms were recorded. Binary logistic regression analysis was used to separately determine associations between hookah and cigarette smoking and the four social norm variables.

RESULTS: Cigarette and hookah smokers had significant differences with nonsmokers in two social norms: "Perceived smoking by important characters" [odds ratio (OR) = 1.35 in cigarette smokers and 1.58 in hookah smokers; $P < 0.001$] and "smoking makes gatherings friendly" (OR = 3.62 in cigarette smokers and 6.16 in hookah smokers; $P < 0.001$). Furthermore, cigarette and hookah smoking were significantly associated with having smoking friends.

CONCLUSION: Highlighting the social norms leading to cigarette and hookah smoking may help policy makers develop comprehensive interventions to prevent smoking among adolescents.

Keywords: Cigarette, Hookah, Smoking, Social Norm

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Introduction

First experiences of smoking usually occur in adolescence and most adolescent smokers continue smoking to adulthood. Due to the deleterious effects of smoking, exposure to tobacco smoke from adolescence increases related morbidity and mortality and leads to premature death.[1] Accordingly, every effort to prevent or decrease the prevalence of smoking should consider this age group. In fact, clarifying the determinants of smoking initiation in the youth is a necessity for effective tobacco control and prevention measures.

In spite of the recent decline in the prevalence of smoking among the youth in developed countries, the problem has become more prevalent in many developing countries.[2] In Iran, the prevalence of smoking has increased from 12.6% in 2000 to 14.3% in 2004.[3,4] A survey on 4361 adolescents living in Tehran (Iran) indicated that 30.7% of boys and 20.6% of girls had smoked hookah.[5]

Research has found the process of cigarette smoking to depend on underlying social and psychological factors such as peer smoking and approval,[6] prevalence estimates of smoking among youth and adults,[6] availability,[7] parental characteristics, smoking, and approval,[8,9] attitudes,[10] family environment, and peer pressure.[8] In other words, young people tend to follow the beliefs and attitudes of the group to which they belong or people they admire. According to the few studies on social correlates of hookah smoking, the smokers consider it as a pleasurable social hobby promoting

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a sense of togetherness. They view it a relatively harmless leisure time activity.[11] Apparently, the attitudes of family and society are more permissive regarding hookah smoking than about any other kind of smoking.[12]

The term "social norms" is a broad term that explains the underlying social factors for many of investigated determinants. It extends from family beliefs to social environments such as school and society. Cigarettes are the most common form of tobacco products in many parts of the world including Iran.[3] In the recent decade, however, the traditional hookah smoking culture has become increasingly popular especially among the youth of Iran and its neighboring countries. Little evidence exists about social norms involved in hookah smoking and its similarities or differences with cigarette smoking particularly among the youth. Social determinants of hookah smoking will undoubtedly differ from those of cigarette smoking due to traditional and cultural backgrounds. This study aimed to compare social norms related to smoking behavior among young cigarette and hookah smokers.

Materials and Methods

This cross-sectional study included all 20-25 year-old students of Isfahan and Kashan Universities (Iran) during 2007. Isfahan and Kashan Universities are the first and second largest universities in Isfahan Province, central Iran. These universities have different majors such as health, science, law, and humanities sciences. Informed consents were obtained from eligible subjects after full explanation of the study. Approvals were obtained from the ethics committee of Isfahan University of Medical Sciences for performing the research. The participants attended a 30-minute interview in which trained health professionals recorded their sociodemographic characteristics, smoking behavior, and attitudes and perceived social norms related to smoking. The questionnaires were completed anonymously and no personally identifiable information was collected.

Sociodemographic characteristics such as age and gender were asked to characterize the sample. The participants were also asked about the age of smoking (either cigarette or hookah) onset and whether there is a smoker in their family. Smoking behavior was assessed by asking "Do you currently smoke tobacco products such as cigarettes or hookah?". Positive answers were followed by another question: "What type(s) of tobacco product(s) do you currently smoke?". The answers could be only cigarettes, only hookah, or both. Those who smoked both hookah and cigarettes were asked "What type of tobacco product do you mainly smoke?". Subjects who did not smoke at the time of the study were categorized as nonsmokers. Students who smoked cigarettes alone or more frequently were categorized as cigarette smokers and those who smoked hookah alone or more frequently were categorized as hookah smokers.

Four aspects of perceived social norms of smoking were measured: (1) perceived smoking of important characters, (2) belief that smoking makes the gatherings friendly, (3) perception that adults disapprove of youth smoking, and (4) the belief that anti-smoking campaigns are disregarded in the community. Cigarette smokers and hookah smokers offered their views toward the tobacco product they smoked mainly and nonsmokers reported their views on both cigarettes and hookah. The participants were asked what they thought about smoking doctors, nurses, teachers, athletes, actors/actresses, and women. They could respond as "The majority of them smoke and this is a personal affair", "He or she should not smoke and few people in this job smoke", and "I have no idea". Respondents with missing data on more than two out of six items were excluded.

The scores of items were summed to create a range of 4 to 12 (Cronbach's alpha = 0.86 for smoking cigarettes and 0.85 for smoking hookah). The participants were also asked if they agreed or disagreed with the statement "Smoking cigarettes/hookah makes the gatherings friendly." or had no idea about it. The subjects could agree or disagree with or have no idea about the perception that adults disapprove youth smoking. In order to evaluate the idea of the participants about anti-smoking campaigns, the statement "The present prevalence of tobacco products is due to the fact that anti-smoking campaigns are not working properly at community level." Was read to them and they were asked if they agreed, disagreed, or had no idea. Finally, the students had to clarify if their fathers or friends smoked.

Statistical analysis

Data was analyzed using SPSS for Windows 15.0 (SPSS Inc., Chicago, IL, USA). Continuous variables are presented as means while qualitative variables are presented as absolute and relative frequencies. Differences between cigarette smokers and none smokers as well as hookah smokers and

none smokers were detected with t-test and χ^2 tests.

Binary logistic regression analysis was used to find associations between cigarette and hookah smoking and four social norm variables and peer and father smoking. The stepwise approach was selected for regression model and two unique models were created for cigarette and hookah smoking.

Independent variables included four aspects of perceived social norms, peer and father smoking, and demographic characteristics (age and gender). Dependent variables were cigarette and hookah smoking in two separate models. P values were based on two-sided tests and were compared to a significance level of 5%.

Results

The sample consisted of 451 girls and 361 boys with the mean age of 21.50 ± 1.04 and 21.80 ± 1.32 years old, respectively. While 71% of the students had never smoked, 9.5% were cigarette smokers and 19.5% were hookah smokers. The mean age of smoking onset was 16.32 ± 3.18 years old in cigarette smokers and 16.38 ± 3.78 years old in hookah smokers. In addition, more than 50% of hookah smokers and approximately 40% of cigarette smokers had smoking friends. Further details of the subjects are shown in table 1.

The response rate of the participants was 95%. The mean response for perceiving cigarette smoking by important characters was 7.45 ± 1.72 among cigarette smokers and 6.24 ± 1.77 in nonsmokers. Also, perceived hookah smoking by important characters was 7.58 ± 2.17 among hookah smokers and 5.92 ± 1.45 in nonsmokers. Cigarette and hookah smokers and nonsmokers were significantly different in this regard.

Of cigarette smokers, 75.3% believed that smoking cigarettes makes gatherings friendlier. Hookah smoking was believed to have the same function in the view of 88.4% of hookah smokers. Again, the two groups of smokers were significantly different with nonsmokers. On the other hand, 72.7% of cigarette smokers and 76.3% of hookah smokers believed that adults disapprove of youth smoking. Anti-smoking campaigns were considered ineffective at community level by 83.1% of cigarette smokers and 89.1% of hookah smokers. The groups did not have significant differences in the two latter factors. The four social norms had low correlations with each other ($0.21 \leq r \leq 0.35$) (Table 1).

Table 1. Personal characteristics of the participants

Personal characteristics	Cigarette smokers (n = 77)	Nonsmokers (n = 579)	Hookah smokers (n = 156)
Gender (male)	66 (85.0)*	191 (32.0)	104 (66.0)**
Age (years)	22.00 ± 1.35*	21.54 ± 1.03	22.34 ± 1.57**
Age at first cigarette smoking†	16.32 ± 3.18	-	-
Age at first hookah smoking†	-	-	16.38 ± 3.78
Family/peer smoking			
Father smokes	10 (12.9)*	44 (7.6)	14 (10.2)**
Friends smoke	31 (40.2)*	88 (15.2)	83 (53.2)**
Social norms			
Perceived cigarette smoking by important characters†	7.45 ± 1.72*	6.24 ± 1.77	-
Perceived hookah smoking by important characters†	-	5.92 ± 1.45	7.58 ± 2.17**
Belief that cigarette smoking makes gatherings friendly	58 (75.3)*	33 (5.7)	-
Belief that hookah smoking makes gatherings friendly	-	224 (38.7)	138 (88.4)**
Perceived adults' disapproval of youth smoking cigarettes	56 (72.7)%	463 (80.0)	-
Perceived adults' disapproval of youth smoking hookah	-	494 (85.3)	119 (76.3)
Belief that anti-cigarette smoking campaigns are disregarded in the community	64 (83.1)	424 (73.2)	-
Belief that anti-hookah smoking campaigns are disregarded in the community	-	407 (70.3)	139 (89.1)

Values are reported as n (%) unless expressed otherwise.
† Mean± SD
* Significant differences between cigarette smokers and nonsmokers ($P < 0.05$)
** Significant differences between hookah smokers and nonsmokers ($P < 0.05$)

Table 2. Odds ratio (OR) and 95% confidence interval (CI) of correlates of smoking (both cigarette and hookah smoking)

	Cigarette smoking OR (95% CI)	Hookah smoking OR (95% CI)
Personal characteristics		
Gender (male)	12.2 (6.60-21.27)*	7.90 (4.35-14.25)*
Age	1.59 (1.11- 3.29)**	0.92 (0.78-1.09)
Family/peer smoking		
Father smokes	1.21 (1.03-3.22)**	1.25 (1.04-1.70)**
Friends smoke	10.68 (3.15-36.06)*	12.09 (4.12-35.44)*
Social norms		
Perceived smoking by important characters	1.35 (1.05-2.70)*	1.58 (1.09-2.27)*
Belief that smoking makes gatherings friendly	3.62 (2.46-12.51)*	6.16 (2.37-9.01)*
Perceived adults' disapproval of youth smoking	0.55 (0.12-2.45)	0.63 (0.15-2.75)
Belief that anti-smoking campaigns are disregarded in the community	1.70 (0.47-6.09)	2.24 (0.47-8.45)

* $P < 0.001$ ** $P < 0.01$

The two multivariate models predicting smoking are presented in table 2. At first, four social norm variables were simultaneously entered in cigarette smoking model and the results were statistically significant, consistent with the bivariate associations explained above (data not shown). These significant relationships were maintained for "perceived smoking by important characters" and "smoking makes the gathering friendly" in cigarette smokers when demographic characteristics were added to the model. In addition, by inserting father and peer smoking to the model, the odds ratios for the two mentioned scales among the cigarette smokers were 1.35 and 3.62, respectively.

Likewise, the four social norm variables were simultaneously entered in hookah smoking model and the results were statistically significant. By entering demographic characteristics and father and peer smoking, the odds ratios were significant for the above-mentioned scales, too (1.58 for "perceived smoking by important characters" and 6.16 for "smoking makes the gatherings friendly").

Discussion

In this study, four social norm variables were assessed. Cigarette and hookah smokers were significantly different with nonsmokers in "perceived smoking by important characters" and "smoking makes gatherings friendly". Moreover, odds ratio was higher in hookah smokers than in cigarette smokers. Both cigarette and hookah smoking were significantly associated with having smoking friends. Odds ratio of this factor was far higher than having a smoking father.

Several studies on the roles of social norms on high risk behaviors such as tobacco use among the youth have indicated that perceiving smoking by significant others and friends as a social value can be a strong predictor of tobacco use.[13] In fact, the youth may mimic the smoking behavior of significant others and acquire the habit of tobacco use.[14] In the current study, smoking by doctors, nurses, or teachers as intelligent individuals, by athletes and actors as role models, and by women who are expected not to smoke could be imitated by the youth. Generally, role models are more widely followed in eastern societies than in western societies. Hence, mimicking persons who are publicly respected or shown in mass media can greatly influence the increased prevalence of cigarette and hookah smoking. Hookah smoking receives special attention in Middle East countries including Iran. As a result, the youths have a better perception of hookah smoking and they tend to smoke hookah much more than cigarettes. Consistent results were found in the present study.

Smoking behaviors are also affected by other social contexts such as family, school, and peer groups. According to a review article in 2003, while some studies have reported peer groups to have stronger effects than families on initiation of smoking, some others consider the role of parents to be greater.[15] Based on the odds ratios calculated in the current study, cigarette and hookah smoking are more influenced by smoking of friends than having a smoking father. This difference was more significant in case of hookah smoking. Iran is a developing country which has faced extensive and rapid social changes in recent decades. Iranian youth and adolescents are thus totally different from their parents and peers can affect each other more. In other words, hookah smoking is seen as a social activity in which everyone can participate and have

an enjoyable time. Hookah smoking can gather people in public places such as coffee shops and tea houses and provide a sense of closeness through using a shared hookah.[16] A study on Arab-American subjects reported similar results about tobacco, and particularly hookah, use.[17]

According to our findings, Iranian females are less likely to smoke cigarettes or hookah. Although the same is true in many countries in the Middle East, recent studies in this region have shown the increased prevalence of smoking, especially hookah smoking, among women.[11,18] In general, hookah smoking is more positively perceived than other methods of tobacco use. Hookah users, especially women, believe that it looks traditional, familiar, social, and attractive. Therefore, hookah smoking may be perceived as a social norm in the Middle East especially among women.[19,20]

The present study had some limitations. First, the results are relational and not causal. Therefore, it cannot be concluded whether social norms are causes or results of youth smoking. Moreover, this study relied exclusively on questionnaires to assess social norms and smoking. On the other hand, our findings cannot be generalized as our sample was restricted to students in Isfahan and Kashan Universities (Iran). Finally, individual traits influencing youth smoking was not considered in this study.

Conclusion

The results of this study indicated that social norms are significantly different in hookah and cigarette smokers. Among hookah smokers, "perceived smoking by important characters" and "smoking makes gatherings friendly" were more effective than among cigarette smokers. In addition, smoking friends had a greater influence than smoking fathers. By highlighting the social norms related to cigarette and hookah smoking, this study may help policy makers develop comprehensive interventions to prevent smoking among adolescents.

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Conflict of Interests

Authors have no conflict of interests.

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Physical activity, sex, and socioeconomic status: A population based study

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Original Article

Abstract

BACKGROUND: The purpose of the present study was to investigate physical activity by socioeconomic status (SES) and sex in an Iranian adult population.

METHODS: In a cross-sectional study, 6622 adults, who participated in the Isfahan Healthy Heart program (IHHP) surveys in 2004 and 2005 and were living in urban areas, were studied. Daily leisure time, household, occupational, and transportation physical activity, and total physical activity were calculated and compared in 3 socioeconomic status groups classified by the two-step cluster analysis procedure.

RESULTS: Statistically significant variations were found in all physical activity levels, except transportation, by sex. Men were more active than women in all fields, except household physical activity. Leisure time physical activity of men and women were significantly higher in higher SES levels. There was an opposite correlation between SES and total physical activity in men.

CONCLUSION: Considering the importance of physical activity as a component of a healthy lifestyle, differences among varying socioeconomic status and sex must be considered while planning for healthy lifestyle programs. Women with low SES, in particular, may need more attention.

Keywords: Physical Activity, Socioeconomic Status, Leisure Time, Gender, Cluster Analysis

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Introduction

There is an international concern about the impact of low levels of physical activity on health.[1] The association between physical activity and health status is well known; active individuals present a lower likelihood of developing several chronic diseases, and physical activity or exercise has been the most common intervention for prevention or management of disability.[2]

Physical activity prevents cardiovascular disease (CVD) by decreasing blood pressure, plasma fibrinogen, viscosity, improvements in glucose metabolism, and blood lipid levels.[3-7] Low levels of physical activity are associated with an increased risk of stroke.[8] It was shown that occupational physical activity reduces woman's risk of breast cancer.[9] A sedentary life style is a major risk factor for type 2 diabetes.[10] Nonetheless, alarming rates of sedentarism are observed in studies on developed and developing countries.[11-13]

In spite of several current initiatives aimed at increasing the activity level of people, socio-economic differences in physical activity are complex.[14] Some studies showed that in men, overall activity levels are the lowest in those with managerial and professional jobs, while the pattern in women is reversed. Overall activity levels vary by household income in men, being the highest among those with mid-range household incomes and lowest at both extremes of the income distribution but no pattern is apparent in women.[15] Previous studies suggested that males are more active than

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females in leisure-time, although not all were consistent.[16] Low leisure-time physical activity has been found to be strongly associated with low income, low education, and low socioeconomic status.[17-19] On the other hand, in the few studies that considered physical activity domains other than leisure-time physical activity, no gender differences were observed.[20] The majority of these studies were carried out in high-income countries, where activity patterns are different from those observed within low and middle-income countries. In this study we examined different types of physical activity by socioeconomic status in a population of Iranian men and women.

Materials and Methods

This study was performed as part of annual surveys of the Isfahan Healthy Heart Program (IHHP), collecting two consecutive cross-sectional data from 2004 and 2005. IHHP is a community based, quasi-experimental demonstration program with the aim of CVD prevention and healthy lifestyle promotion.[21,22] After the baseline survey on adults aged 18 years and over residing in three cities in central Iran (Isfahan, Najaf-Abad, and Arak, with nearly similar socio-demographic situations), the IHHP interventions began in late 2001 and continued for 5 years. In all surveys, participants were selected by multistage cluster random sampling method according to the regional population distribution. Full explanation and sampling details were previously given.[21] Due to essential differences in the lifestyle of rural and urban areas, this study focused on 6622 participants in the urban population. The response rates were 91.6% and 93.2% in 2004 and 2005, respectively. Non-respondents were substituted to reach original sample size. Written informed consents were obtained from all participants. Ethical approval was obtained from the Ethics Committee of Isfahan Cardiovascular Research Centre (ICRC), a WHO collaborating centre.

The validity of the questionnaire was confirmed by three experts. The reliability of the questionnaire was 0.73 (Cronbach's Alpha). Based on the existing categorizations and the purpose of each activity done during the day, physical activities are divided into four main fields (leisure time, occupational, household, and transportation physical activities).[23] Particular items in each field were selected based on the usual Iranian life style.

During a structured interview, based on a researcher made questionnaire, the above items in the everyday life of the participants were asked. The duration of activities in each session and their frequency per week were also asked.

The amount of each physical activity was calculated by multiplying its intensity (in the unit of metabolic equivalent of the task (Met)) and duration (minutes) per day.[23]

$$[\text{MET}-\text{minutes}/\text{day} = \frac{\text{times}/\text{week} * \text{duration}/\text{times}}{7} \times \text{Mets}]$$

One MET is reflective of energy expenditure during rest (1 metabolic unit = oxygen consumption of 3.5 mL/min kg-1).[24] To obtain each field's value, the amounts of physical activities in items related to each field were added together.

Indicators of socioeconomic status (SES), including income, education level, and occupation type, were determined based on a combination of NS-SEC model (National Statistics Socio-Economic Classification), other similar studies, and WHO recommendation on measuring socioeconomic inequalities in health.[25-27] Dependency ratio, an indicator used in population studies to measure the portion of the population that is economically dependent on the active age group, was added as the fourth factor. It was calculated by the number of those aged under 18 or over 65 being divided by the number of those aged 18 to 64.

Reported jobs were categorized into four groups; namely upper white-collar employees, lower white-collar employees, manual workers, and self-employed persons.[28] The unemployed, retired, and housewife groups were added to the mentioned pattern. Education level was defined as illiterate, primary school, guidance school, high school, associate or bachelor degree, and master's degree or higher. Income was reported in Iranian currency unit (RIALs), and as table 1 shows it was categorized into 4 groups.

Statistical analysis

Data entry was done using EPI info™. All data were analyzed by SPSS for Windows (SPSS Inc., Chicago, IL, USA; version 15). Two-step cluster analysis procedure was done to explore SES grouping of participants using income, education, and occupation as categorical variables, and dependency ratio as continuous variable. This procedure seeks to identify homogeneous subgroups of cases in a population. Number of clusters was limited to three (high, moderate, and low SES), and analysis was performed separately for each gender. To compare various components of physical activity among the three SES groups, ANOVA and Tukey's post-hoc test were used.

Student's t-test was used to compare between men and women. Spearman correlation was used to determine the relationship of physical activity with age. In order to include age as an important related factor, multiple regression analysis was carried out using sex and age as covariates. The averages are reported as mean ± standard deviation. For all analyses, statistical significance was assessed at a level of 0.05 (2-tailed).

Results

The mean age of the 6622 participants in the survey was 45.2 ± 17.2 years. 3401 (51.3%) of the participants were women. Table 1 describes the distribution of SES indicators; the SES levels (three different clusters produced by cluster analysis) were identified based on them. SES levels (high, moderate, and low) were attributed to clusters of people based on the distribution of indicators. Occupational factors were overlapped between low SES and moderate SES in both genders, but other factors perfectly differentiated SES levels. Income, occupation, and education were all used to significantly determine clusters. However, dependency ratio was statistically significant for high SES in women, and both high SES and moderate SES in men. 353 (10.4%) men and 300 (9.3%) women were excluded by cluster analysis.

The mean age of the men did not differ significantly between different SES groups, nor did that of the women. No important relationships were found between physical activity and age in various fields. The most significant correlation was shown to be between age and both Leisure time physical activity ($r = -0.25$, $P < 0.001$), and total physical activity ($r = -0.23$, $P < 0.001$) in women. In men, maximum correlation was between age and total physical activity ($r = -0.27$, $P < 0.001$). Table 2 shows the sex separated differences in various fields of physical activity among three defined socioeconomic status levels; low socioeconomic status (LSES), moderate socioeconomic status (MSES), and high socioeconomic status (HSES).

Leisure time Physical Activity

The average amount of leisure time physical activity (MET - minutes per day) was 147.6 ± 289.3 (Median: 62.1). It was significantly higher in men than women (198.6 ± 355.9 vs. 99.4 ± 198.6, $P < 0.001$; Median: 90 vs. 45, respectively). In women the estimated amount of MET - minutes in leisure time physical activity was significantly higher for HSES participants than MSES, and also higher for HSES in comparison with LSES (Figure 1). In men the estimated amount of leisure time physical activity was also greater for HSES participants than MSES as well as HSES and LSES. The age and sex adjusted model yielded a significant regression coefficient for SES level ($B = 11.5$, $R2 = 0.046$, $P = 0.03$).

Occupational Physical Activity

Mean occupational physical activity for 2433 (36.7%) of employed participants was 635.1 ± 510.5. They consist of 2196 (68.1%) men and 237 (6.9%) women. Men had more occupational physical activity than women (659.4 ± 520.5 vs. 427 ± 353.5, $P < 0.001$). According to high frequency of housewives in women of MSES, no occupational physical activity was reported in this level. There was no significant difference between occupational physical activity of women of LSES and HSES (Table 2). In spite of the results in women, occupational physical activity was less in HSES men than MSES men, and also than LSES men. The age and sex adjusted model yielded a significant regression coefficient for SES level ($B = -68.3$, $R2 = 0.035$, $P < 0.001$).

Household Physical Activity

Household physical activity was reported by 4305 (65%) participants with the average amount of 360.8 ± 307.9. Recorded household physical activity was higher in 3390 (99.6%) women than 915 (28.4%) men (421.1 ± 296.1, 137.2 ± 240.5, respectively), and the difference was significant. In women, the values of this field in all three levels of SES were significantly different ($P < 0.001$) (Table 2). However household physical activity was higher in MSES than HSES and LSES; it was lower in HSES than LSES. No significant differences were found between various SES levels of men. The age and sex adjusted model yielded a significant regression coefficient for SES level ($B = -38.3$, $R2 = 0.169$, $P < 0.001$).

Transportation Physical Activity

The mean of transportation physical activity was 63.8 ± 120 (Median: 25.7) MET - minutes in the study sample. There was higher transportation physical activity in men than women (84.5 ± 154.4 vs. 44.21 ± 68.3; Median: 38.5 vs. 25.7); the difference was statistically significant. No significant difference was reported in transportation physical activity for three SES levels neither in men nor in women (Table 2). The age and sex adjusted model did not show a significant relationship for SES ($P = 0.555$).

Table1. Distribution of socioeconomic indicators in three levels of socioeconomic status (clusters)

		Female n (%)				Male n (%)				Total↓
		Low SES	Moderate SES	High SES	All↓	Low SES	Moderate SES	High SES	All↓	
Income	≤ 1,000,000 Rials	471 (100)	0	0	898 (26.4)	376 (71.2)	0	152 (28.8)	614 (19.1)	1512 (22.8)
	1,000,000-3,000,000 Rials	0	1661 (81.2)	384 (18.8)	2200 (64.7)	10 (0.5)	1193 (59.8)	793 (39.7)	2176 (67.6)	4376 (66.1)
	3,000,000-5,000,000 Rials	0	0	211 (100)	221 (6.5)	120 (37.2)	0	203 (62.8)	332 (10.3)	553 (8.4)
	5,000,000-10,000,000 Rials	0	0	46 (100)	49 (1.4)	5 (7.7)	0	60 (92.3)	68 (2.1)	117 (1.8)
	≥ 10,000,000	0	0	5 (100)	5 (0.1)	3 (33.3)	0	6 (66.7)	9 (0.3)	14 (0.2)
Education	Illiterate	351 (46.6)	368 (48.9)	34 (4.5)	969 (28.5)	90 (23.2)	93 (24)	205 (52.8)	458 (14.2)	1427 (21.5)
	Primary school	191 (22.9)	590 (70.7)	54 (6.5)	902 (26.5)	193 (27.5)	476 (67.7)	34 (4.8)	791 (24.6)	1693 (25.6)
	Guidance school	70 (19.2)	253 (69.3)	42 (11.5)	386 (11.3)	108 (23.5)	296 (64.5)	55 (12)	488 (15.2)	874 (13.2)
	High school	104 (13.4)	450 (57.8)	225 (28.9)	806 (23.7)	116 (13.6)	284 (33.2)	456 (53.3)	935 (29)	1741 (26.3)
	Associate and bachelor degree	25 (8.3)	0	275 (91.7)	321 (9.4)	7 (1.5)	44 (9.3)	424 (89.3)	507 (15.7)	828 (12.5)
	Master's degree and higher	0	0	16 (100)	17 (0.5)	0	0	40 (100)	42 (1.3)	59 (0.9)
Occupation	Upper white-collar employees	3 (23.1)	0	10 (76)	13 (0.4)	1 (0.8)	0	124 (99.2)	128 (4)	141 (2.1)
	Lower white-collar employees	9 (7.2)	0	116 (92.8)	131 (3.9)	3 (0.8)	0	389 (99.2)	406 (12.6)	537 (8.1)
	Manual Workers	9 (17.6)	0	42 (82.4)	53 (1.6)	248 (32.2)	508 (65.9)	15 (1.9)	812 (25.2)	865 (13.1)
	Self-employed persons	7 (25%)	0	21 (75)	32 (0.9)	154 (26.1)	408 (69.3)	27 (4.6)	621 (19.3)	653 (9.9)
	Housewife	663 (26.1)	1661 (65.4)	217 (8.5)	2860 (84.1)	0	0	0	0	2860 (43.9)
	Unemployed	50 (17.2)	0	240 (82.8)	303 (8.9)	108 (10.3)	277 (26.5)	659 (63.1)	1158 (36)	1461 (22.1)
	Dependency Ratio (mean ± SD)	0.47 ± 0.58	0.47 ± 0.54	0.41 ± 0.46§	0.46 ± 0.54	0.71 ± 1.03§	0.47 ± 0.52	0.39 ± 0.47§	0.48 ± 0.64	0.47 ± 0.59
	Total	741 (21.8)	1661 (48.8)	646 (19)	3401*	514 (16)	1193 (37)	1214 (37.7)	3221*	6622

↓Percentages are pertaining to columns

* In females 353 cases (10.4%) and in males 300 (9.3%) cases could not be inserted to any cluster by cluster analysis and were excluded.

§ Significantly participate in cluster definition (P < 0.05).

SES: Socioeconomic status

Table 2. The mean of physical activity (95% confidence interval) calculated as MET min/day in three different socioeconomic status levels

Socioeconomic Status	Leisure time physical activity	Occupational physical activity	Household physical activity	Transportation physical activity	Total physical activity
Men					
High	218 (197-239)	564 (525-602)	114 (93.4-135)	79.6 (73-86.2)	600 (565-635)
Moderate	187 (168-206)	710 (676-745)	131 (102-160)	88.2 (77.8-98.7)	877 (830-924)
Low	176 (142-210)	690 (632-748)	147 (104-189)	84.2 (71.1-97.2)	877 (798-956)
P-value	0.032	< 0.001	0.325	0.385	< 0.001
Women					
High	144 (125-163)	448 (339-497)	331 (309-354)	48 (41.9-54.2)	678 (636-721)
Moderate	88.5 (80.4-96.6)	- *	482 (486-497)	43.5 (40.7-46.3)	619 (600-637)
Low	98.7 (83.1-114)	381 (219-543)	404 (382-425)	45.3 (39.6-51.1)	566 (534-598)
P	< 0.001	0.357	< 0.001	0.364	< 0.001

*No occupational physical activity was reported due to high frequency of house wives in MSES level.

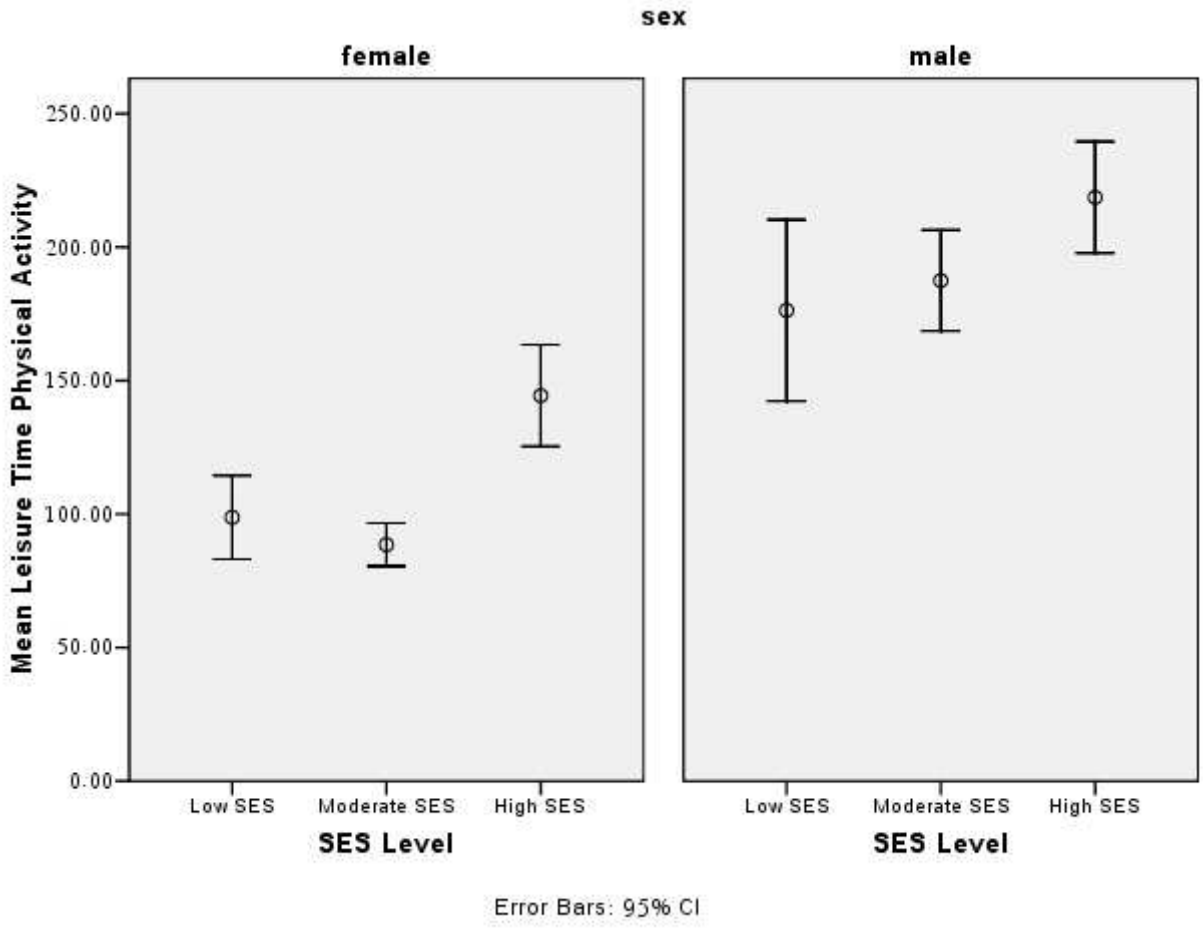

Figure 1. Leisure time physical activity (MET min/day) in different socioeconomic status levels (Error Bars: 95% CI)

SES: socioeconomic status

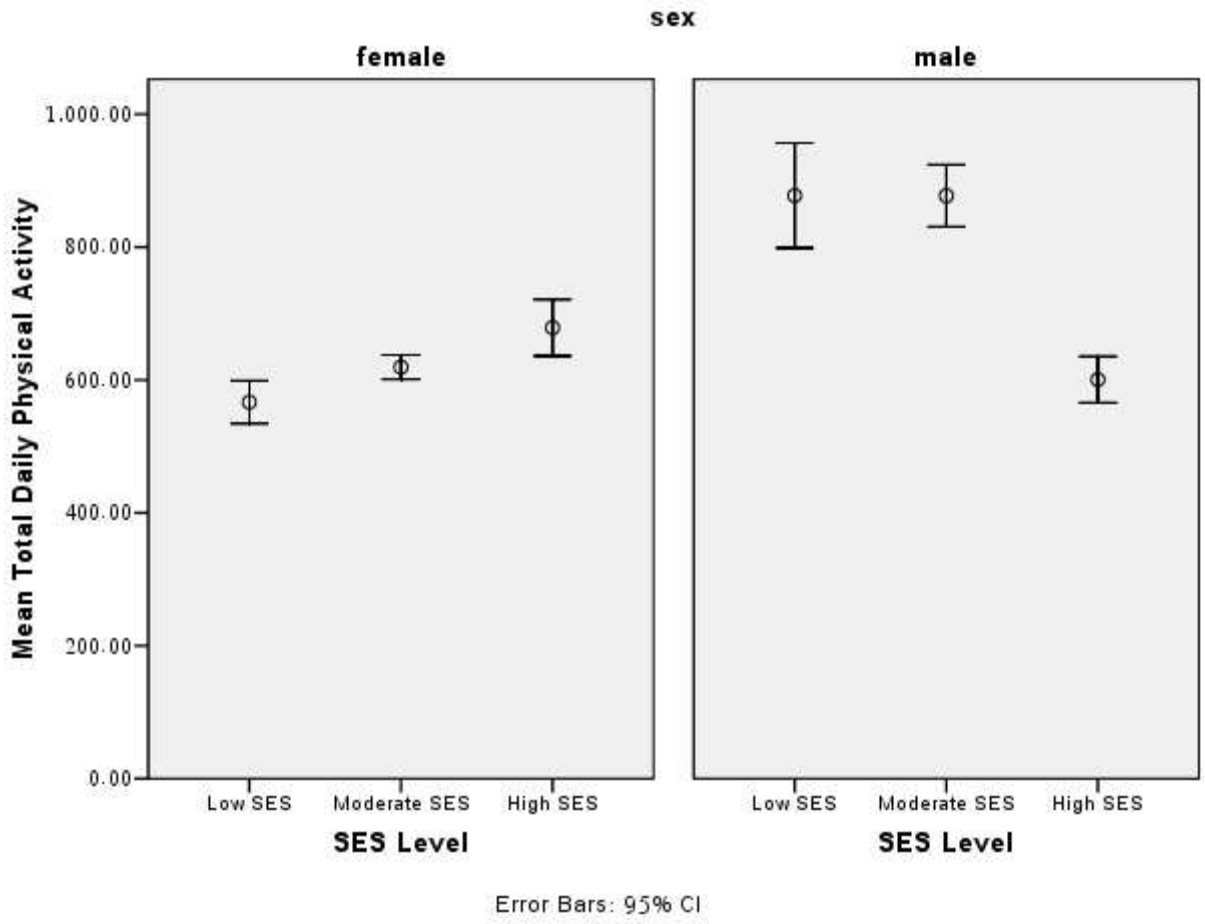

Figure 2. Total daily physical activity (MET min/day) in different socioeconomic status levels (Error Bars: 95% CI)
SES: socioeconomic status

Total Physical Activity

Total physical activity in the sampled population was 677.5 ± 624. It was higher in men (756.6 ± 766) than women (602.71 ± 437.10), and the difference was significant. Total physical activity of women was higher in HSES than MSES and LSES; it was the same for MSES in comparison with LSES. In contrast with these findings, in men the total daily physical activity was higher in LSES than HSES, and also was higher in MSES than HSES. However, there was no significant difference between total physical activity of participants in LSES and MSES (Figure 2).

The overall differences of men and women in most physical activity fields have been followed similarly in each level of SES. However, the occupational physical activity differences of men and women in LSES were greater in comparison with the overall differences. It was the same in MSES level for household physical activity. Moreover, differences in total physical activity were greater than the overall differences between men and women in LSES and MSES level, but it was less in HSES. The age and sex adjusted model yielded a significant regression coefficient for SES level (B = -97.9, R2 = 0.060, P < 0.001).

Discussion

In this study we found statistically significant differences in the extent of leisure-time, household, occupational, and total physical activity based on SES but not in transportation physical activity.

It seems that none of the socioeconomic factors alone can define the precise socioeconomic level of people in non-industrial countries, like Iran, due to being in a transitory period from traditional to modern conditions. Consequently, in this study we used multivariable method (cluster analysis) to categorize people according to their real SES characteristics, like education or income, etc. It is obvious that the relative importance of leisure-time physical activity has increased over time.[29,30] Reports from developed and developing countries showed that men are more active than women in leisure-

time.[12,16,31,32] In their study, Droomer et al. have found lower levels of leisure-time physical activity in lower educated, lower income level, and in general low socioeconomic status groups.[2,33-36] These findings seem to have two main reasons. The first is internal barriers, such as lack of motivation and free time, and special attitudes in women, who do not think that household physical activity is insufficient for health. The second is external barriers such as lack of appealing public places for physical activity, not enough knowledge about exercise related issues, and low income.[37]

We believe that low SES men were more active than high SES in occupational physical activity due to accumulation of handworkers in this category.

While higher SES is positively associated with leisure time physical activity, lower SES is positively associated with occupational physical activity.[38] It has been suggested that health outcomes depend not on absolute income, but rather on equality or how resources are distributed in society. However, access to health care explains only part of the difference in health status among various SES groups.[38]

Furthermore, it is interesting to note that as the result of using more technology and spending less time in the house, women who had occupational physical activity had less household activity.

Men were prominently more active in transportation physical activity than women. Moreover, in contrast with other studies, gender difference was observed when all domains of activity practice were considered.[20] Nonetheless, no important differences were found between SES levels, which implicate the general behavior of the population apart from SES levels. However, overall values of this field in both genders and all SES levels are trivial. It can be an issue for health policy makers to plan for promoting more active transportation instead of using motor vehicles.

Although higher levels of household physical activity was seen among women, the effect of having lower activity level in other domains of physical activity causes low total physical activity in women. This may be due to cultural characteristics of Iranian women about social behavior, jogging or cycling less than men, or less tendency or opportunity to have a job, and considerably less opportunity to leave the home. As we have shown men were considerably more active than women during leisure time in all 3 levels of SES (the difference was more than 70 Met - minute per day). Similar pattern were shown in total physical activity except in high SES men, who were less active than women. In both sexes fewer but more important differences were found between SES levels, especially high SES and low SES. However, we should be cautious in our interpretation in men due to overlapping 95%CI compared to significant P-value.

In line with other studies, our finding showed that association between SESs and total physical activity levels was exactly the opposite in men; the lower the SES level, the higher the rate of physical activity.[22] However, in women this pattern has not been shown. Although the pattern of physical activity and SES for women were similar in leisure time physical activity (as the most important field) and total physical activity (as life style marker), the HSES men with the most leisure time physical activity had the least total physical activity. This supports the fact that although they have high leisure time physical activity, they have an inactive lifestyle. Although leisure time physical activity was less in LSES than HSES, higher level of occupational physical activity cause higher total physical activity in these groups. On the contrary, the HSES group had more leisure physical activity, but less occupational physical activity.

In the past, physical activity was simply a part of ordinary life. However, in the modern and new life style of humanity many activities have been transferred to machines. This trend has finally affected people with different SES levels, even if begun in high SES's. Consequently, the role of leisure time physical activity has gradually become more important. In Iran, such activities need extra costs, and are not a part of daily routines in the traditional culture. For these reasons, it seems that leisure time physical activities are considered to be a special behavior rather than a routine. Hence, it is less probable that low SES people have leisure time physical activities. Moreover, they might not be aware of the important role of such activities, and think that the costs are unnecessary. Therefore, attempts to develop these habits among low SES groups, decrease costs, and increase easy available facilities should be taken into account as a part of health policies.

The improvements of the physical environment, eliminating physical barriers, group physical exercise instead of individuals ones, and community and workplace policies may promote physical activity in a population.[39-41] The results presented in this paper emphasis the fact that women of low and moderate SES who live in these areas need particular measures to increase their physical activity. They

not only have low leisure time, but also low total physical activity. Although there are many cultural and social differences between the Persian society and neighbor countries in the Middle East, some similarities like religion or economy may make these results generalizable to them.

This study has a number of strengths. The large sample size provided statistical power to examine associations within subgroups. This study reveals special physical activity patterns related to socioeconomic (that was not clear before) and exaggerated gender differences, and complete profile of physical activity fields (leisure time, occupational, household, and transportation) in Iran. The questionnaire included a wide range of subjects to prepare a more accurate estimation of physical activity together with more variation. Using Mets to report physical activity in this study provides quantifiable values based on calorie expenditure, which is more accurate than physical activity duration, but it leads to some difficulties in comparison with other studies.

Some of the limitations of our research are that assessments of physical activity via a questionnaire may not accurately reflect physical activity. Participation in active sports may be particularly overestimated, considering the strong Iranian social attitudes towards the desirability of an active lifestyle. Furthermore, information on income was self-reported and may be affected by prestige bias, or underestimation to avoid taxation. Our findings emphasize the need for a better understanding of social and environmental barriers, and special considerations for women in the low and moderate socioeconomic status in order to make social and health policies particularly in unindustrialized countries similar to Iran. More research is needed to examine the effect of other constructs of social class, such as acculturation, safety, and social support, in promoting successful interventions to increase physical activity.

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Conflict of Interests

Authors have no conflict of interests.

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Parental perceptions of weight status of their children

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Original Article

Abstract

BACKGROUND: Understanding the knowledge, attitudes, and beliefs of parents is important for planning appropriately to control their children's weight. We aimed to study these variables in parents of normal, underweight, overweight, and obese children.

METHODS: This cross-sectional study targeted the parents of normal, underweight, overweight, and obese children, who were selected using multistage random sampling method. The parents' knowledge, attitudes, beliefs, and behaviors about the weight status of their children, weight management, obesity, diet, lifestyle, and related psychosocial factors were evaluated using a validated questionnaire. The questionnaire, which had been validated, consisted of 12 demographic, 8 knowledge, 19 attitude and beliefs, and 25 behavior questions. Mean knowledge, attitude and beliefs, and behavior scores were compared across three subgroups of parents. Student's independent t-test, ANOVA, and Kruskal-Wallis test were used to study the correlation between different demographic and socioeconomic factors, and the studied variables.

RESULTS: 90% of parents were aware that obesity is a disease, and 92% knew that eating too much fast food would lead to obesity in children. Only 5% assumed that obese children are healthier than non-obese children. The mean scores of the three subgroups showed no significant difference in knowledge, attitude and beliefs, and behavior. Families with fathers, whose education level was higher than high school diploma, rated their children's weight status as overweight or obese significantly less than families with fathers, whose education level was high school diploma or lower (8.5% vs. 16.5%, respectively, $P = 0.014$). Only 12% of parents tried to help their children lose weight at least once, and only 6% arranged sport activities for the family members. In 57% and 41% of families, the child, respectively, decided how much time was enough to watch TV, and how much chocolates and sweets to eat. 46% of children watched TV for more than 2 hours/day, and 49% of children watched TV while eating meals. The mean total score of boys' parents was significantly lower than that of girls' parents ($P < 0.05$). Families with low income, with no medical insurance, or not owning a house thought that the cost of registration in sport activities for children was too high ($P < 0.03$).

CONCLUSION: Some parents unreasonably rated the weight status of their children as overweight/obese. It is suggested that further studies be carried out to evaluate and improve parents' knowledge, attitudes, and behaviors regarding their children's weight.

Keywords: Children, Obesity, Overweight, Knowledge, Attitude, Belief, Behavior

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Introduction

The epidemic of obesity in children has become one of the main concerns in developed and many developing countries.[1-5] The prevalence of overweight (BMI of 85th to 95th percentile) and obesity (BMI > 95th percentile) in our country were about 5% and 10%, respectively.[6] Childhood obesity is related to some chronic diseases in adulthood such as hypertension, diabetes mellitus, and cardiovascular disease.[7-10] In addition, overweight and obese adults demonstrated less successful economic and social patterns.[1] Complex interactions of genetics, sedentary lifestyle, poor nutrition, and psychosocial and environmental factors are essential in inducing excess body weight in children around the world.[1,11,12] Overweight and obese children are more likely to eat fatty and salty food, and spend more time watching TV rather than being physically active. They are also less likely to consume enough vegetables, fruits, and whole grains.[13] Moreover, there are some psychosocial factors that endorse the risk of being overweight and obesity in children. For example, some parents believe that the larger the body size, the healthier the child. In other words, they are even satisfied with their children's obesity or overweight. Some parents also consider their overweight children as strong and/or solid.[14] The social acceptance of being overweight leads to less pressure on children to lose weight. This results in less frequent seeking of appropriate weight management strategies. There are similar trends in many cultures. Understanding the thinking patterns of caregivers of overweight and obese children is the first step in the modification of their behaviors. Appropriate planning may also help to promote a healthier lifestyle in children, and to tackle the epidemic of obesity. The current study evaluated a sample of parents of normal, overweight, and obese children in order to assess their knowledge, attitudes, beliefs, and behaviors related to obesity and weight management in their children.

Materials and Methods

Sampling, Recruitment, and Data Collection

In 2011, a qualitative study was performed as the initial step of a large study, named TABASSOM study, on obesity determinants in adults and children. It was conducted to investigate the knowledge, attitudes, and behaviors toward obesity variables.[15] Then a questionnaires was developed for adults and adolescents and validated to be used in this study.[16] The current study has been approved by the Ethical Committee of Isfahan Cardiovascular Research Center (a WHO collaboration center). 320 families were randomly selected through multistage random sampling after clustering urban health centers. They were randomly selected from each health center from the list of families with children aged 15 years and under. The parents were called, informed about the study, and asked if they were willing to take part in the study between January 2011 and December 2011. Appointments were made, and trained interviewers went door to door and completed the questionnaire. All participating parents gave their consents before enrollment in the study. Each questionnaire started with demographic and socioeconomic questions (family structure, parent's education, employment, family income, and medical insurance) followed by knowledge, attitude, beliefs, and behavior questions. Questions on barriers or facilitators of weight management strategies from the parents' points of view were included.

Measurement Tool, Development, Validity, and Reliability

The parents' knowledge, attitudes, beliefs, and behaviors about their children's weight and its management were measured using a validated instrument.[16] The measurement tool was developed based on the literature review and qualitative study conducted previously.[15] In brief, the qualitative study evaluated weight status, physical activity, and nutritional, environmental, and psychosocial issues affecting weight control in children. Textbooks, scientific literatures, and published questionnaires were also used to extract the questions. A panel of experts, including nutritionists and psychologists, was asked to review the instrument for content validity, accuracy, and suitability of different items.[16] In order to check the face validity, a number of lecturers of the Social Medicine Department, Isfahan University of Medical Sciences (Isfahan, Iran) were asked to answer the questionnaire. The answers were prepared in scales or multiple choices. According to the recommendations and feedbacks of the expert panel and the lecturers, the items were either kept unchanged, removed, or revised. The modified instrument was pretested with 10 parents for readability and transparency of the overall questionnaire, items, answers, and scales. A few corrections were made according to the new feedbacks of parents. Cronbach's alpha coefficient of the questionnaire ranged between 0.6 and 0.8.[16] The final questionnaire consisted of 12 demographic, 8 knowledge, 19 attitude and belief, and 25 behavior questions. The knowledge questions consisted of obesity and its relationship with the following factors:

diet quality, physical activity, psychosocial factors, obesity control and prevention, and associated diseases. Each knowledge question had three answers of true, false, and I don't know. Every correct answer was assigned 1 point, and every incorrect response or I don't know answer was assigned 0 points. Attitude and belief questions corresponded to the personal values and beliefs on 6 obesity related constructs of body image, diet, active or sedentary lifestyle and related cultural, educational issues, and psychosocial issues. The first 16 attitude and belief questions were assessed using five-point Likert scale answers, ranging from strongly agree to strongly disagree. The answers were given 1 to 5 points according to the correctness of the response. 3 other attitude and belief questions had favorable and unfavorable options, and were scored accordingly. Behavior questions represented behaviors of both parents and children evaluated by different questions in the following domains: physical activity and sedentary lifestyle, diet pattern, parent-child communication, and weight management education and interventions. The first 17 behavior questions had five-point Likert type scales, ranging from everyday to never. The correct behavior was given 5 points, and the other choices were ranked accordingly. The rest of the behavior questions were assessed according to the multiple choice answers. The correct response was given one point and other choices were given 0. The higher the scores, the higher the knowledge, right attitudes, correct beliefs, and appropriate behaviors.

Data Analysis

Frequency distributions of demographic and socioeconomic information of families and of the parental knowledge, attitudes, beliefs, and behavior patterns were determined. The scores of each section of knowledge, attitude and belief, and behavior and the total score for every person were calculated. Parents were divided into three subgroups based on their perceptions of children's weight status (underweight, normal weight, and overweight and obese). The mean knowledge, attitude and belief, and behavior scores among three subgroups and across different demographic and socioeconomic factors were compared using independent t-test, ANOVA, and Kruskal-Wallis. SPSS for Windows (Version 15; SPSS Inc., Chicago, IL., USA) was used for data analysis.

Results

Demographic and Socioeconomic Status

Parents of 146 boys and 139 girls participated in the study. The mean age of boys and girls were 9.6 ± 2.6 and 9.4 ± 2.7, respectively. The age range of children was 5-14 years in both genders. 21%, 51%, and 28% of families had one, two, and three or more children, respectively. In 270 children, the father and mother were living together. 15 children lived with single parents (parents were divorced and separated in 5 and 3 cases, respectively) and one parent was not alive in 7 children. Five fathers and five mothers were illiterate (2%), whereas 157 fathers (56%) and 167 mothers (59%) had a high school diploma or college/university degree. 262 mothers were housewives. Monthly income was equal or less than US$ 300 in 69 families, and equal or greater than US$ 1000 in 3 families. 171 and 191 families owned a house and 1 or more cars, respectively. 221 families were covered by medical insurance.

Knowledge, Attitude and Belief, and Behavior about Obesity and Overall Health

Participating parents had a reasonable knowledge of obesity. About 90% knew that obesity is a disease, 91% were aware that it is possible to become obese at all ages, 89% knew that the possibility of becoming obese in adulthood is higher for obese children, and 95% were aware of the good chance of preventing childhood obesity. 98% knew that having a normal weight is important in maintaining children's overall health. 93%, 95%, and 96% were aware that obesity may lead to diabetes mellitus, cardiovascular diseases, and hypertension, respectively. When asked "Have you ever been informed about the risks of obesity and overweight in children?" 69% of parents responded yes. However, when the same question was asked about their children, the positive answer dropped to 40%. 54% of parents found their information about the risk of obesity through TV and radio, whereas in 32%, books, journals and newspapers were the sources of information.

Knowledge, Attitude and Belief, and Behavior about Obesity and Physical Activity

Although 91% of parents knew that children with less physical activity are more prone to become obese, only 6% arranged exercise and sport activities, such as walking and mountain climbing, for the family members. About 42% of parents talked to their children about the advantages of sport activities. In 57% of families, the child decided how much TV to watch and 46% of children watched TV for more than 2 hours per day. In 13% of families, the child worked on the computer for more than 2 hours per day. One-third of parents believed that the time of sport activities in their children's schools was not enough and

assumed that there was not enough space for sport activities in their children's schools. 28.5% of parents thought the children did not have enough time for sport activities because of the pressure of the school's science programs. Nearly half of the parents believed that the cost of registration of their children in sport activities was too high. Only the latter item was significantly different based on the sex of the child and the family's economic status. In other words, 58% of boys' parents and 39% of girls' parents believed that the cost of registration of children in sport activities was too high ($P = 0.001$). Furthermore, families with low income, no medical insurance, or those who did not own a house similarly thought that the cost of registration in sport activities for children was too high ($P < 0.03$).

Knowledge, Attitude and Belief, and Behavior about Obesity and Dietary Habits

About 92% of parents knew that eating too much fast food would lead to obesity in children. Although 34% thought not having fast food could be difficult for their children, only 5% and 13% declared that their children were regularly eating fast foods (such as pizza, or sandwich) and snacks (such as chips, cheese balls, biscuits, or chocolates). 52% stated that educational programs on appropriate nutrition were not frequently conducted in schools. 39% believed that selling some snacks such as chips and cheese balls in schools made their children consume them more frequently, and 53% thought that by their children's friends eating snacks their children ate more snacks. In 49% of families, the children watched TV while eating meals and 57% believed that TV advertisements on some snacks such as chips and cheese balls led the children to consume them more frequently. 65% of children were regularly eating breakfast, 81% were eating fruits every day, and 63.5% had healthy snacks such as bread and cheese, nuts, or dried fruits between the meals. 78% of parents selected the type of food consumed at home, 14% prepared fried food for their children, 3% chose chips, cheese balls, or chocolates to reward the children's good behavior, 25% locked some foods such as sweets or chocolates out of access of children, and 45.5% talked to children about the advantages of having healthy foods. In 41% of families, the child was authorized to decide how much chocolates and sweets to eat. Only the last item was significantly different based on father's education; in 36% of families with father's education of lower than high school diploma, and in 50% of families with father's education of higher than high school diploma, children were rarely or never authorized to decide how much chocolate and sweets to eat ($P < 0.02$).

Knowledge, Attitude and Belief, and Behavior about Obesity and Psychosocial Issues

About 72% of parents believed that children of obese parents are more probable to become obese. Only 5% assumed that obese children are healthier than non-obese children. 79% believed that obesity caused the isolation of children from other children at school, 83% thought obese children might become depressed and 81% assumed that obesity might decrease self-confidence in children. When asked "How important is the normal weight of your child to you and your spouse?" 96% and 87% responded it is very important to me, and it is very important to my spouse, respectively. The parents ratings of their children's weight status was very interesting; 25% of parents rated their children as thin or very thin, 62% considered them to be about the right weight, and only 13% selected overweight or obese as the body shape of their children. Only 12% had tried to help their children lose weight. Of the latter group (35 children) the parents of 16 children consulted with a nutritionist or a medical doctor to get help on reducing the child's weight. 11 children lost weight with no return, and 9 lost weight and regained the weight. The following methods were used by this group of children to lose weight: diet (12 children), exercise (7 children), and both (16 children). When asked "Which one of the following behaviors was more difficult to control for your child?" the answers were as follows: self-regulation of eating (14 children), exercise (4 children), and both (7 children).

Comparison of Knowledge, Attitude and Belief, and Behavior Scores

Few significant differences were found between the knowledge, attitude and belief and behavior scores across different demographic and socioeconomic factors (Table 1). The mean scores of knowledge, attitude and belief, and behaviors were not significantly different between boys' parents and girl's parents. However, the mean total score of boys' parents was significantly lower than that of girl's parents ($P < 0.05$). Families with fathers' education of lower than high school diploma had significantly lower mean knowledge, behavior, and total scores than those of families with fathers' education of high school diploma or higher (Table 1).

One question evaluated the parents' perception on their children's weight status. The mean scores of the three subgroups (underweight, normal weight, and overweight and obese) were compared and no significant difference in knowledge, attitude and

Table 1. Mean knowledge, attitude and beliefs, behaviors, and total scores across various demographic and socioeconomic factors

Demographic and socioeconomic factors		Knowledge		Attitudes and beliefs		Behavior		Total	
		Scores	P	Scores	P	Scores	P	Scores	P
Sex of child*	Boys	0.90 ± 0.14	0.7	0.76 ± 0.13	0.08	0.51 ± 0.15	0.08	0.69 ± 0.09	0.03
	Girls	0.91 ± 0.13		0.78 ± 0.13		0.54 ± 0.16		0.72 ± 0.09	
Number of children in the family	One	0.87 ± 0.15	0.15**	0.75 ± 0.14	0.31**	0.52 ± 0.13	0.49**	0.69 ± 0.08	0.15***
	Two	0.91 ± 0.12		0.78 ± 0.13		0.53 ± 0.16		0.71 ± 0.09	
	≥ Three	0.91 ± 0.13		0.77 ± 0.11		0.51 ± 0.17		0.69 ± 0.11	
Father education*	< High school diploma	0.88 ± 0.15	0.02	0.76 ± 0.14	0.07	0.49 ± 0.15	0.01	0.68 ± 0.10	0.001
	≥ High school diploma	0.92 ± 0.12		0.79 ± 0.12		0.54 ± 0.15		0.72 ± 0.09	
Family income	≤ 300,000	0.87 ± 0.16	0.2**	0.75 ± 0.13	0.3**	0.53 ± 0.16	0.3**	0.69 ± 0.09	0.4***
	301,000-600,000	0.91 ± 0.12		0.78 ± 0.13		0.53 ± 0.15		0.71 ± 0.09	
	≥ 601,000	0.89 ± 0.13		0.77 ± 0.15		0.53 ± 0.18		0.70 ± 0.11	
Number of automobiles*	≥ 1	0.90 ± 0.13	0.8	0.78 ± 0.12	0.2	0.52 ± 0.15	0.35		0.8
	0	0.90 ± 0.14		0.75 ± 0.15		0.54 ± 0.16			
House*	Owned	0.89 ± 0.16	0.5	0.78 ± 0.12	0.35	0.51 ± 0.15	0.2	0.70 ± 0.09	0.6
	Not owned	0.91 ± 0.13		0.76 ± 0.14		0.54 ± 0.16		0.71 ± 0.10	
Medical insurance*	Yes	0.91 ± 0.13	0.1	0.77 ± 0.13	0.97	0.53 ± 0.16	0.1	0.71 ± 0.09	0.1
	No	0.88 ± 0.16		0.77 ± 0.16		0.49 ± 0.15		0.69 ± 0.09	

* Independent t-test was applied.
** Kruskal-Wallis test was used.
*** ANOVA was employed.

Table 2. Comparison of mean and/or median scores of knowledge, attitudes and beliefs, and behaviors across three subgroups of parental ratings of children's weight status

Parental perception of children's weight status	Knowledge scores			Attitudes and beliefs scores			Behavior scores			Total scores	
	Median (IQR)	Mean ± SD	P	Median (IQR)	Mean ± SD	P	Median (IQR)	Mean ± SD	P	Mean ± SD	P
Underweight (n = 71)	0.87 (0.75, 1)	0.88 ± 0.15		0.79 (0.71, 0.86)	0.77 ± 0.14		0.5 (0.37, 0.64)	0.51 ± 0.16		0.69 ± 0.1	
Normal (n = 177)	1 (0.87, 1)	0.91 ± 0.13	0.37	0.79 (0.71, 0.86)	0.77 ± 0.13	0.99	0.5 (0.43, 0.64)	0.53 ± 0.15	0.46	0.71 ± 0.09	0.55
Overweight and Obese (n = 37)	1(0.87, 1)	0.93 ± 0.09		0.79 (0.71, 0.86)	0.77 ± 0.13		0.5 (0.36, 0.64)	0.49 ± 0.17		0.69 ± 0.08	

beliefs, behaviors, and total scores were found among them (Table 2).

Moreover, parental perception about children's weight status had no significant relationship with the sex of the child or the number of children in the family. However, families with fathers' education of lower than high school diploma rated their children's weight status as overweight or obese significantly less than families with fathers' education of high school diploma or higher (8.5% vs. 16.5%, respectively, P = 0.014).

Discussion

Although some parents enrolled in this study had overweight or obese children, the majority of parents didn't think that their children were either overweight or obese. This finding is important given that parents had good or very good knowledge about obesity and its health related consequences. They were aware that obesity is a disease, causes psychosocial problems in children, and leads to chronic diseases later in life. Furthermore, the majority of the subjects stated that their children consumed fruits and vegetables every day, and two-thirds ate breakfast and healthy snacks, regularly. However, in half of the families, the children watched TV while eating meals, a finding that may explain the high level of overweight and obesity in our society.[5] The Ministry of Health has banned TV advertisement on non-healthy snacks in Iran which further helps reduce the consumption of non-healthy snacks. However, the effect of international media including internet, and satellites may be more effective. Overall, some parents were not able to recognize the correct body shape of their children in the current study. Therefore, they were not expected to intervene to modify the children's, and probably their own, unhealthy lifestyles and to treat this disease. That's why only 12% had ever tried to help their children lose weight. Parents' underestimation or misperception of children's weight status has also been demonstrated by other studies.[17-35] This finding seems more important when we learn that the scores of knowledge, attitude and beliefs, and behaviors of parents who perceived their children as overweight and obese in the current study were not significantly different than those who rated their children's weight as normal or underweight. It seems that increase in knowledge of parents is not enough for them to perceive the correct weight status, and prevent or treat overweight or obesity in their children. Some researchers gave three reasons for parental misperception of children's weight status; gender-based different viewpoints of parents, ethnic-based different perspectives, and low education and income levels.[14,21,32] Our study demonstrated no difference between the parents of boys and girls in rating the children's weight status. The level of income of parents also caused no difference in parental rating of children's body shape. A previous local research found that overweight children were significantly more prevalent in average-income families than in high-income families, and in lower-educated mothers than in higher-educated ones in our city.[5] In the current study, the higher the level of education of fathers, the higher the possibility of rating the weight status of children as overweight or obese.

Overweight and obesity in children are prevalent in our country.[5,6,36-40] Furthermore, their prevalence decreased significantly in girls, though it increased in boys following the interventional activities of the Heart Health Promotion from Childhood as one of the ten interventional projects of the Isfahan Healthy Heart Program.[12,41,42] Body weight increases gram by gram and obesity develops very slowly. Thus, its development in children might not be noticeable for parents. They see their children every day since their birth. Day to day weight increase in children is not large enough for parents to perceive in day to day interaction with them. For parents, the child's body shape today is similar to the picture taken yesterday. Many parents have a fixed image of the child in their minds which is most often a healthy portrait. They do not see what the health care providers see.[33] Some parents do not see the ongoing increase in weight unless it is acute. Acute changes or events are perceived immediately but chronic ones are not. As long as the children have a good appetite, do not complaint of any symptoms, and are active in their school homework, the parents' attention may not be directed towards their body shape.[14] Some parents do not care about the gradual weight changes of their children.[21] On the other hand, parents may know obesity but may not be able to diagnose it; because they may either compare their children with extreme cases of obesity or assess their weight status visually. They do not trust or use clinical measures.[27] Besides, parents know fever and cough but cannot easily diagnose whether they are due to common cold, sinusitis, bronchitis, or pneumonia. Increase in weight is a sign not a symptom. People come to the medical doctor with symptoms whereas the signs are mostly picked up by doctors. The information

on symptoms and signs directs the doctor towards correct diagnosis. Obesity is not a symptom or sign, but a disease. It is probably too much to expect of parents to diagnose this disease given their various responsibilities and stresses. Overweight and obesity can be detected actively by health care providers rather than passively by the parents. It is important to mention that the results of the current study demonstrated that only 40% of parents were educated about the risks of obesity in their children. It seems that the main focus on overweight and obesity detection might shift from families to schools. Teachers or school health care providers could be continually educated on this issue. They probably can easily detect overweight and obesity and inform the parents about the weight status of their children in a non-stigmatizing and non-offensive way.[43] This can raise the parents' concerns about this issue. The parents are aware of the long-term consequences of obesity on biopsychosocial aspects of their children's lives and they know that they can largely shape the lifestyles of their school-aged children.[44,45] As soon as parents acknowledge the children's overweight or obesity they can start appropriate interventions. In other words, although the parents are principal keys in weight management of children, they need assistance and guidance by public health programs to successfully perceive the problem. Increasing the knowledge and awareness of parents is important and should be continued but to translation this knowledge into perception needs further practical strategies. Otherwise, underestimation of the weight status of children by their parents will be an important barrier in preventing the epidemic of obesity among children.

Conclusion

Recognition of the correct body shape of children by parents needs special attention. Further action-oriented studies are necessary to build practical steps in order to improve the practice and behaviors of parents towards tackling the epidemic of overweight and obesity in their children.

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Conflict of Interests

Authors have no conflict of interests.

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Differences in the prevalence of metabolic syndrome in boys and girls based on various definitions

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Original Article

Abstract

BACKGROUND: The prevalence of metabolic syndrome (MetS) is increasing among children and adolescents. However, the prevalence of this disorder varies based on its different definitions. This study aimed to determine the prevalence of MetS in Iranian adolescents in junior high and high schools according to the definitions provided by the International Diabetes Federation (IDF) and De Ferranti.

METHODS: Overall, 1039 junior high school and 953 high school students were selected using multistage random sampling. Demographic data was collected using validated questionnaires. Fasting blood sugar, total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) levels were determined. Waist circumference and blood pressure were measured by trained individuals. Subjects with MetS were selected according to two definitions provided by the IDF and De Ferranti. Chi-square and Fisher's exact tests were used to compare the prevalence of MetS and its components based on sex, school level, and the two definitions.

RESULTS: The mean age of junior high and high school students was 13.11 ± 1.21ad 15.93 ± 1.07 years old, respectively. The prevalence of MetS among all participants was 4.8% and 12.7% according to the definitions by the IDF and De Ferranti, respectively. It was significantly higher among boys compared to girls. According to the IDF definition, low HDL-C and hypertension were the most frequent components. Based on the De Ferranti, abdominal obesity and hypertriglyceridemia were the most frequent components.

CONCLUSION: The prevalence of MetS was higher in both groups of students based on De Ferranti definition compared to the IDF definition. The prevalence was not significantly different in boys and girls. Further studies to investigate the most suitable definition of MetS for Iranian adolescents are necessary.

Keywords: Metabolic Syndrome, Adolescence, International Diabetes Federation and De Ferranti

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Introduction

The prevalence of metabolic syndrome (MetS) is on the rise as a result of the global epidemic of obesity among children and adolescents.[1] There are different definitions of MetS including those provided by the Third National Health and Nutritional Survey (NHANES III), the International Diabetes Federation (IDF), and the World Health Organization (WHO).[2,3] The prevalence of MetS differs within the same population based on each definition.[4,5] Different studies have shown that MetS increases with age, but the frequency depends on the studied population and the applied definition. The

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NHANES IIIreported the prevalence of MetS as 4.2% in teenagers.[6] A study on 9-10 year-old children in Tehran (Iran) suggested the prevalence of MetS based on IDF, NHANES III, the American Heart Association (AHA), and Adult Treatment Panel III (ATP III) as 1.5%, 5.9%, 17.8%, and 5.8%, respectively. It found the values to be significantly higher in boys than in girls. It also showed the prevalence of MetS based on the ATP III definition to be 2.2% among normal weight children and 62.2% among obese children.[7] Weiss et al. showed that increased prevalence of MetS was directly related to obesity in children and adolescents.[8] The difference in the frequency of this syndrome in children and adolescents is related to different definitions used.[5,9-11] The cut-off point specified for MetS definition differs probably due to the lack of a gold standard for the diagnosis of MetS in adolescents. The place of residence is also important in determining the prevalence of MetS. A previous study calculated the prevalence of MetS in urban and rural adults of Isfahan (Iran) as 24.2% and 19.5%, respectively.[12]

The definitions developed by IDF and De Ferranti and Osganian[5] (which we call the De Ferranti's definition throughout this paper) appear to be more efficient for determining the prevalence of MetS in adolescents.[3-5] Increasing prevalence of MetS has an important role in the increased prevalence of other diseases and mortality at older ages. To the best of our knowledge, no Iranian study has evaluated MetS in school children based on the two mentioned definitions. Due to the absence of estimates of the prevalence of the MetS using the mentioned definitions, we analyzed data from an American sample of children and adolescents to estimate the prevalence of the syndrome and to examine demographic variation in its prevalence. Our results provide the first data of the prevalence of the MetS using the definitions provided by the pediatric IDF and De Ferranti among a representative sample of Iranian adolescents.

Materials and Methods

This study was a part of the Healthy Heart from Childhood (HHC) project which was in turn one of the 10 projects forming the Isfahan Healthy Heart Program (IHHP) conducted from 2000 to 2007 in Isfahan, Najafabad, and Arak (all in Iran).[13,14] The IHHP was a community-based interventional program that was performed to prevent and control cardiovascular diseases and to promote healthy lifestyle. While the intervention community comprised urban and rural regions in Isfahan and Najafabad, Arak was studied as the control area. Details relating to the methodology, sampling, and study populations of HCC are noted elsewhere.[15]

In summary, 1039 junior high school and 953 high school students in Isfahan and Najafabad were selected by multistage random sampling. Validated questionnaires were used to collect sociodemographic data. Parents of all participating students signed informed consent forms. This study was approved by the Ethics Committee of the Isfahan Cardiovascular Research Center (a WHO collaborating center).

Fasting blood samples were taken from all participants to measure blood sugar, total cholesterol, and triglyceride levels using the enzymatic methods. The amount of high-density lipoprotein cholesterol (HDL-C) was determined by heparin-manganese precipitation. LDL was estimated using the Friedewald equation.[15] All tests were performed at the laboratory of the Isfahan Cardiovascular Research Center which had been validated by national and international authorities. In order to measure weight, height, and waist circumference (WC), the participants were asked to wear light clothes and to take off their shoes. They stood upright on a scale after it had been reset and their weight was measured to a standard error of 1%. The participants' right hand blood pressure was measured twice after a five-minute rest and the mean value was recorded as their blood pressure. All measurements were performed by trained individuals.

MetS was defined according to the definitions suggested by the IDF and De Ferranti.[3-5] The IDF defines MetS as the presence of at least three of the following criteria: 1) WC ≥ 90th percentile, 2) serum triglyceride ≥ 150 mg/dl, 3) HDL-C < 40 mg/dl, 4) systolic and diastolic blood pressure ≥ 90th percentile, and 5) fasting blood sugar (FBS) > 100 mg/dl. De Ferranti De Ferranti consider all the above-mentioned criteria except for WC ≥ 75th percentile and serum triglyceride > 100 mg/dl.[5]

Statistical analysis

Data was entered in Epi Info 2000 and analyzed with SPSS for Windows 15.0 (SPSS Inc., Chicago, IL, USA). Comparisons of the prevalence of MetS based on sex in the two school levels were performed using chi-square test and Fisher's exact tests (if required). P values less than 0.05 were considered significant.

Results

Of the 978 female adolescents (500 junior high

school and 478 high school students) and 1014 male adolescents (539 junior high school and 475 high school students), 1532 students were from urban areas and 460 from rural regions. The mean age of the junior high school and high school students was 13.11 ± 1.21 and 15.93 ± 1.07 years old, respectively.

In general, the prevalence of MetS was 4.8% based on the IDF's definition and 12.7% based on the De Ferranti's definition (Table 1). Based on the IDF's definition, the prevalence of MetS in boys of all grades was significantly higher than in girls. However, there was no significant relation between the prevalence of MetS and school grade either boys or girls. Similarly, the definition provided by De Ferranti revealed the prevalence of MetS to be significantly higher in male junior high school students than in girls of the same level (15.8% vs. 10.2%; P = 0.012). However, no significant difference was observed between boys and girls in high school (11.5% vs. 13.0%; P = 0.510). Furthermore, the overall prevalence of MetS was higher in all grades and both sexes according to the De Ferranti's definition compared to the IDF's definition (13.2 and 12.3 vs. 5.3 and 4.2).

Table 2 shows the components of MetS stratified based on sex, school, and the two definitions. Using both definitions, the prevalence of hypertriglyceridemia, low HDL-C, and hypertension was higher than other components. Based on the IDF's definition, low HDL-C and hypertension and based on the De Ferranti's definition, abdominal obesity and hypertriglyceridemia were the most prevalent components. In junior high school students, hypertension and high FBS level were significantly higher in boys than in girls. Moreover, boys in junior high schools had significantly higher blood pressure than boys in high schools. Although the prevalence of MetS in male and female high school students was not significantly different, a significantly higher prevalence was observed in boys in junior high schools than in the girls of the same age.

Base on the IDF's definition, the frequency of hypertriglyceridemia in girls was higher in junior high schools than in high schools (15.1% vs. 6.4%; P < 0.001). In addition, the frequency of hypertriglyceridemia in boys was significantly higher than that in girls (P = 0.003). Based on the De Ferranti's definition, the frequency of hypertriglyceridemia in girls in junior high schools was higher than that in boys of the same age and higher than that in high school girls. Using both definitions resulted in significantly higher frequency of abdominal obesity among junior high school boys than in girls (P < 0.001). However, this difference was not significant in high school students.

Discussion

This was the first study to compare the prevalence of MetS in female and male junior high school and high school students from two districts in Iran based on definitions provided by the IDF and De Ferranti. The prevalence of MetS was three-fold higher when our measurements were based on the De Ferranti's definition compared to the IDF's definition irrespective of sex and school grade. Previous studies on MetS in adolescents and adults have reported different results in different parts of the world. The prevalence of MetS has been calculated as 3.0-11.0% in Europe,[16] 2.5-12.9% in the U.S.,[17] 3.6% in Brazil,[18] and 4.8% in Greece.[19]

Table 1. Prevalence of metabolic syndrome based on sex and school level according to the definitions by the International Diabetes Federation (IDF) and De Ferranti and Osganian[5]

Metabolic syndrome			Girls	Boys	Total	P
Based on the IDF's definition	Junior high school	Number	14	37	51	0.005
		Percent (SE)	3.1 (0.8)	7.2 (1.1)	5.3 (0.7)	
	High school	Number	11	28	39	0.008
		Percent (SE)	2.4 (0.7)	5.9 (1.1)	4.2 (0.7)	
	Total	Number	25	65	90	<
		Percent (SE)	2.8 (0.5)	6.6 (0.8)	4.8 (0.5)	0.001
	P		0.530	0.430	0.280	---------
Based on the De Ferranti's definition	Junior high school	Number	46	81	127	0.012
		Percent (SE)	10.2 (1.4)	15.8 (1.6)	13.2 (1.1)	
	High school	Number	52	61	113	0.510
		Percent (SE)	11.5 (1.5)	13.0 (1.5)	12.3 (1.1)	
	Total	Number	98	142	240	0.022
		Percent (SE)	10.9 (1.0)	14.4 (1.1)	12.7 (0.8)	
	P		0.540	0.210	0.540	---------

SE: Standard error P values were obtained from chi-square test.

Table 2. Frequency of metabolic syndrome components based on sex and school level according to the definitions by the International Diabetes Federation (IDF) and De Ferranti and Osganian[5]

Component of metabolic syndrome			Girls	Boys	Total	P
High blood pressure	Junior high school	Number	117	167	284	0.007
		Percent (SE)	23.7 (1.9)	31.2 (2.0)	27.6 (1.4)	
	High school	Number	83	87	170	0.780
		Percent (SE)	17.7 (1.8)	18.4 (1.8)	18.0 (1.3)	
	Total	Number	200	254	454	0.020
		Percent (SE)	20.8 (1.3)	25.2 (1.4)	23.0 (0.9)	
		P	0.021	< 0.001	< 0.001	--------
Low high-density lipoprotein cholesterol	Junior high school	Number	114	133	247	0.87
		Percent (SE)	25.3 (2.1)	25.8 (1.9)	25.6 (1.4)	
	High school	Number	102	147	249	0.004
		Percent (SE)	22.7 (1.9)	31.3 (2.1)	27.1 (1.5)	
	Total	Number	216	280	496	0.031
		Percent (SE)	24.0 (1.4)	28.4 (1.4)	26.3 (1.0)	
		P	0.36	0.056	0.45	--------
High fasting blood sugar	Junior high school	Number	11	38	49	0.001
		Percent (SE)	2.4 (0.7)	7.4 (1.1)	5.1 (0.7)	
	High school	Number	15	28	43	0.058
		Percent (SE)	3.3 (0.8)	5.9 (1.1)	4.6 (0.7)	
	Total	Number	26	66	92	< 0.001
		Percent (SE)	2.9 (0.5)	6.7 (0.8)	4.9 (0.5)	
		P	0.440	0.370	0.670	--------
High triglyceride base on the IDF's definition	Junior high school	Number	68	63	131	0.190
		Percent (SE)	15.1 (1.7)	12.2 (1.4)	13.6 (1.1)	
	High school	Number	29	57	86	0.003
		Percent (SE)	6.4 (1.1)	12.1 (1.5)	9.3 (0.9)	
	Total	Number	97	120	217	0.340
		Percent (SE)	10.8(1.0)	12.2(1.0)	11.5(0.7)	
		P	< 0.001	0.940	0.004	--------
High TG Base on De Ferranti's definition	Junior high school	Number	244	232	476	0.004
		Percent (SE)	54.2 (2.3)	45.0 (2.2)	49.3 (1.6)	
	High school	Number	179	199	378	0.450
		Percent (SE)	39.7 (2.3)	42.2 (2.3)	41.0 (1.6)	
	Total	Number	423	431	854	0.15
		Percent (SE)	46.9 (1.7)	43.7 (1.6)	45.2 (1.1)	
		P	< 0.001	0.360	< 0.001	--------
High waist circumference base on the IDF's definition	Junior high school	Number	30	65	95	0.001
		Percent (SE)	6.1 (1.1)	12.1 (1.4)	9.2 (0.9)	
	High school	Number	35	49	84	0.100
		Percent (SE)	7.4 (1.2)	10.4 (1.4)	8.9 (0.9)	
	Total	Number	65	114	179	<0.001
		Percent (SE)	6.7 (0.8)	11.3 (1.0)	9.1 (0.6)	
		P	0.410	0.390	0.810	--------
High waist circumference base on the De Ferranti's definition	Junior high school	Number	79	141	220	< 0.001
		Percent (SE)	16.0 (1.6)	26.3 (1.9)	21.3 (1.3)	
	High school	Number	92	108	200	0.190
		Percent (SE)	19.5 (1.8)	23.0 (1.9)	21.2 (1.3)	
	Total	Number	171	249	420	< 0.001
		Percent (SE)	17.7 (1.2)	24.8 (1.4)	21.3 (0.9)	
		P	0.150	0.220	0.940	--------

P values were obtained from chi-square test.

The prevalence of MetS in Germany was 4.0%,9.5%, 7.6%, and 9.6% based on a definition suggested by Cook et al.,[9] the De Ferranti's definition, the Jolliffe and Janssen's definition,[11] and the IDF's definition, respectively.[5]

In the present study, based on both the De Ferranti's and the IDF's definitions, the prevalence of MetS was higher among boys than among girls in all grades. While based on the IDF's definition, the prevalence of MetS was higher in junior high school girls than in high school girls, evaluations based on the De Ferranti's definition did not show a similar significant difference. In contrast, applying the De Ferranti's definition revealed higher prevalence of MetS in junior high school boys than in high school boys. These differences are related to differences in the cut-off points for WC and serum triglycerides in the two definitions. The prevalence of hyper-triglyceridemia was higher among girls than among boys in junior high schools using both definitions. This difference can be attributed to the age of puberty in girls which can affect triglyceride levels.

Various definitions of pediatric MetS have been used in different populations. Cook et al. reported lower prevalence in adolescents since they used more limited lipid and abdominal obesity cut-off points. They in fact translated the adult definition of MetS to pediatric percentiles. For instance, a higher triglyceride cut-off point of 110 mg/dl represents the 85th to 95th pediatric percentiles which is higher than the adult range (75th to 85th percentiles). The HDL-C level of 40 mg/dl represents the 10th to 25th percentiles in boys and the 10th to 15th percentiles in girls (lower than the 40th percentile in adults).[9] Moreover, their waist circumference cut-off point of the 90th percentile[9] is higher than the 75th percentile used in the present study. In contrast to other criteria, De Ferranti De Ferranti considered the effects of gender, age, and puberty and provided a pediatric definition based on the more inclusive ATP III adult criteria.[5]

The definitions suggested by De Ferranti and Osganian[5] and the IDF have been used more commonly than other definitions of MetS in recent years. Although their prevalence and cut-off points differ, it seems that both definitions are effective in determining MetS in adolescents.[20] The advantage of the De Ferranti's definition is that it is completely based on the ATP III which is recommended as a standard definition for determining the prevalence of MetS in adults.[2] A study in Mashhad (Iran) reported the prevalence of MetS based on ATP III to be 6.5% in high school girls.[21]

Although the etiology of MetS is not yet known, factors such as genetics, metabolism, and several environmental factors affect its occurrence.[22] The high prevalence of MetS in junior high schools compared to high schools can be attributed to the lifestyles of adolescents at this age, e.g. immobility,[23] interest in processed food, and entertainment devices such as computers and television. On the other hand, high school students pay more attention to their appearance, shape, and weight.

The importance of MetS in childhood is its impact on the health of adults. What is worrying about our studied population is the higher prevalence of other risk factors in junior high school students. In addition, we found higher prevalence of high blood pressure and FBS in junior high school boys than girls of the same age. Their prevalence was also higher among junior high school students than in high school students. Burns et al. showed that those who suffer from MetS in childhood will have systolic and diastolic hypertension, hypertriglyceridemia, and a higher body mass index in adulthood.[24] A cohort study in Japan with seven years of follow-up indicated that as the number of MetS components increased at the beginning of the study, the probability of cardiovascular diseases increased in the following years.[25]

The prevalence of obesity, which is the starting point of acquiring MetS in children and adolescents, is increasing in most parts of the world, especially in developing countries.[26] Acquiring the Western lifestyle and reduced physical activity can be responsible in this regard. It seems that obesity in one family member impacts MetS in adolescents. According to previous research, having an overweight or obese family member increases the prevalence of MetS to 7.0% in the boys and 8.1% in the girls of the family.[27,28] As obesity is turning into an epidemic among Iranian families,[22] it is necessary to pay more attention to children's lifestyle.

Conclusion

Compared to the IDF's definition, employing the De Ferranti's definition resulted in higher prevalence of MetS among junior high and high school students. Furthermore, the prevalence of MetS was higher in boys than in girls. Hence, more attention has to be paid to the definition used in determining the prevalence of MetS in adolescents. Further studies may introduce a standard definition specific for different societies and age groups.

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Conflict of Interests

Authors have no conflict of interests.

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Socioeconomic characteristics and controlled hypertension: Evidence from Isfahan Healthy Heart Program

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Original Article

Abstract

BACKGROUND: Hypertension is a major risk factor for cardiovascular diseases. It affects approximately 18.0% of Iranian adults. This study aimed to estimate age-adjusted prevalence of hypertension and its control among Iranian persons older 19 years of age. It also tried to find and socioeconomic factors associated with hypertension control in Iranian population.

METHODS: In Isfahan Healthy Heart Program (IHHP) subjects were selected by multistage random sampling. The participants completed questionnaires containing demographic information, lifestyle habits, medical history, and consumption of relevant medications, especially antihypertensive agents. Income, marital status, and educational level were considered as socioeconomic factors. Hypertension was defined as systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or taking antihypertensive medications. Controlled hypertension was considered as systolic blood pressure < 140 mmHg and diastolic blood pressure < 90 mmHg among hypertensive subjects.

RESULTS: The prevalence of hypertension and controlled hypertension was 18.9% and 20.9%, respectively. We found significant relationships between hypertension and marital status, education, and income. At age ≥ 65 years old, odds ratio (OR) was 19.09 [95% confidence interval (CI): 15.01-24.28] for hypertension. Middle family income (OR: 0.71; 95% CI: 0.58-0.87) and education level of 6-12 years (OR: 0.29; 95% CI: 0.25-0.35) were significantly associated with increased risk of hypertension (P = 0.001). Among subjects aging 65 years old or higher, the OR of controlled hypertension was 2.64 (95% CI: 1.61-4.33). Married subjects had a higher OR for controlled hypertension (OR: 2.19; 95% CI: 1.36-3.52). Obesity had no significant relationships with controlled hypertension.

CONCLUSION: The IHHP data showed significant relationships between some socioeconomic factors and controlled hypertension. Therefore, as current control rates for hypertension in Iran are clearly unacceptable, we recommend preventive measures to control hypertension in all social strata of the Iranian population.

Keywords: Socioeconomic Factor, High Blood Pressure, Control

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Introduction

Hypertension is a serious public health problems in Iran with a prevalence of approximately 18.0% in Iranian adults.[1,2] Since hypertension increases the risk of non-communicable diseases such as heart disease and stroke, it is considered as the most important cause of death among Iranian population.[3,4] Numerous studies have documented

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the prevalence of hypertension in Iran during different periods.[1,5,6] It seems that between 2000 and 2007, the prevalence of hypertension did not change, but control of hypertension increased among individuals with hypertension.[1] Although awareness, treatment, and control of hypertension significantly improved from 2001 to 2007, almost half of adults with hypertension did not have controlled blood pressure.[2,7] As hypertension plays an important role in cardiovascular diseases (CVD), the Isfahan Healthy Heart Program (IHHP), a community-based intervention program, was designed and implemented to prevent CVD and control its related risk factors by promoting healthy lifestyle.[8] The IHHP used high risk intervention strategies on general population to prevent CVD. This study aimed to estimate the prevalence and control of age-adjusted hypertension among persons over 18 years of age and to determine their relationship with socioeconomic disparities in Iranian population.

Materials and Methods

As a secondary analysis of the IHHP, this study was conducted by Isfahan Cardiovascular Research Center (Isfahan, Iran). Full details of the program have been reported elsewhere.[9] Data of the last phase (2007) was used in this study. The methods were in accordance with ethical standards of the ethics committee of Isfahan Cardiovascular Research Center. Trained interviewers completed questionnaires for each subject. The questionnaire contained demographic information, lifestyle habits,[10] medical history, and consumption of relevant medications especially antihypertensive agents. Subsequently, the participants were invited to certain health centers where physical examination and blood sampling (after 12-14 hours of fasting) were carried out.[11]

Marital status, education level, occupation, and income were considered as socioeconomic factors. Based on the Iranian education system, education was categorized as 0-5, 6-12 and more than 12 years. Monthly incomes of less than 300000, 300000 to 500000, higher than 500000 were considered as low, middle, and high, respectively. Since the definition of marriage varies according to different cultures, we categorizes the participants only as married and single (including separated, divorced, and widowed).

Blood pressure was calculated by averaging two blood pressure readings taken during the physical examination in the IHHP examination center.[1] Hypertension was defined as having systolic blood pressure (SBP) ≥ 140 mmHg, having diastolic blood pressure (DBP) ≥ 90 mmHg, or taking antihypertensive medications.[1] Controlled hypertension was defined as SBP < 140 mmHg and DBP < 90 mm Hg among hypertensive patients. The prevalence of hypertension and controlled hypertension was analyzed based on demographic factors (sex, age, marital status, education level, and family income) and health factors (diabetes and obesity).

Univariate t-tests were used to assess significant differences between groups. All significance tests were two-sided (level of significance = 0.05). Multivariate regression tests were used to determine prognostic factors for hypertension and controlled hypertension.

Results

The prevalence of hypertension and controlled hypertension among our participants was 18.9% and 20.9%, respectively. In 2007, there were significant relations between the prevalence of hypertension and age, marital status, education, income, diabetes, and obesity (Table 1). The prevalence of hypertension increased with increasing age and decreased with higher education and income level. Diabetic subjects had a significantly higher prevalence of hypertension than those without diabetes (51.9% vs. 15.3%). A similar difference was observed between obese and non-obese individuals (32.7% vs. 14.3%).

The overall age-adjusted prevalence of controlled hypertension among hypertensive subjects was 20.9% (Table 2). Unemployed 19-44 year-old individuals with higher education had a lower prevalence of controlled hypertension than older subjects. The prevalence of controlled blood pressure in women was significantly higher than men (29.2% vs. 12.7%; P = 0.001). Obese and non-obese participants did not have a significant difference in terms of controlled hypertension (21.5% vs. 20.2%).

Univariate analysis showed that poor control of hypertension was related only with employment among all social factors. Middle-income patients had approximately two times higher probability to have controlled hypertension than uncontrolled hypertension (unadjusted odds ratio: 1.99; 95% confidence interval: 1.2-3.31).

Multivariate logistic regression showed older patients (≥ 65 years old) to have more than fifteen fold increased risk for hypertension than younger patients (adjusted odds ratio: 14.96; 95% confidence interval: 11.11-20.14).

Table 1. Sociodemographic characteristics of the participants with controlled and uncontrolled hypertension

Characteristics	Uncontrolled hypertension		Controlled hypertension	
	n (%)	OR (95%CI)	n (%)	OR (95%CI)
Sex				
Female	404 (17.6)	Reference	116 (29.2)	Reference
Male	404 (18.0)	1.02 (0.88-1.19)	51 (2.7)	0.35 (0.25-0.51)*
Age (years)				
19-44	227 (7.2)	Reference	27 (12.0)	R
44-64	341 (35.4)	7.10 (5.88-8.59)	77 (23.0)	2.19 (1.36-3.52)**
≥ 65	240 (59.6)	19.09 (15.01-24.28)*	63 (26.5)	2.64 (1.61-4.33)*
Marital Status				
Married	660 (19.2)	Reference	133 (20.5)	Reference
Single	148 (13.6)	1.51 (1.25-1.83)*	34 (23.0)	1.16 (0.76-1.78)
Education (years)				
0-5	486 (30.5)	Reference	110 (22.9)	Reference
6-12	235 (11.5)	0.29 (0.25-0.35)	42 (18.1)	0.74 (0.50-1.11)*
> 12	85 (9.6)	0.24 (0.19-0.31)	15 (17.9)	0.73 (0.40-1.33)
Employment				
Housewife	381 (19.7)	Reference	109 (29.1)	Reference
Manual jobs	120 (12.8)	0.59 (0.48-0.75)*	8 (6.7)	0.17 (0.08-0.37)*
Non-manual jobs	129 (15.6)	0.75 (0.60-0.93)	16 (12.5)	0.35 (0.19-0.62)
Retired	134 (53.2)	0.27 (0.27-1.37)	29 (22.1)	0.57 (0.37-0.89)**
Unemployed	32 (11.5)	-	2 (6.3)	-
Student	5 (1.9)	-	1 (20.0)	-
Family income				
Low	619 (19.5)	Reference	122 (19.9)	Reference
Middle	141 (14.7)	0.71 (0.580-0.87)	37 (26.4)	1.44 (0.94-2.20)
High	46 (12.2)	0.57 (0.42-0.79)	8 (18.2)	0.89 (0.41-1.97)
Obesity				
No	520 (14.3)	Reference	104 (20.2)	Reference
Yes	269 (32.7)	2.90 (2.44-3.45)*	57 (21.5)	1.58 (0.75-1.55)

OR: Odds ratio; CI: confidence interval * P value obtained from chi-square test.
** Data expressed as OR (95% CI) was obtained from univariate logistic regression

Table 2. Associations between social factors and controlled hypertension among the studied population

Variable	Uncontrolled hypertension		Controlled hypertension	
	OR (95% CI)	P	OR (95% CI)	P
Sex				
Male/female	2.05 (1.24-3.39)	0.005	0.32 (0.12-0.93)	0.036
Age (years)				
19-44	Reference	Reference	Reference	Reference
44-64	5.29 (4.25-6.59)	< 0.001	2.20 (1.29-3.74)	0.004
≥ 65	14.96 (11.11-20.14)	< 0.001	3.36 (1.80-6.29)	< 0.001
Marital status				
Married vs. single	0.93 (0.73-1.19)	0.582	0.66 (0.40-1.10)	0.108
Education (years)				
0-5	Reference	Reference	Reference	Reference
6-12	0.88 (0.70-1.11)	0.286	1.36 (0.83-2.25)	0.228
> 12	0.89 (0.63-1.26)	0.512	1.48 (0.67-3.30)	0.332
Income				
Low	Reference	Reference	Reference	Reference
Middle	1.06 (0.83-1.35)	0.662	1.99 (1.2-3.31)	0.008
High	1.00 (0.68-1.47)	0.986	1.45 (0.58-3.62)	0.424
Job				
Housewife	Reference	Reference	Reference	Reference
Manual jobs	0.57 (0.33-0.96)	0.035	0.67 (0.22-2.05)	0.477
Non-manual jobs	0.52 (0.31-0.89)	0.017	1.04 (0.34-3.18)	0.944
Retired	-	-	-	-
Unemployed	-	-	-	-
Student	-	-	-	-
Comorbid disease				
Obesity	2.34 (1.91-2.87)	< 0.001	0.96 (0.65-1.42)	0.842

OR: Odds ratio; CI: confidence interval
Data expressed as OR (95% CI) was obtained from multivariate logistic regression adjusted for other variables. Variables entered in the model were sex and age in the first step and marital status, educational level, income, job, diabetes, and obesity in the second step.

Discussion

The results of this study demonstrated significant relationships between socioeconomic factors, such as income and education, and controlled hypertension. We found older housewives with lower education to have a greater tendency to control their hypertension. On the other hand, obesity and diabetes were not related with controlled hypertension. Unlike our results, other studies showed controlled hypertension was much less common among older persons and ex-smokers.[12]

In the present study, controlled hypertension was more common among subjects with middle income. However, in contrast with other studies, we failed to establish a significant relationship between income and controlled hypertension. A previous research suggested patients at higher income level to have better awareness and treatment.[13] Apparently, better awareness and control of hypertension have no strong relationship with income among Iranian population. According to our findings, lower level of education (e.g. having primary school degree) was associated with awareness about control of hypertension. This is justifiable considering the role of mass media in improving self-care and self-awareness among the target audience. Controlled hypertension was more common among subjects aware of their hypertension diagnosis and those who undertook lifestyle modification.[12] Tian et al. reported controlled hypertension to be much less common among older persons and ex-smokers.[12]

Many studies have shown interactions between blood pressure and socioeconomic factors, lifestyle, and female hormones. Improved lifestyle following the implementation of IHHP interventions[14] resulted in significantly better awareness, treatment, and control of hypertension in all groups with different body mass indexes (BMI).[1] Nevertheless, Khosravi et al. emphasized on the necessity of further educational programs on hypertension control for Iranian youth.[1] Additionally, the First National Health and Nutrition Examination Survey revealed that compared with younger hypertensive individuals, older patients have a lower control rate despite being equally likely to be treated.[15-17] On the contrary, another study reported higher awareness and control rates among older hypertensive people and found patients of younger age to be under-treated.[18] Therefore, close monitoring of blood pressure and relevant adjustment of ntihypertensive treatment are necessary to reduce the risk of cardiovascular events in patients.[19]

Obesity seems to have be associated with uncontrolled hypertension among male hypertensive patients of higher age. In women, on the other hand, abdominal obesity (high waist circumference) plays a major role.[20] In fact, a strong relationship between decreased abdominal obesity and controlled hypertension has been reported specifically in women.[21] Many studies proposed the benefits of comprehensive programs to improve blood pressure control after identification, follow-up, and lifestyle modification in hypertensive subjects.[22]

Conclusion

As current control rates for hypertension in Iran are clearly unacceptable, lifestyle modifications, i.e. maintaining a healthy body weight, adopting a diet rich in fruits, vegetables, and low-fat dairy products with reduced levels of saturated and total fat, reducing sodium intake, and participating in regular aerobic physical activity, are recommended in all social groups.

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Conflict of Interests

Authors have no conflict of interests.

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Renal ablation for treatment of hypertension without Symplicity catheter: The first human experience

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Original Article

Abstract

BACKGROUND: Hypertension (HTN) treatment has remained insufficient. New modalities such as "Symplicity method" for the treatment of HTN are a priority, especially in patients with resistant hypertension. In this study, we describe our first experience with a novel percutaneous treatment modality, without using Symplicity catheter.

METHODS: 30 Patients who were resistant to at least three types of antihypertensive medical therapy were selected. Patients received percutaneous renal artery denervation, without Symplicity catheter method, and were followed up for 1 week, 1, 3, and 6 months later after treatment. Ambulatory 24-hour blood pressure (BP) Holter was performed 1 week before intervention and after 1 month. The primary outcome was change in 24-hour ambulatory BP and change in office and home-based BP measurements.

RESULTS: The mean age of the studied patients was 52 ± 15.4 years and 43.3% (n = 13) were female. Systolic and diastolic BP at baseline was 163 ± 17.2 and 95 ± 8.2 mmHg, respectively. Patients took 3.6 ± 1.3 hypertensive medications. Systolic and diastolic BP at 1-week, 1-month, 3-month and 6-month after renal denervation significantly decreased compared to the baseline ($P < 0.0001$). Average BP derived from 24-hour ambulatory BP monitoring changed in parallel with office-based BP measurements. Most of patients (50%) who underwent renal denervation had reductions of 10 mmHg or greater in systolic BP and 56.7% of them had reductions of 5 mmHg or greater in diastolic BP. 33.3% of patients also achieved the target of systolic BP less than 140 mmHg and 60% achieved the target of diastolic BP less than 90 mmHg. No patients showed vascular damage at final angiography.

CONCLUSION: Catheter based renal ablation was associated with a significant reduction in both systolic and diastolic BP, on top of maximal medical therapy, which persisted throughout 6 months follow-up in the first-in-man study without the Symplicity catheter.

Keywords: Renal Denervation, Resistant Hypertension, Catheter

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Introduction

About 30% of populations in the world have hypertension (HTN). Furthermore, its prevalence is increasing in developing countries. HTN is known as "silent killer" and often is asymptomatic. It is a major risk factor for death worldwide. HTN is also a financial problem for governments and their population.[1] HTN treatment has remained insufficient. About 30% of patients with HTN were aware of their disease. Of those aware patients, about 60% were treated. Of those patients treated, about 40% had blood pressure at optimal level.[2] Therefore, new modalities for the treatment of HTN are a priority, especially in patients with resistant HTN. Only 10-15% of patients with resistant HTN are optimally treated.[3]

Sympathetic nerves of renal arteries are essential for occurrence of systemic HTN. Old methods for denervation such as radical surgery for sympathetic nerves were associated with high morbidity/mortality and many complications.[4] Nowadays, catheter-based approach for disruption of renal sympathetic nerves is done[5-9] without long term complications. Percutaneous renal denervation resulted in meaningful reduction in systolic and diastolic blood pressure during medical therapy,

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which persisted for 12 months follow-up in the first human study. The recently published trial "Symplicity 2", which was the first randomized controlled study in this field, confirmed the findings of the first human study. In this study, we wanted to do the first Iranian experience regarding this novel treatment modality and the first human experience of renal ablation without Symplicity catheter.

Materials and Methods

This study was approved by the ethical committee at Vice Chancellor of Research in Isfahan University of Medical Sciences and all patients provided written informed consent. This trial was registered with IUMS.ac.ir number 391001.

Screening was done at HTN clinic in Chamran Heart Hospital, a large teaching, referral heart hospital. Patients were asked to record triple daily automated home blood pressure measurements and to document drug compliance for 10 days before ambulatory 24-hour blood pressure Holter monitoring. Patients were treated with the renal denervation procedure between September 2011 and January 2012, with subsequent 6 months follow-up.

Outpatient (OPD) assessment included patient's characteristics, vital sign, past medical history, physical examination, number and type of medications, blood chemistries (like creatinine and potassium) and ambulatory 24-hour blood pressure Holter. We did follow-up assessments at 1 week and 1, 3, and 6 months, consisted of office blood pressure measurements, surveillance for adverse events, 24-hours blood pressure Holter, serum creatinine and HTN drugs. Office blood pressure measurements were performed in a seated position in at least two visits (1st visit and 2 weeks later) in both arms. Ambulatory 24-hour blood pressure Holter was performed 1 week before intervention and at 1 month follow-up.

Patients aged at least 15 years were eligible for inclusion, with a systolic blood pressure of 160 mmHg or more (≥ 150 in patients with type-2 diabetes) and/or diastolic blood pressure of 90 mmHg or more, despite at least three antihypertensive drugs or confirmed intolerance to medication. The renal artery anatomy was considered suitable in case of a vessel diameter of ≥4 mm and ≥20 mm length, no significant stenosis, no previous renal artery intervention and no more than one main renal artery.

Exclusion criteria included patients with any known secondary hypertension and a glomerular filtration rate estimated at ≤ 45 ml/min/1.73m² and patients with a history of unstable angina or cerebrovascular accident in the previous 6 months or pregnancy. We did not exclude patients with type 1 diabetes, implantable cardioverter defibrillations and advanced congestive heart failure. Patients whose all blood pressure measurements were below the enrolment criteria for blood pressure in 24-hour BP Holter monitoring were excluded.

Patients were pretreated with 2 mg midazolam and 25 mg pethidine. Using local anesthetics, cannulation of the femoral artery was performed by the standard Seldinger technique. Firstly, a 7 Fr sheath was introduced and heparin was given using an intravenous bolus of 10 IE/Kg with a target activated clotting time (ACT) ≥ 250 S. Then, using an 8 Fr coronary sinus (CS) sheath and a 6 Fr soft tip Rt Judkins catheter, a steerable catheter with radiofrequency energy electrode tip was delivered into the renal artery. Before starting the denervation, 50 μg fentanyl and at least 1 cc ketamine were given to patient by anesthesiologist. We applied discrete, radiofrequency ablations lasting 2 minutes each and of 15 watts or less to obtain six ablations separated both longitudinally and rotationally with a minimum of 5 mm distance in between and with a pullback from distal to proximal within each renal artery. During ablation, the catheter system monitored tip temperature and impedance, altering radiofrequency energy delivery in response to a predetermined algorithm. A non-selective renal angiography was performed before and after the procedure. Intraprocedural diffuse visceral pain restricted to the duration of energy delivery was managed with intravenous narcotics.

After procedure till one month, changes to baseline doses of all antihypertensive drugs were not allowed, unless medically judged necessary. At 1 month after the procedure, we repeated ambulatory 24-hour blood pressure monitoring with readings taken every 30 minutes in day time and every 60 minutes at night time. We calculated average values obtained during the day and night for every patient. Patients were instructed to remain adherent to their prescribed antihypertensive drugs.

The primary outcome was change in 24-hour ambulatory blood pressure and change in office and home-based blood pressure measurements. Secondary end points were procedural safety and composite cardiovascular end points such as myocardial infarction, cerebrovascular accidents, and congestive heart failure.

Statistical analysis

Continuous variables were described with mean ±

standard deviation. Other variables were reported as numbers (percentage). For comparison within different time points, a paired t-test was used.

Role of the funding source

The study was designed by Chairperson of Hospital and Cardiology Department of Isfahan University of Medical Sciences and the sponsor (Chamran Hospital). Procedure was done and data were monitored, collected and managed by an interventional fellow. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between September 2011 and January 2012, of 45 patients with resistant hypertension who assessed for eligibility, 12 (27%) patients did not meet the inclusion criteria and were not entered the study (7 subjects because of blood pressure < 160 mmHg at baseline visit when it was confirmed that patients took drugs for two weeks, and 5 ineligible anatomy). Three (6%) patients also did not enter the study because of not consenting to participate in the trial. Finally 30 (67%) patients underwent renal denervation and were followed up for 6 months (Figure 1).

Table 1 shows baseline characteristics of the patients. The mean age of the studied patients was 52 ± 15.4 years and 43.3% (n=13) were female. Systolic and diastolic blood pressure at baseline was 163 ± 17.2 mmHg and 95 ± 8.2 mmHg, respectively. Patients took, on average, 3.6 ± 1.3 hypertensive medications. Most of them [43 (96%)] received angiotensin converting enzyme inhibitors or angiotensin receptor blockers.

All patients had 24-hour ambulatory blood pressure monitoring at baseline and at follow-up. The mean of systolic and diastolic blood pressure were decreased after renal denervation compared with mean of blood pressure at baseline (Figure 2). Table 2 shows the mean of blood pressure during 6 months of followed-up. Systolic and diastolic blood pressure at 1-week, 1-month, 3-month and 6-month after renal denervation significantly decreased compared to the baseline ($P < 0.0001$).

Mean of reduction of office blood pressure at 1 week, 1, 3, and 6 months after renal denervation is shown in figure 3. As shown, systolic blood pressure, 1 week after procedure was further reduced at 1, 3, and 6 months. Similarly 1 month after renal denervation diastolic blood pressure was further reduced through subsequent assessments up to 6 months. Thus, average blood pressure derived from 24-hour ambulatory blood pressure monitoring changed in parallel with office-based blood pressure measurements.

Figure 4 shows the proportions of patients achieving defined thresholds of systolic and diastolic blood pressure reduction at 6 months. Most of patients (50%) who underwent renal denervation had reductions of 10 mmHg or greater in systolic blood pressure and 56.7% of them had reductions of 5 mmHg or greater in diastolic blood pressure. 33.3% of patients also achieved the target of systolic blood pressure less than 140 mmHg and 60% achieved the target of diastolic blood pressure less than 90 mmHg.

No patients showed vascular damage at final angiography; however, renal angiographic studies identified focal renal artery irregularities immediately after radiofrequency (RF) energy delivery, none of which was flow limiting at the end of procedure.

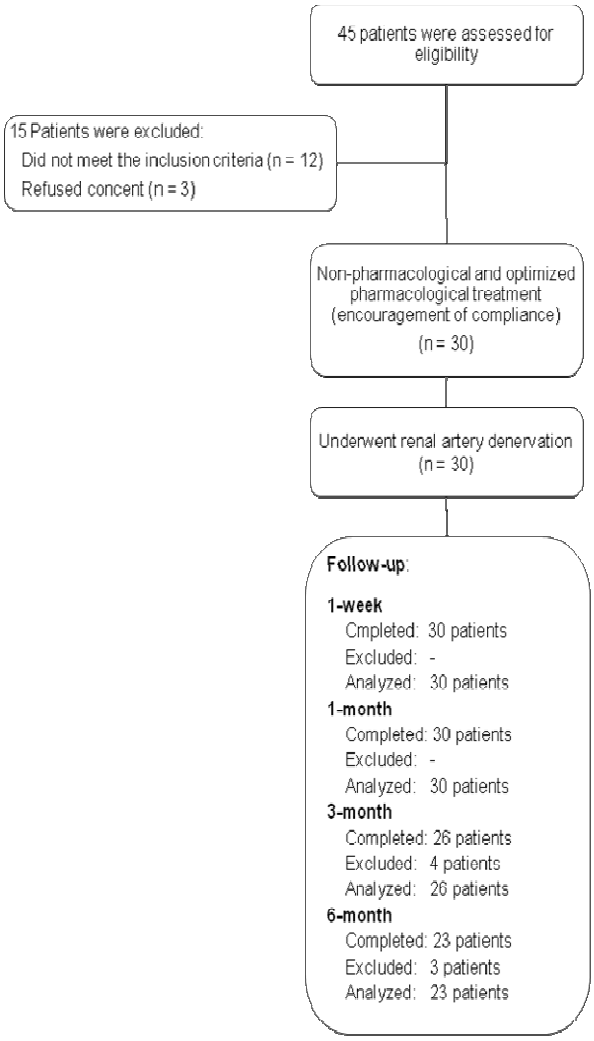

Figure 1. Study profile

Table 1. Baseline characteristics of 30 patients with resistant hypertension who underwent renal denervation

Age (years)	52 ± 15.4
Sex	
Male	17 (56.7)
Female	13 (43.3)
Body mass index	30.6 ± 4.7
Medical history	
Coronary artery disease	16 (54.3)
Type 2 diabetes	5 (17.7)
Hyperlipidemia	8 (26.7)
Cerebrovascular accident	2 (6.7)
Smoking	8 (26.7)
Alcohol use	0
Congestive heart failure	4 (13.3)
Baseline systolic blood pressure (mmHg)	163 ± 17.2
Baseline diastolic blood pressure (mmHg)	95 ± 8.1
K	4.2 ± 0.56
Number of antihypertensive medications	3.6 ± 1.3
Drug history	
Beta blockers	3 (10)
Alpha blockers	8 (26.7)
Vasodilators	2 (6.7)
Diuretics	19 (63.3)
Calcium channel blockers	19 (63.3)
ACE inhibitors/ARBs	27 (81.8)
Serum creatinine (µmol/L)	1 ± 0.12

Data are presented as mean ± SD or number (percent)

In total, an average of 5.2 ± 1 RF ablations was performed in the left renal artery, and 5.8 ± 1 RF ablations in the right renal artery. The mean use of contrast was 80 ± 20 ml. Mean fluoroscopy time was 11 ± 2 minutes. The mean time of the procedure (i.e. from puncture of the femoral artery to closure) was 38 ± 8 minutes. After the procedure, there was no change in serum creatinine (1 ± 0.12 µml/L compared with 1 ± 0.11 µml/L; P = 0.93). No changes in medication was noted at 1-month follow-up; however; 18 (60%) of patients who underwent renal ablation had drug reductions prior to 6-month follow-up and none of them had drug increases prior to 6-month. In general, there was no a per-procedural complication or complications during follow-up.

Table 2. Comparison of 24-hour baseline ambulatory blood pressure monitoring with follow-up period in 30 patients with resistant hypertension who underwent renal denervation

	SBP (mmHg)	DBP (mmHg)
Baseline (n=30)	163 ± 17.2	95 ± 8.1
1-week (n=30)	136.2 ± 13.1	85.3 ± 8.9
P	< 0.0001	< 0.0001
1-month (n=30)	137.8 ± 8.5	80.7 ± 8.2
P	< 0.0001	< 0.0001
3-month (n=26)	136.4 ± 9	81.8 ± 6
P	< 0.0001	< 0.0001
6-month (n=23)	145.7 ± 10.1	86.3 ± 5.6
P	< 0.0001	< 0.0001

Data are presented as mean ± SD; SBP: Systolic blood pressure; DBP: Diastolic blood pressure

P-values calculated by paired samples t-test compared to the baseline

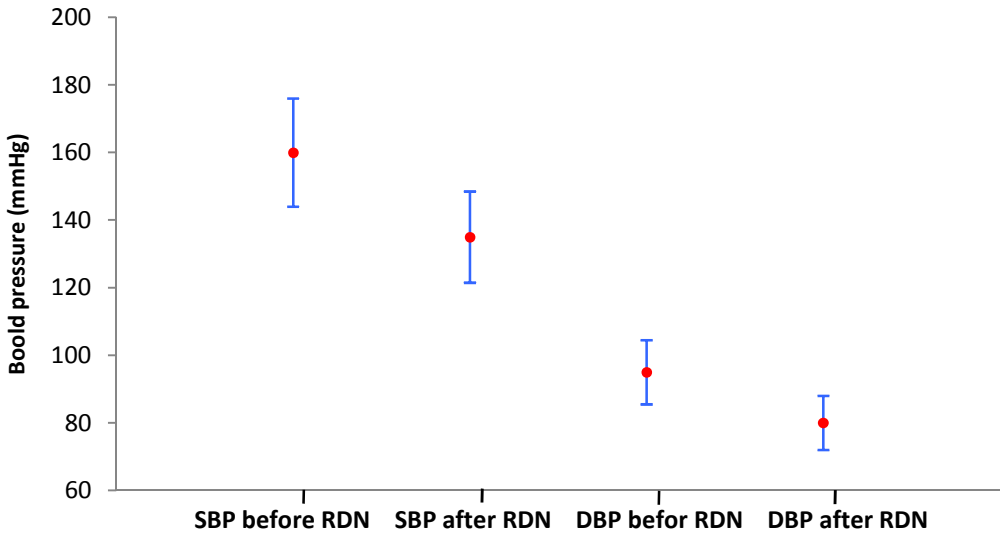

Figure2. Mean of 24-hour ambulatory blood pressuremonitoring for systolic and diastolic blood pressure before and after renaldenervation in 30 patients with resistant hypertension
RDN: Renaldenervation; SBP: Systolic blood pressure; DBP: Diastolicblood pressure

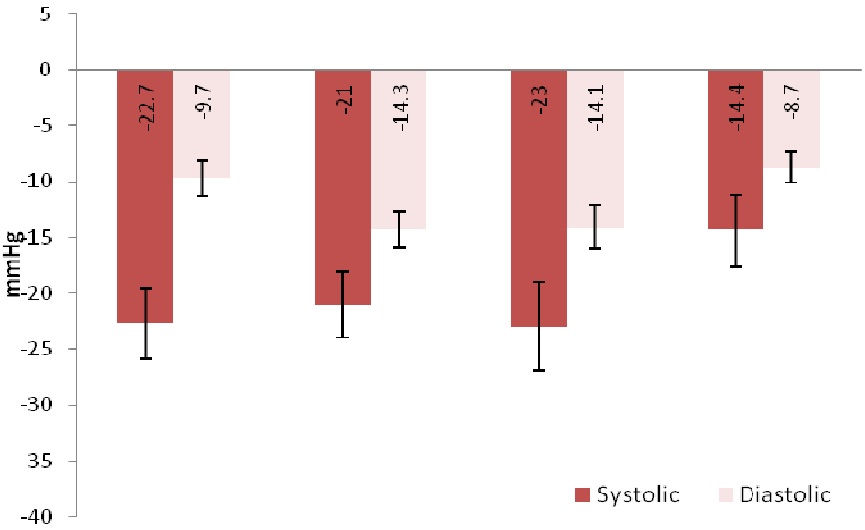

Figure 3. Change in office-based measurements of systolic and diastolic blood pressures at 1 week, 1 month, 3 months, and 6 months for renal denervation. Error bars are Standard Error

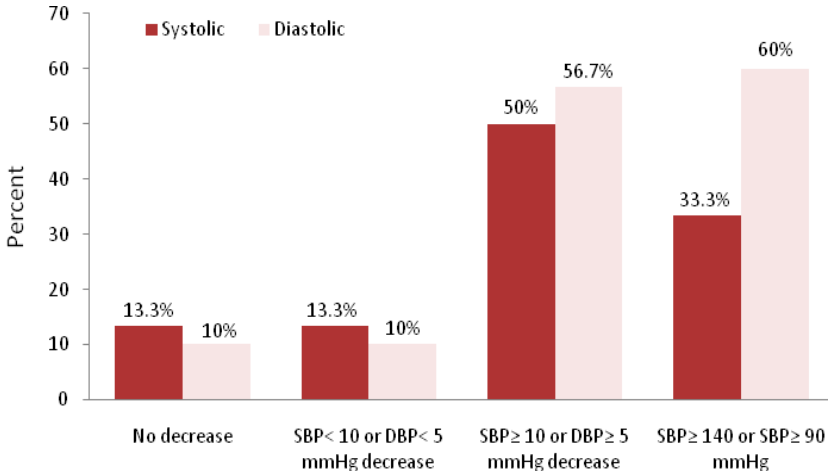

Figure 4. Proportion of blood pressure status after renal denervation after 6 months based on 24-hour ambulatory blood pressure monitoring (n = 30)
SBP: Systolic blood pressure; DBP: Diastolic blood pressure

Discussion

Uncontrolled hypertension is a common clinical condition and causes significant morbidity and mortality such as cardiovascular and cerebral events. Thus, appropriate control of HTN result in prevention of cardiovascular morbidity and even mortality. A new catheter system has been developed, making the endovascular approach to renal denervation an attractive therapeutic option in patients with resistant hypertension. The "Symplicity Catheter System" (Medtronic-Ardian) was the first and only system available.[3] Previous studies about radiofrequency renal-nerve ablation in patients with resistant hypertension showed the feasibility and safety of it and reported encouraging blood pressure reductions, with no major complications due to the technique.[4-7] In our study, novel catheter-based treatment of resistant hypertension without using of "Symplicity" catheter was assessed and to the best of our knowledge this

is the first human experience. Our results showed that after renal denervation, systolic and diastolic blood pressure decreased compared with blood pressure at baseline. Moreover, systolic and diastolic blood pressure at 1-week and 1, 3 and 6 months after renal denervation significantly decreased compared to baseline. Reductions of 10 mmHg or greater in systolic blood pressure and 5 mmHg or greater in diastolic blood pressure occurred in 50% and 56.7% of patients, respectively.

The Symplicity Catheter System as a new approach to renal denervation was studied in several trial, the first study, a cohort study, was done on 50 patients with resistant hypertension, renal sympathetic ablation was achieved using a radiofrequency ablation catheter inserted through the femoral artery and selectively engaging the renal artery bilaterally (Symplicity, Ardian Inc., Palo Alto, Calif, USA). This study showed safety of denervation of renal sympathetic nerve endings. However, two complications were occurred but not related to ablation itself (complication of site of puncture). Then authors carried out a randomized controlled trial, the Symplicity HTN 2 study, on 106 patients with resistant hypertension, to compare the antihypertensive efficacy of this procedure plus drug treatment with that of drug treatment alone. They reported that catheter-based renal denervation can safely be used to substantially reduce blood pressure in treatment resistant hypertensive patients with a low incidence of immediate per-procedural complications and short- and medium-term renal and vascular complications.[5] In another study in 2010, a total of 11 patients who were resistant to at least three types of antihypertensive medical therapy, underwent treatment by renal artery radiofrequency ablation using Symplicity catheter and concluded that catheter-based renal denervation seems an attractive novel minimally invasive treatment option in these patients, with no serious adverse events per-procedurally or at follow-up.[7]

Our findings showed that a significant reduction in blood pressure, based on 24-hour blood pressure monitoring, can be achieved with catheter-based renal denervation in patients with resistant hypertension which was uncontrolled despite treatment with three or more antihypertensive drugs. Also no vascular damage at angiography or per-procedural complications was observed. This finding supports the results of previous investigations[4-7] even though, the procedure was different in present study, which was catheter-based treatment of resistant hypertension without using of Symplicity catheter, compared to other studies that used Symplicity catheter.

The main limitation of present study is that this was not a randomized controlled trial and factors such as regression to the mean and Hawthorne effect need to be considered in the interpretation of these results, because there is no control group with which to make evaluations about blood pressure responses over time. On the other hand, patients in our study were followed for 6-month whereas the efficacy of this new treatment should be investigated in long-term follow-up not only in the short-term. It seems randomized controlled clinical trials are required to confirm this primary experience in long-term follow-up. Accordingly, renal artery denervation without using of Symplicity catheter, which is not ready in any cathlab and is an expensive catheter, opens new opportunities for the treatment of patients with resistant hypertension and further researches are needed to identify groups of patients who might benefit from this intervention such as patients with milder forms of hypertension, patients intolerant to medication and in several other conditions.

In conclusion, previous studies in catheter-based renal denervation represented an advanced new technique to effectively reduce blood pressure in patients with resistant hypertension. Similarly, findings of this study indicated that renal nerve ablation achieved by a catheter-based approach without using of Symplicity catheter has the potential to improve blood pressure control in these patients, simpler and less expensive. For example, in our country, each Symplicity catheter is about $300 while the catheters for our technique are less than $30. The Symplicity system is about $30000 but we did renal nerve ablation by radiofrequency ablation system of our electrophysiology (EP) cathlab. However, randomized controlled clinical trials are needed to compare these two techniques.

Acknowledgements

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Conflict of Interests

Authors have no conflict of interests.

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Alteration in unhealthy nutrition behaviors in adolescents through community intervention: Isfahan Healthy Heart Program

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Original Article

Abstract

BACKGROUND: Primary prevention of chronic diseases has been suggested to initiate health promotion activities from childhoods. The impact of Isfahan Healthy Heart Program (IHHP), a comprehensive community trial, on unhealthy snacks and fast food intake changes was evaluated in Iranian adolescents between 2001 and 2007.

METHODS: Healthy Heart Promotion from Childhood (HHPC) as one of the IHHP interventional projects was conducted in adolescents aged 11-18 years, selected randomly by multistage random sampling. Isfahan and Najafabad districts were intervention areas (IA) and Arak district was reference area (RA). The baseline and post-intervention surveys were conducted on 1941 and 1997 adolescents, respectively.

Healthy lifestyle interventions were performed during the 2nd phase of the study targeting about 410000 students in urban and rural areas of the IA via education, environmental and legislation activities. Dietary intake was assessed annually using a fifty-item food frequency questionnaire in both communities.

RESULTS: The interaction of year×area demonstrated that the consumption of unhealthy snacks decreased significantly in middle school boys of RA compared to IA (P for interaction=0.01). However, middle school girls (P for interaction = 0.002) and both sexes of high school students in IA showed a significant reduction in fast food consumption against RA (P for interaction < 0.001).

CONCLUSION: The HHPC interventions made some improvement in fast food consumption. It did not show significant decrease regarding unhealthy snacks in adolescents. Proper and higher dose of interventions may be effective in achieving this goal.

Keywords: Nutrition, Dietary Behaviour, Adolescent, Lifestyle, Community Trial

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Introduction

Increasing evidence over the past 4 decades indicates that the progression of atherosclerosis begin early in life is affected by some modifiable and non-modifiable risk factors of cardiovascular diseases (CVD).[1-3] Furthermore, the patterns of behavioral and biological risk factors originate in early childhood and influence CVD risk factors in adolescence and usually persist until adulthood.[1-2]

Dietary behaviour modification has a main effect on the occurrence of chronic diseases and their risk factors.[3-5] Therefore, it has been suggested for primary prevention of chronic diseases, to initiate health promotion activities from childhood.[4] Moreover, a healthy dietary pattern in childhood is an important public health issue.[6] A previous study in Iran indicated that excess weight gain and its cardiometabolic outcomes were common in adolescents and it should be considered as a national health priority.[7] Unhealthy snacks consists of sausage, sandwiches, crisps and cheese balls, creamy wafers, cakes, chocolate and toffee were the

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most common snacks consumed by Iranian children and adolescents.[8]Among the reasons that led to the recent habit changes are the long time spent by women working outside homes, inexpensiveness of unhealthy food and their good taste.[9-11] Americans eat outside home four times per week and one third of American children and adolescents consume fast food one time per week,[12,13] while Iranian adults consume fast foods on average one time per week.[14] It seems Iranian adolescents consume fast foods more.

Since schools are the best place to work with children and adolescents, they are the best place for health promotion and lifestyle modification and for implementing favorable environmental changes through the availability of healthy foods and physical exercise.[15]

Several successful school-based health promotion programs were carried out in developed countries.[15-18] Therefore, Heart Health Promotion from Childhood (HHPC) project was performed as one of interventional projects of a comprehensive community-based program entitled Isfahan Healthy Heart Program (IHHP) with school-based approach[19] to improve lifestyle behaviour and cardiometabolic risk factors among children and adolescents. HHPC targeted students in middle and high schools. The current study focused on the impact of HHPC nutrition interventions on unhealthy dietary behaviour changes of Iranian adolescents.

Materials and Methods

IHHP was carried out by Isfahan Cardiovascular Research Center (ICRC) (a WHO Collaborating Center), and Isfahan Provincial Health Office, both affiliated to Isfahan University of Medical Sciences. Ethics committees of Isfahan University of Medical Sciences approved the study. IHHP was a quasi-experimental community trial with reference area and different types of evaluation.[20,21] The study was launched in 1999-2000 and conducted 2001-2007, in three phases as pre-intervention (baseline), intervention and post-intervention phase.[21] Written informed consent was obtained from the parents or legal guardians of students.

Design and participants: This study reports part of data of the HHPC project. The impact of all interventional projects in IHHP was reported before.[22] In the 1st phase, the baseline status was assessed on 2000 students in middle and high schools (1000 girls and1000 boys) aged 11-18 years, selected from Isfahan and Najafabad districts, as the intervention areas (IA) and Arak district as the reference area (RA) in 2001.[20,23] Both areas are industrial and located in the center of Iran with similar socio-economic and demographics. Recruitment was performed by multistage cluster random sampling method from 56 middle and high schools of different urban and rural areas. Sampling details were presented elsewhere.[19,23] Based on the results of the baseline study, multidisciplinary interventions were conducted during the 2nd phase (2002-2006) of the study in IAs, but not in Arak. Lifestyle behaviors were evaluated annually by questionnaires in IA and RA. Post-intervention outcomes comprising behaviour, physical and biochemical measurements were done similar to the 1st phase but on independent random sample in 2007. Process evaluation was done in the IA only.[24] Overall, 1941students in both communities were studied at baseline and 1997 students in post-intervention survey. Trained nurses carried out data collection.[23] The study design has been described elsewhere.[20,21]

Interventions: HHPC interventions' design was based on findings of the baseline survey and needs assessment considering the existing health and human resources.[22] Target groups were middle and high school students, their parents and teachers in urban and rural areas of IA. Healthy nutrition was one of the main fields of interventions in the program which was performed based on educational, environmental and legislative strategies. The details of IHHP interventions were presented elsewhere.[21,22] In the beginning, HHPC activities were carried out in 1769 (45%) schools in IA; however, until 2004 it increased to3654 (92.9%) schools with about 410000 students of Isfahan and Najaf-Abad.[25]

Briefly, HHPC public education was done through mass media, pamphlets, booklets, face-to-face meetings, proposing role models among students, arranging different competitions with the subject of healthy heart, serving healthy snacks, establishing healthy heart buffets, reinforcing healthy eating habits in schools, and gathering parents at least yearly to train healthy nutrition.[19]

Dietary assessment: The common foods consumed in Iran were assessed by a validated 50-item-food frequency questionnaire (FFQ). The FFQ was adopted from the Non communicable Disease Intervention program questionnaire.[26] Four experts in nutrition and pediatrics assessed the content validity of the FFQ. Moreover, its criterion validity was evaluated by 24-hour recall questionnaires that were completed three times. The criterion validity

was acceptable for unhealthy snacks and fast food consumption. Unhealthy snacks included salty, sweeten and fatty snacks that were assessed by4 questions and frequency consumption of fast foods included sausages, pizza and hamburgers were evaluated by 3 questions.

Evaluation: Evaluation consisted of impact, outcome and process types that were done as integrated elements of the program. The detail of evaluation was described previously.[21,24,25] The impact of interventions on dietary behaviour was carried out by implementing annual dietary surveys during 2001-2006 and the outcome evaluation was done at baseline (2001) and post-intervention (2007) phases. Both impact and outcome evaluations were performed on independent samples in both communities, while process evaluation was done only in IA during the study.[24] Following the request of Isfahan University of Medical Sciences for undertaking an external evaluation of the whole IHHP, all component of the program including implementation of interventions as well as all evaluation studies was done by international experts.[25]This study reports the results of impact evaluation on unhealthy nutrition behaviors.

Statistical analysis: The mean frequency consumption of foods was compared between pre- and post-intervention in independent sample surveys using t-test and in terms of frequency of students by chi-square. The year × area interaction was determined by General Linear Model-univariate analysis to compare variable changes in intervention vs. reference community by adjustment for residency (urban/ rural). Data were analyzed using the SPSS statistical package version 15.0 for windows (SPSS Inc., Chicago, USA).The significance level was set at $P < 0.05$.

Results

The frequency of studied population in IA were 969, 1000, 629, 518, 389, and 972 subjects in 2001, 2002, 2003, 2004, 2005 and 2007, respectively. In RA, it was 977, 999, 798, 707 and 1020 subjects, in 2001, 2002, 2003, 2004, and 2007, respectively. Due to budget limitations, the repeated study was not done in RA in 2005. The basic characteristics of adolescences in 2001 and 2007 are presented in table 1. The mean age of students was not significantly different across the years. The differences were not significantly significant at baseline and final surveys in IA and RA based on sex, grade as well as place of residence.

Table 2 indicates the mean of unhealthy food consumption in IA vs. RA based on the school grade during the study. There was no significant difference between unhealthy snacks consumption in pre- and post- intervention phases in both sexes of middle and high school students in IA as well as high school students of RA. However, it showed a significant decrease in middle school boys ($P = 0.001$) and girls ($P < 0.001$) of RA. Furthermore, the interaction of year ×area demonstrated the consumption of these snacks decreased significantly in middle school boys of RA compared to IA (P for interaction=0.011).

Table 1. Basic characteristics of study population in intervention and reference area before and after intervention

	Baseline 2000-2001		Post-intervention 2007	
	Intervention	Reference	Intervention	Reference
Age (year)		Mean ± SD		
Middle school	12.92 ± 1.14	12.63 ± 1.11	13.17 ± 1.26	13.04 ± 1.15
High school	15.36 ± 1.02	15.36 ± 1.19	16.02 ± 1.00	15.85 ± 1.12
Sex		Frequency (%)		
Boy	501(51.7)	500(51.2)	467(48.0)	511(50.1)
Girl	468(48.3)	477(48.8)	505(52.0)	509(49.9)
Grade				
Middle school	500(51.6)	486(49.7)	524(53.9)	515(50.5)
High school	469(48.4)	491(50.3)	448(46.1)	505(49.5)
Residency				
Urban	613(63.3)	638(65.3)	857(88.2)	675(66.2)
Rural	356(36.7)	339(34.7)	115(11.8)	345(33.8)
Total	969	977	972	1020

In IA, mean of fast foods consumption had a significant reduction in middle school girls (P <0.001), in high school boys (P =0.002) and girls (P =0.008), while it increased significantly in both sexes of high school students in RA (in boys: P =0.026 and in girls: P =0.006). Moreover, it showed a significant reduction in middle school girls (P =0.001) and both sexes of high school students in IA vs. RA across the years (P <0.001). Figures 1 and 2 illustrate the trend of unhealthy snacks and fast food consumption (per week) based on sex and grade in IA vs. RA areas across years of study.

Table 2. The mean of unhealthy food consumption (per week) in intervention vs. reference area based on school grade between 2001 and 2007

	Intervention			Reference			Interaction P
	Baseline	Post-intervention	P	Baseline	Post-intervention	P	
	Mean±SD*	Mean±SD		Mean±SD	Mean±SD		
Unhealthy snacks (per week)							
Middle schools							
Boys	6.47 ± 0.29	6.46 ± 0.26	0.99	9.15 ± 0.31	7.700 ± 0.27	0.001	0.011
Girls	7.08 ± 0.28	6.61 ± 0.30	0.23	9.75 ± 0.29	8.26 ± 0.29	<0.001	0.079
High schools							
Boys	6.61 ± 0.32	6.27 ± 0.32	0.49	7.94 ± 0.30	7.98 ± 0.30	0.93	0.55
Girls	7.63 ± 0.32	7.10 ± 0.32	0.23	8.87 ± 0.31	9.10 ± 0.29	0.59	0.22
Fast foods(per week)							
Middle schools							
Boys	1.23 ± 0.09	1.11 ± 0.08	0.32	1.42 ± 0.09	1.44 ± 0.08	0.86	0.4
Girls	1.41 ± 0.08	0.92 ± 0.08	<0.001	1.17 ± 0.08	1.18 ± 0.08	0.98	0.002
High schools							
Boys	1.58 ± 0.09	1.13 ± 0.09	0.002	1.30 ± 0.09	1.54 ± 0.09	0.026	< 0.001
Girls	1.34 ± 0.08	1.04 ± 0.08	0.008	1.02 ± 0.08	1.33 ± 0.07	0.006	< 0.001

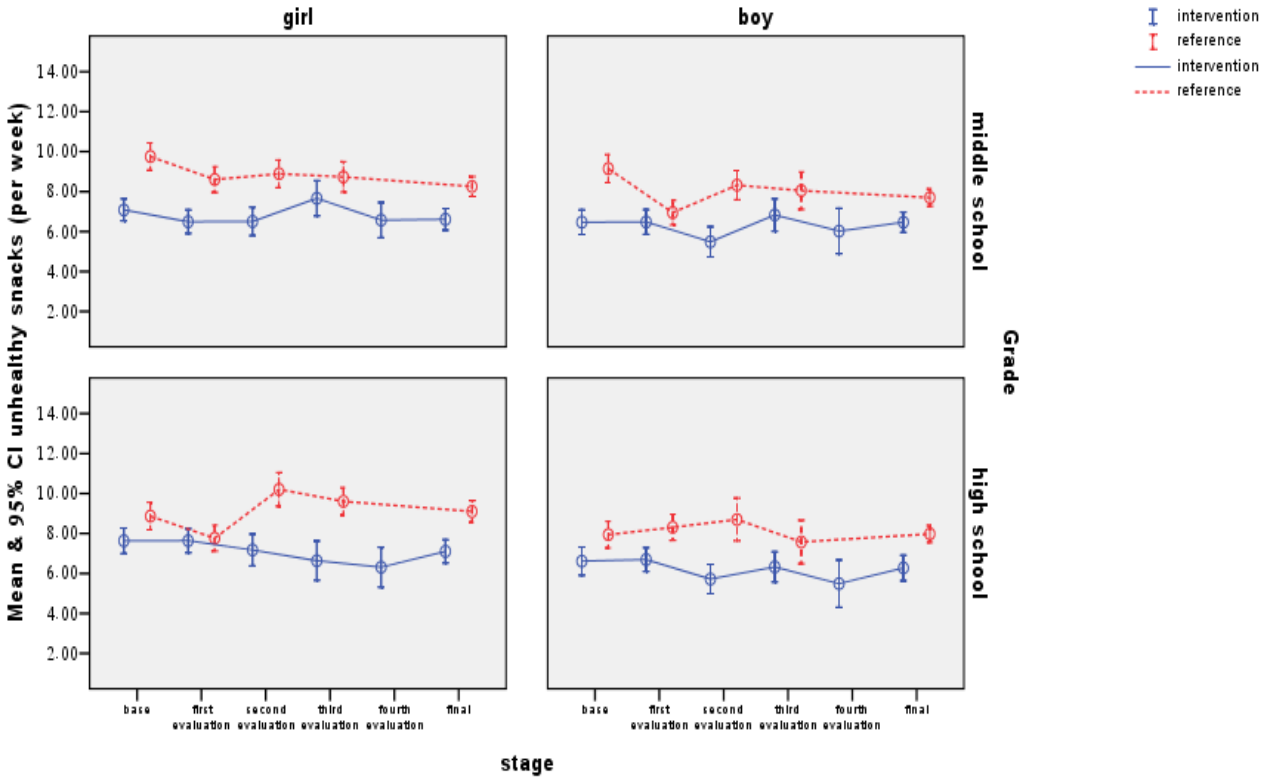

Figure 1. The trend of unhealthy snacks consumption (per week) based on sex and school grade in intervention vs. reference area between 2001 and 2007

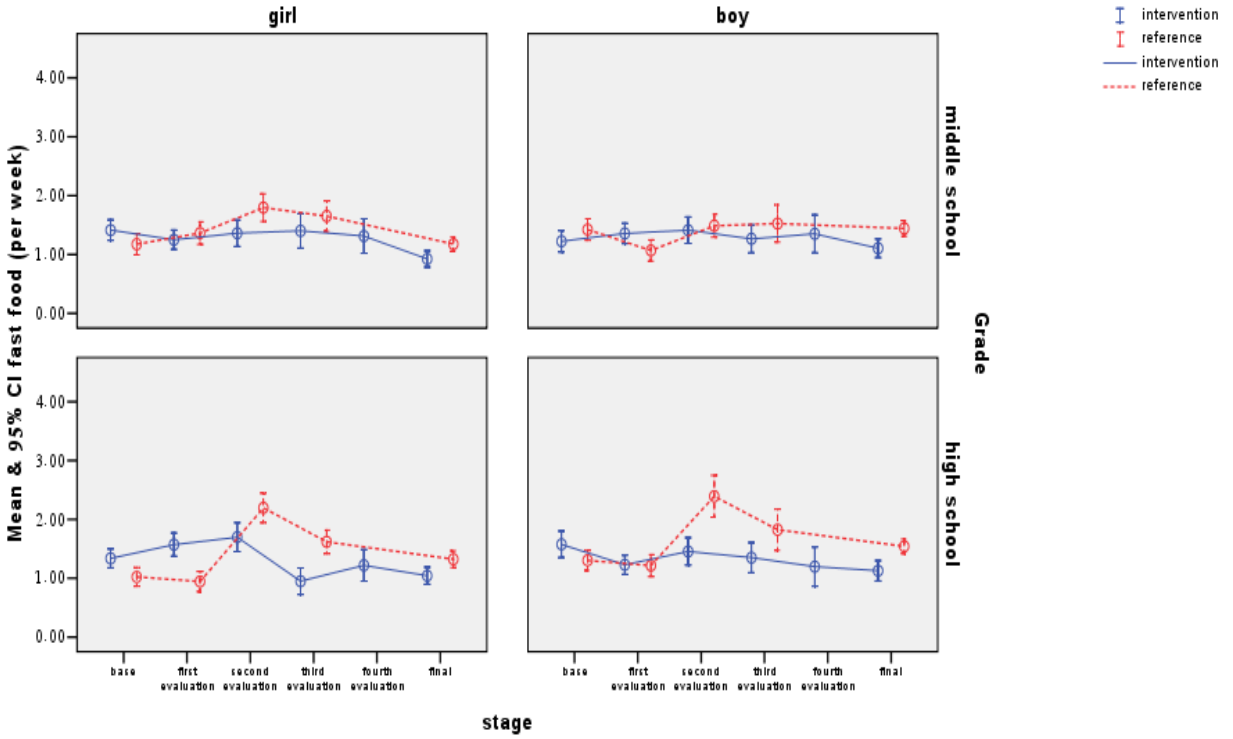

Figure 2. The trend of fast food consumption (per week) based on sex and school grade in intervention vs. reference areas between 2001 and 2007

Discussion

IHHP is the first community-based trial with quasi-experimental design and RA to assess the impact of comprehensive, multidisciplinary interventions on lifestyle improvement, and CVD and its risk factors prevention in a developing country setting. Our findings indicated that the HHPC, as one of IHHP intervention projects, made some positive changes in unhealthy dietary behaviors. There were no significant changes in unhealthy snacks consumption in middle and high school adolescents in IA vs. RA, except for unexpected reduction of unhealthy snacks in middle school girls of RA compared to IA, whereas fast food consumption showed a significant reduction in IA vs. RA in both sexes of high school students and middle school girls.

Lifestyle modification programs in other countries indicated contradictory findings.[27-37] A cohort study of dietary intake tracking in Mexican-American and white children aged 4 to 12 years found that dietary intake was steady over 8 years and was better in younger ages compared with older children.[27] It may be the purpose of not improving unhealthy snacks consumption in middle schools students in our study. Another study was done in elementary school children to ease obesity and improve lifestyle behaviors through nutrition education and serving lower fat and sodium lunch in intervention schools during 2 years. Although the lunch in these schools showed significantly less energy, fat, sodium, and more fiber, only sodium intake had significant difference in intervention vs. control schools.[34]This study concluded that dietary intake outside schools may be the cause of no differences between intervention and control schools.[34] Another study in adolescence from Tehran(Iran) indicated that there was no association between nutrition knowledge and behaviors,[8] the same as other countries.[38,39] Therefore, it seems that nutrition education and serving healthy food in schools could not improve nutrition behaviors of adolescents.

Obesity epidemic and nutrition transition is increasing in developing countries. Thus the non-significant improvement of unhealthy snacks consumption might be considered as favorable impact of interventions in IA. Conversely, the trend of fast food consumption was increased in all students' categories of RA. Although it was insignificant in some groups, it might be significant if our sample size was larger. Planet Health study in middle schools of Massachusetts communities which was focused on decreasing high-fat foods

consumption and increasing fruit and vegetable intake, illustrated only increase in fruit and vegetable consumption without any change in high-fat foods intake and smaller increment in total energy intake among girls.[33]

Conversely, the Child and Adolescent Trial for Cardiovascular Health (CATCH) in USA during 3 school years,[29] a short-term school-based interventional study in rural communities in USA,[32] and a small scale multi-component intervention study in India managed to improve knowledge and healthy dietary behaviors by nutrition and lifestyle education model in children and adolescences.[28] Another school based health behaviour intervention program in England led to significant decrease in carbonated drink consumption.[31] Implementing a multi component obesity prevention program in elementary schools of American Indian communities made significant improvement in dietary fat intake.[36] Moreover, there was some differences in nutrition behaviour changes among boys and girls in a controlled trial in Perth, Western Australia, which was conducted on children aged 10-12 years old, as change was larger in sugar intake in boys compared to girls, while fat intake showed contradictory changes.[37]

Although comprehensive community-based lifestyle interventions of IHHP were successful in improving some dietary behaviour, fast food consumption had no reduction in adults of IA. Since it increased in the adults of RA, the trend of fast food consumption indicated a significant improvement in IA vs. RA.[14,22] However, we found a significant reduction in fast food consumption of adolescents in IA, as well as significant reduction in IA compared to RA. Attained healthy information from other IHHP projects could increase the dose of interventions to improve the parents' life style and consequently had some beneficial effect on their children.[20,21]

Unhealthy snack consumption showed no improvement, especially in middle school students. Moreover, unhealthy snack was consumed more than healthy snack in adolescents from Tehran.[8]Non-communicable diseases prevention from childhood needs an intersectoral collaboration of governmental, non-governmental, national and international organizations, media, general population, and food producers. Although school-based programs that focused on improving knowledge could improve knowledge and attitude; however, it has less beneficial impact on lifestyle behaviors of students; because it has been affected by socioeconomic status, culture, and environment.[19] Therefore, there may be need for supportive policies and change in environment besides improving knowledge and behaviors.[19]

Furthermore, urban-rural residency, parents education (especially mothers), and family income may predict dietary changes during lifestyle modification program in developing countries with social and economic transitions. Wang et al. suggested children in higher income family, urban residency and with higher educated mothers are more likely to track unhealthy nutrition habits related to chronic disease. Although these mothers had better access to the media and to healthy nutrition awareness, their behaviors illustrated that they had no consideration about higher fat foods.[40] Unfortunately, these data were not gathered in our study. Therefore, it might have diluted the impact of our interventions. Considering the main role of parents in the dietary behaviors of their children, more emphasis on parents and their diet may improve adolescents' nutrition habits.[41,42]In addition, advertisements in television have great effect on adolescences' nutrition behaviors.[18] Although there are limited unhealthy food advertisements in Iran, especially after the enforcement by IHHP and the close collaboration with the Iranian Ministry of Health officials,[22] these advertisements have been increased in computer digital games or movies on compact disks (CD). Therefore, as adolescents are getting used to watching video and computer CDs even more than TV, they are influenced by unhealthy food advertisement. Since the companies that produced these CD's were private, forbidding the advertisements was impossible. The attractive package of unhealthy snacks is another influential choosing factor[8] that if had been considered in our interventions, we might have had better results in terms of unhealthy snacks.

Strength and limitation: The novelty of the data, assessing the impact of the comprehensive community-based interventions with quasi-experimental design and having reference area in several annual surveys in a developing country setting were the main strength of the present study.

The implemented FFQ was qualitative; therefore, the estimation of food intake was not precise. Furthermore, according to the limited food list, the frequency of categories choice and the difficulty in remembering foods were sources for bias.[43] Another limitation of the study was the small sample size in some annual surveys, which might be

the reason of non-significant results in some group. Mother education and family income might influence adolescences' dietary behaviour, but the data was unavailable.

Conclusion

The HHPC interventions had some improvement in fast food consumption. It did not show significant decrease regarding unhealthy snacks in adolescents; however, the insignificant change might be considered as favorable impact of interventions in IA in which a fast epidemic toward more consumption of these foods has been recently seen. Proper and higher dose of interventions may be effective in achieving this goal.

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Conflict of Interests

Authors have no conflict of interests.

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Effects of citrus sinensis juice on blood pressure

Sedigheh Asgary[(1)], Mahtab Keshvari[(2)]

Original Article

Abstract

BACKGROUND: Citrus sinensis juice (CSJ) is a rich source of dietary flavonoids which reduce the risk of adverse cardiovascular events. This study aimed to examine the effects of four-week intake of natural and commercial orange (*Citrus sinensis*) juice on blood pressure in healthy volunteers.

METHODS: In this single-blind randomized crossover study, 22 healthy subjects (age: 18-59 years old) were included and randomly divided into two groups of 11. Group A consumed commercial CSJ during the first four-week period. After a two-week washout period, they consumed natural CSJ for another four weeks. The procedure was reversed in group B. The participants were asked to drink 500 ml/day of either natural or commercial CSJ twice a day with breakfast and dinner. The effects of orange juice on blood pressure were evaluated.

RESULTS: After drinking commercial CSJ, diastolic and systolic blood pressure were significantly decreased (5.13%; P = 0.03 and -5.91%; P = 0.003, respectively). However, consumption of natural CSJ did not have significant effects on either diastolic or systolic blood pressure.

CONCLUSION: Commercial CSJ significantly decreased blood pressure. Higher flavonoid, pectin, and essential oils content of concentrated products compared to natural juice might have been responsible for this finding. Nevertheless, further studies to focus on dose-response effects are recommended.

Keywords: Citrus Sinensis Juice, Hypertension, Blood Pressure

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Introduction

Hypertension is a major risk factor for cardiovascular diseases (CVD) whose global prevalence is predicted to be as high as 30% by 2025. Approximately 25% (6.6 million) 25-64 year-old have hypertension and 46% (12 million) have prehypertension.[1,2] A growing number of epidemiological studies have consistently shown the protective effect of polyphenol-rich foods (fruit, tea, wine, cocoa or chocolate, and special citrus fruits) against some intermediate risk factors for CVD including high low-density lipoprotein (LDL) cholesterol, high blood pressure, and endothelial dysfunction.[3-5] Orange *(Citrus sinensis)* juice is also considered a good source of essential nutrients such as vitamin C, folate, and potassium. Vitamin C has recently been found to protect endothelial cells and LDL from intra- and extracellular oxidative stress[6] and to reduce the risk of atherosclerosis.[7] In addition, folic acid can lower plasma homocysteine concentrations and to revert endothelial dysfunction in patients with cardiovascular diseases.[8] Potassium, on the other hand, may contribute to lower blood pressure.[6-9] Four-week consumption of orange juice in healthy middle-aged, normal-weight men has been suggested to reduce diastolic blood pressure (DBP). Since DBP is an indicator of peripheral vessel resistance, orange juice can have particular health benefits.[10]

Citrus sinensis juice (CSJ) consumption has become a worldwide dietary habit. As a result, the consumption of frozen concentrated juice has also increased steadily over years. Not surprisingly, the market share of this product is now much greater than that of natural fruit, especially in developed countries.[11] Furthermore, it was hypothesized that

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natural and commercial orange juice consumption have different effects on blood pressure in healthy volunteers. This study aimed to examine the effects of four-week intake of natural orange (*Citrus sinensis*) juice and commercial CSJ on blood pressure in healthy volunteers.

Materials and Methods

Subjects

This single-blind, randomized, crossover study was conducted on 22 healthy volunteers (age: 18-59 years old) with no evidence of chronic, metabolic, and endocrine diseases. The exclusion criteria were using medications, antioxidants, or vitamin supplements, intense physical activity (five hours a week), smoking, and vegetarian or other restrictive dietary habits.

Using a protocol approved by the ethics committee of Isfahan Cardiovascular Research Center (Isfahan, Iran), this study mainly aimed at comparing the effects of four-week consumption of natural and commercial orange juice on blood pressure in healthy volunteers. The subjects were hence allocated to two groups of 11 using computer-generated random numbers. Group A received commercial orange juice for four weeks, had a two-week washout period, and consumed natural orange juice for another four weeks. The reverse order was used in group B. Commercial orange juice without preservatives, extra vitamin C, or other additives was purchased. Natural fruits were also bought at the fruit market, crushed, and then squeezed. Both types of juice were stored in one-liter bottles at 20°C. The subjects were asked to drink 500 ml/day of orange juice twice a day with breakfast and dinner.

In order to measure blood pressure, the participants made four visits to the clinical research unit, i.e. before and 30 days after each experimental period. All measurements were performed in the morning and after a 20-minute rest using a stethoscope and a sphygmomanometer (Accutorr 1A, Datascope, Japan) and according to a standard protocol.[12]

The collected data was reported as means ± standard deviation (SD). A paired t-test was performed to analyze data obtained by the crossover design before and after juice supplementation and to determine possible significant differences in blood pressure between time points. A paired t-test between baseline values (before either natural or commercial orange juice supplementation) was used to establish the correct performance of the washout. A paired t-test was also used to compare the mean values obtained before and after the experiment period. Data was compared by repeated-measures analysis of variance with Dunnett's post-test for nonparametric data. In all cases, P values less than 0.05 were considered statistically significant. All statistical analyses were performed using SPSS for Windows 15.0 (SPSS Inc., Chicago, IL, USA).

Results

Overall, 22 subjects were included. The mean age of the participants was 34.36 ± 11.54 years old in group A and 35.91 ± 12.80 years old in group B (P = 0.769). The mean SBP in groups A and B was 112.00 ± 8.50 and 110.91 ± 7.01 mmHg, respectively (P = 0.555). The mean DBP was 78.0 ± 11.35 mmHg in group A and 72.73 ± 4.67 in group B (P = 0.130).

Blood pressure was measured at the beginning and at the end of each experimental period. There was a statistically significant difference in DBP between the two groups the first and second experimental periods. However, within group comparisons did not reveal statistically significant differences in DBP and SBP (Table 1).

Table 1. Comparison of the two groups before and after each experimental period

Characteristics	Group	T1	T2	P	T3	T4	P
Systolic blood pressure (mmHg)	Group A	112.00 ± 8.50	108.00 ± 7.89	0.020	112.55 ± 8.20	110.91 ± 11.36	0.271
	Group B	110.91 ± 7.01	106.36 ± 6.74	0.129	110.91 ± 7.01	104.55 ± 8.20	0.053
	P	0.555	0.917	0.860	0.630	0.119	0.840
Diastolic blood pressure (mmHg)	Group A	78.00 ± 11.35	72.00 ± 7.89	0.050	75.45 ± 11.28	76.36 ± 10.27	0.792
	Group B	72.73 ± 4.67	70.91 ± 7.01	0.317	72.91 ± 5.39	69.09 ± 5.39	0.050
	P	0.130	0.400	0.204	0.011	0.146	0.490

Group A consumed commercial Citrus sinensis juice during the first period and natural Citrus sinensis juice during the second. Group B consumed natural Citrus sinensis juice during the first period and commercial Citrus sinensis juice during the second.
T_1: Before the first period T_2: After the first period
T_3: Before the second period T_4: After the second period

Table 2. Changes in systolic and diastolic blood pressure (SBP and DBP) after the intervention compared to baseline

Characteristic	Commercial orange juice users (n = 22)	Natural orange juice users (n = 22)
SBP (mmHg)	-5.91%	-3.63%
DBP (mmHg)	-5.13%	-0.61%

SBP: Systolic blood pressure; DBO: diastolic blood pressure

In addition, DBP and SBP had significant reductions after commercial orange juice consumption (-5.13% and -5.91% respectively). Nevertheless, commercial orange juice resulted in a significantly lower DBP reduction compared to natural orange juice (Table 2).

Discussion

The main finding of this study is that four-week consumption of commercial CSJ significantly decreased DBP and SBP in healthy subjects. Morand et al. reported similar findings.[13] Hara showed that four-week consumption of orange juice reduced DBP in healthy middle-aged, normal-weight men.[14] Moreover, studies have shown consumption of flavanone-rich fruit juice to have a significant beneficial effect on blood pressure in hypertensive subjects.[10,14] Focus on flavanones is particularly relevant considering their high content in citrus and high consumption of citrus fruits, and particularly orange juice, worldwide.[15] Concentrated citrus products have a greater flavonoid (polymethoxylated flavones, hesperitin and naringin) content compared to natural juice.[16] This is due to the grinding process which uses the entire fruit to produce the juice. Pectin and essential oils contained in the peel are also found in greater amounts in the concentrated juice.[16] Naringin and hesperidin are mainly present in grapefruits and oranges. They have been reported to possess antioxidant, antihypertensive, and hypocholesterolemic effects and to offer some kind of protection against mutagenesis and lipid peroxidation.[17,18] In healthy, middle-aged, moderately overweight men, regular postprandial consumption of Citrus sinesis juice (CSJ) has been found to decrease DBP and increase endothelium-dependent microvascular reactivity. Hesperidin was suggested to cause the beneficial effect of orange juice.[13] Law et al. showed that a 3-4 mmHg reduction in DBP would reduce the incidence of coronary artery disease by 20%.[19]

The possible mechanisms by which these flavonoid-rich foods lowered blood pressure may involve a chronic increase in the production of nitrogen oxide (NO) by vascular endothelium. Other mechanisms such as an inhibitory effect on angiotensin-converting enzyme could also be responsible for the blood pressure-lowering effects of flavanones.[13,20,21] Endothelium dysfunction causes the endothelium to become permeable to plasma components such as LDL which are deposited in the subendothelial space. Consequently, endothelial dysfunction can be considered as the first step in atherogenesis and development of arteriosclerotic lesions.[22-24]

In general, association between flavonoid intake and blood pressure is a theory which requires more research.

Conclusion

Commercial orange juice has a significant effect on blood pressure. As concentrated products have greater contents of flavonoids, pectin, and essential oils compared to natural juice, they are more effective on blood pressure. Future studies to examine dose-response effects are recommended.

Conflict of Interests

Authors have no conflict of interests.

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Psychological factors and coronary heart disease

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Review Article

Abstract

BACKGROUND: Although psychological factors play an important role in coronary heart diseases (CHD), it seems there is a need for more researches in this respect. The present study aimed to review psychological factors, including depression, anxiety and stress related to etiology and prognosis of CHD.

METHODS: This was a review on medical and psychological literatures, particularly in the years 1995-2012.

RESULTS: As protective factor or risk factor, psychological factors play an important role in CHD.

CONCLUSION: Given the findings of this study, it seems necessary that we pay attention to psychological factors, as independent risk factors or protective factors for CHD.

Keywords: Coronary Heart Disease, Psychological Factors, Depression, Anxiety, Stress

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Introduction

Coronary heart disease (CHD) is one of the most important health issues of the twenty first century, and the most important cause of mortality in our community.[1-3] According to statistics, 2 million Iranians are suffering from coronary heart disease. The Research Committee of the Iranian Society of Cardiac Surgeons has announced that the age of exposure to cardiovascular disease in Iran is approximately 7 to 10 years less than other countries. In developed countries, people are exposed to this disease in the sixth decade of their lives. However, people in Iran are exposed to this disease during the fifth decade of their life. There are about 50 thousand heart surgeries performed annually in Iran. In China, with a population of one billion and 300 million, the same amount of heart surgeries are performed.[4]

Although most of the studies on CHD are mainly focused on the biological risk factors and life style, some evidences have revealed that psychological and psychiatric factors have a very important role in the etiology, development, duration, and outcome of this disease.[1,5,6] The most important factors are depression,[7-29] anxiety,[12-40] and stress.[30-32,41-53] Increasing evidence suggests that psychological factors, as independent risk factors, have an important part in physical chronic diseases, particularly coronary heart disease.[5,9,38,48,53-58]

The purpose of this paper is to review psychological risk factors of CHD such as depression, anxiety and stress. Then via a computerized literature search in ProQuest, Elsevier, and PubMed covering the period from 1995 to 2012, all studies focusing on psychological factors in the etiology and prognosis of CHD were reviewed.

In recent years, researchers and clinicians have been attempting to reduce CHD occurrence by primary and secondary prevention strategies such as behavioral changes and risk factor modification.[34-36] Secondary prevention of CHD is also a main objective that results in the reduction of cardiac events especially acute myocardial infraction.[59]

Psychological risk factors in CHD

The biological risk factors for CHD have been studied in many researches, but this paper focused

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exclusively on psychological risk factors for CHD etiology, prognosis and mortality.[60,61]

Depression

Depression is a risk factor for morbidity and mortality in patients with coronary heart disease, especially following acute coronary syndrome.[7-29] Most studies showed depression as an important disorder that leads to an increase in cardiovascular events, re-admission to hospital and CHD mortality.[16] Depression is common among CHD patients; there is ample evidence that prevalence of depression is 20% higher in patients with heart failure than in healthy individuals.[11,31,47,62-65]

Depression has been found to be a risk factor in the etiology of CHD.[16,64-70] However pervious research has had several potential limitations concerning causal inference. The greatest challenge in research on prospective association between depression and CHD is the possibility that both depression and subsequent CHD are caused by subclinical manifestation of cardiovascular disease.[68] Atherosclerosis, the underlying pathophysiological mechanism of CHD, is known to develop during the decade before the first clinical symptoms. Therefore, atherosclerosis may facilitate depressive symptoms even before clinical CHD symptoms.[48,68]

Balog et al. studied depression symptoms associated with job stress and stress in marital relationships in women with and without coronary artery disease.[17] They found that in women, marital stress is associated with depression symptoms and results in the intensification of CHD. Therefore, it appears that depression has a mediating role for marital stress that ultimately results in CHD.

Anxiety

Although evidence suggests that anxiety has an adverse impact on prognosis in CHD patients independent of depression, the role of anxiety as an etiological risk factor is less clear.[68,71-74]

In a systematic review, 12 studies evaluated clinical endpoints, such as myocardial infarction (MI) and cardiac death, 5 studies reported significant association, 3 studies reported marginally significant associations, and 4 studies reported no association between indexes of anxiety and cardiac patients.[75]

Roest et al. (2010) in their meta-analysis studied the connection between anxiety and the risk factors of coronary artery disease, and found that anxiety is an independent risk factor for CHD and cardiac deaths. However, the association between anxiety and CHD was somewhat less than the corresponding association between depression and CHD, but this connection was stronger than the relationship between anger and CHD occurrence.[38]

A survey conducted about physical and psychological symptoms of anxiety in CHD patients revealed that anxiety is correlated with physical factors such as palpitation without any physical exercise, anger and redness in the face, abnormal heart beat, and muscle tension that increases the risk of CHD especially in women.[76]

A research showed that somatic symptoms of anxiety were associated with an increased risk of CHD in women. This finding lends support to the physiological pathway for the relation between psychological factors, anxiety in particular, and CHD.[37]

A longitudinal research conducted by Janszky et al. over a period of 37 years on 49321 young Swedish men aged 18-20 years evaluated the effects of anxiety and early depression on risk factors of coronary artery disease. This research revealed that both anxiety and depression are associated with low physical activity and high rate of cigarette smoking. Depression was also associated with high levels of alcohol consumption and anxiety had a connection with high blood pressure. Finally, this study indicated that anxiety independently predicted subsequent CHD events such as morbidity and mortality. In contrast, it found no support for such an effect concerning early onset of depression in men.[28]

In another study, it was indicated that high and low levels of trait anxiety do not have a different effect on cardiovascular reaction. Expressing and inhibiting styles of anger did not have a different effect on cardiovascular reactions, but anger expression and management styles and trait anxiety levels had an opposite effect on cardiovascular reactions. This means that the outward (behavioral) expression of anger with high level of anxiety is associated with low cardiovascular reaction (heart beat), and the outward expression of anger with low level of anxiety is associated with high cardiovascular reaction. In contrast, inner expression of anger with high level of anxiety is associated with high cardiovascular reaction, and inner expression of anger with low level of anxiety is associated with low cardiovascular reaction.[77] In addition to depression, other psychological factors such as anger, hostility and anxiety are associated with increase in risk factors of cardiovascular disease.[78-81,34]

Stress

To fully understand the relationship between cardiovascular disease and stress is simply not

possible, but empirical evidence indicates a relationship between the heart and mind.[81]

A number of experts have suggested that those variables that are commonly regarded as components of stress include: depression and anxiety, social isolation and lack of social support, acute and chronic life events, psychosocial work characteristics, and type A behavior and hostility.[66]

Depression and anxiety

The association between depression and anxiety with CHD has been previously discussed in this essay. [11,16,31,34,37,47,61-64,67-70,75-77,80-84]

Social isolation and lack of social support

In many studies lack of social support was indicated as a predictor of onset and prognosis of CHD, and mortality among both sexes; however, it was more consistent in males.[47,84,85] The risks are increased 2–3-fold and 3–5-fold for females and males, respectively. The association between social isolation and lack of social support with CHD exists for subjects who live in different countries and are of various age groups.[47] A study aimed to investigate and identify psychological factors in patients with ischemic heart disease within 4 months after discharge.[14] This study indicated that coping style, social network and social support, within 4 months after discharge, caused these patients to be less focused on their illness and feel less threatened in comparison with the control group that did not have these types of support. These patients were also less excited and benefited more from the health services provided by the professionals. Moreover, people who suffered from this disease for the first time were seeking social support and coping style more in comparison to those that had previous history of hospitalization due to ischemic heart disease.[14] In another study, loneliness and social support were studied in patients with heart failure (CHF). They realized that loneliness is one of the important risk factors for patients with heart failure, and the more the patients feel lonely the more severe the heart failure is.[86]

Acute and chronic stressors

Some studies have shown that acute and chronic psychological stressors are associated with acute coronary syndromes (ACSs).[87] Acute stressors such as earthquakes or loss of a child may trigger death.[88,89] However, it is very difficult to study and quantify the magnitude of effects.[6] Moreover, there has been less focus on how chronic and low-key stress of everyday life affects mortality rate of individuals.[90]

Psychosocial work characteristics

This topic refers to the characteristics of the work environment. Few associations supported the hypotheses that high job demands, low decision latitude, or job strain are associated with increased levels of CHD risk factors.[91] When the results for job control, demands and strain were studied, there was not a preponderance of positive over negative studies. The expert working group found no consistency between this review and the other two reviews of work-related stressors.[6,64,92] A study on the association between adverse psychosocial characteristics at work and risk of coronary heart disease among males and females with low job control, reported a higher risk of newly reported coronary heart disease during follow up. Subjects with low job control on both follow-ups had an odds ratio for any subsequent coronary event compared with subjects with high job control at both follow-ups.[93] One study characterised occupational cohort of British men well. This study reported that the association between psychosocial factors at work and CHD was largely independent on family history of CHD, education, paternal education and social class, number of siblings, and height.[93,94] Therefore, the results of these studies were heterogeneous. Future research will need to clarify this subject with the role of moderator variables.

Type A behavior and hostility

Early research data indicated that type A behavior pattern, which is primarily characterized by hostility, intense ambition, competitive drive, constant preoccupation with deadlines, and a sense of time urgency, was related to the development of CHD. However, these original findings were not supported by subsequent research.[51,95,96] Recent studies do not confirm the correlation between type A behavior and coronary artery diseases.[64]

Studies on American and European populations have demonstrated that high levels of anger and hostility are predictive of coronary heart disease (CHD) mortality.[97] Moreover, a Japanese study indicated that higher levels of cynical hostility increased the risk of acute myocardial infarction syndrome (AMIs), and that anger-control strategies could have some benefit in reducing the risk of AMIs in middle-aged Japanese men.[96] However, another review indicated that there was no evidence of such an association.[64] Beside some studies demonstrated no clear association between hostility and CHD.[6] More research is needed in order to understand this

relationship in the future.

Materials and Methods

This study was conducted through searching in related books and articles. The related articles were retrieved from authorized database such as ProQuest, Elsevier and PubMed using keywords such as (psychological factors), (psychological risk factors), (depression, anxiety, stress), (social isolation and lack of social support, acute and chronic life events, psychological work characteristics, Type A behavior and hostility) (coronary heart diseases) from 1995 to 2012. Accordingly, articles that were most related to the subject were selected and the relationship of psychological factors to coronary heart disease were studied.

Results

This study showed that psychological factors as protective or risk factors have an important role in CHD; the most important of which are depression, anxiety, stress, occupational status, and[94-97] social support.[4,6,7-29,30-40,41-53,48,62-66,80,82,86-89,94-98] Strong evidences regarding the role of depression in enhancing morbidity and mortality of CHD showed that depression is an independent predictor.[8,13,14,68,99-105] Depressed people are 64% more at the risk of suffering from CHD than non-depressed people.[68] Depression is also a negative predictor for improvement of CHD. Conducted studies have illustrated that after controlling demographic variables, low social support and anxiety were also independent risk factors for mortality.[106] Moreover, the results of these studies have demonstrated that anxiety, stress, and type of stress, such as lack of social support and psychological work characteristic, were associated with coronary artery disease.

One of the major protective factors for CHD is social support. Some studies have shown that perceived social support during hospitalization decreases depressive symptoms in subsequent months.[107] In addition, many studies have shown that after myocardial infarction the rate of depression depends upon the amount of social support.[14] This study also showed different types of stress such as anxiety, depression, social isolation, social support, acute and chronic life event, hostility, and type A behavior. Among these variables, social support is more important than other variables. Not only is the lack of social support associated with the occurrence of CHD, but it is also an independent risk factor for mortality.[6,66,71,108]

Research has highlighted the importance of stresses caused by acute and chronic life events in CHD incidence. Acute life event stressors can trigger CHD events, but it is very difficult to study and quantify the magnitude of these effects. Although the deleterious physiological effects of acute stressors as CHD triggers are well documented, the role of chronic stressors in CHD onset and prognosis remains unclear.[6] Many researches on hostility as type A behavior were inconsistent. Some studies confirm the role of hostility in the etiology of coronary artery disease, while other researches refute this assumption.[64,72] Moreover, some studies have conflicting views about the role of hostility in the etiology and prognosis of coronary artery disease.[6,109]

Discussion

Coronary artery diseases are caused due to insufficient blood and oxygen flow to the heart muscle and will be the main cause of death until the year 2020.[110,111] The risk factors of CHD are divided into unchangeable factors (age, and genetic factors) and changeable factors (smoking, obesity and psychosocial factors).[112,113] Only half of the variances of CHD are explained by unchangeable factors (such as age and genetic factors).[113] Due to the high expenses of treatment of these diseases and their complications, appropriate scientific approach, and prevention and treatment of these diseases result in saving millions of Rials in health costs. In this regard, it seems necessary to concentrate on the changeable factors that are mostly the psychosocial factors and life style.

Different reasons such as increasing prevalence in developing countries, like Iran, the high expenses of surgical and other treatment programs, side effects, and the resultant inability make CHD one of the most important medical and health issues.[74] Although most of the researches on CHD are focused on the biological risk factors and life style, evidence shows that psychological and psychosocial factors have an important part in etiology, development, continuity and the consequence of this illness.[1,5,9,47,64,112] Today, psychological factors are considered as independent risk factors in chronic diseases.[112,113]

However, psychosocial factors are not recognized clinically. Cardiologists frequently state that the psychosocial factors identified in the literature are not apparent in clinical practice. There are probably three reasons for this. First,

psychosocial factors are risks rather than inevitable causes; they vary widely in importance for different patients, and will not be apparent in every case. Second, psychological characteristics such as hostility may only be elicited under appropriate provocation. Therefore, they are unlikely to be expressed during a typical clinical consultation. Finally, there is a tendency to search for psychosocial explanations only for patients who do not have other clear risk factors such as hypertension, diabetes, or smoking. Many clinicians work based on implicit models that place biological and psychosocial causes as alternatives. However, psychosocial factors may be associated with other risk factors.[54] For example, the Whitehall II study by Marmot et al. showed that social isolation, lack of control at work, and hostility are more prominent in low social class groups where smoking, insulin resistance, and other factors are clustered. Therefore, 10,308 women and men, all of whom were employed in the London offices of the British Civil Service, would provide advice to patients, and refer more extreme cases to psychiatric or psychological services.[114]

Most studies discussed depression and anxiety as an important disorder that results in increase of cardiovascular incidents, re-admittance to hospital, and death in coronary artery patients.[34,36] Depression is common among coronary artery patients; extensive research evidence showed that prevalence of depression in patients with heart failure is more than 20%.[47,62-64,115]

The health system in Iran is experiencing different problems such as unfair and inadequate access to health services for the society, high cost of health care, emphasis on health care and neglect of preventive care, intervention on the individual level and neglect of community intervention, lack of balance between the interests of patients, society and the health system, and especially little attention to mental health. Furthermore, the age of exposure to cardiovascular disease, mainly heart failure, is decreasing in Iran and is reaching the teenage years. This is mostly due to psychological and life style reasons, therefore, a new psychological perspective to CHD is crucial. It is obvious that today one of the main aims of psychology is the prevention of psychosomatic disease, that results in decreasing expenses and improving health and quality of life.[116,117] The new trend in psychology under the name of health psychology, and extensive research and publications in this field are a confirmation of this matter. Thus, by knowing the psychological risk factors and protective factors of coronary artery disease, prevention, control and adjustment can be performed. These performances result in a decrease in risk factors, decrease in treatment expenses, improvement in life quality, and eventually decrease in illnesses and inabilities.[68,105,117,118]

Conclusion

This study dealt with this topic using a modern psychological perspective and with the aim to evaluate the role of psychological factors in the etiology and prognosis of coronary heart diseases. The findings of this study showed that although psychological factors are independent risk factors for CHD, the diagnostic and therapeutic procedures of this illness had a favorable process. Prevention is better than cure; therefore, considering the increase in CHD risk factors during recent years, it is necessary that more attention be paid to psychological factors and preventive actions. Without doubt, performing psychological and educational interventions in the community and increasing people's awareness about the psychological factors of CHD can have an effective role in promoting the people's health in the future.

Conflict of Interests

Authors have no conflict of interests.

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Dabigatran, a direct thrombin inhibitor, can be a life-saving treatment in heparin-induced thrombocytopenia

Ahmad Mirdamadi[1]

Case Report

Abstract

BACKGROUND: Several studies have emphasized thrombosis associated with thrombocytopenia as a potentially fatal complication of heparin. A number of agents are used for this condition. As a new oral, reversible direct thrombin inhibitor, dabigatran has been approved for short-term thromboprophylaxis after elective hip and knee replacement surgery. We present a case of dabigatran administration in a patient with femoral fracture.

CASE REPORT: A 67-year-old woman referred to the orthopedic ward of Shariati Hospital (Isfahan, Iran) due to femoral fracture following an accident. Immediately after surgery, she was found to be suffering from deep vein thrombosis (DVT) in her lower extremity despite sufficient prophylaxis by enoxaparin. Laboratory data showed severe thrombocytopenia. Considering the clinical history, an initial diagnosis of heparin-induced thrombocytopenia was made. Doppler ultrasound confirmed the diagnosis. Heparin was thus replaced with dabigatran which increased platelet count to the normal range and improved DVT.

CONCLUSION: Dabigatran can be a life-saving treatment in heparin-induced thrombocytopenia. However, it is contraindicated in patients with renal dysfunction since it may cause potentially catastrophic results.

Keywords: Heparin Induced Thrombocytopenia, Heparin, Enoxaparin, Dabigatran

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Introduction

Thrombosis associated with thrombocytopenia has been emphasized in several studies as a potentially fatal complication of heparin. After searching PubMed, Sid and Elsevier, we found 7 case reports that described several types of heparin-induced thrombocytopenia (HIT) treatment. The use of lepirudin infusion,[1,2] argatroban,[3,4] danaparoid,[5] plasma exchange,[6] and streptokinase[7] has been indicated. Oral thrombin inhibitors are new agents for prevention and treatment of HIT. Melagatran, an oral thrombin inhibitor, is no longer available due to its hepatic toxicity. While several other thrombin inhibitors such as lepirudin and desirudin are used via parenteral administration, bivalirudin and argatroban are less convenient for patients and health care providers.[8] As a new oral, reversible direct thrombin inhibitor, dabigatran has been approved for short-term thromboprophylaxis after elective hip and knee replacement surgery.[9] This paper presents a case of dabigatran administration in a patient with femoral fracture.

Case report

A 67-year-old woman with left femoral fracture ward of Shariati Hospital (Isfahan, Iran). She received sufficient thromboprophylaxis with enoxaparin for 6 days and then underwent orthopedic surgery.

Five days after surgery, the patient experienced swelling, pain, and tenderness in her left thigh and leg. Doppler sonography was ordered to confirm the suspected deep vein thrombosis (DVT). Dilation of the left common femoral, superficial femoral, popliteal, and posterior tibial veins was detected without any blood flow in them and with no compressibility as well. In the other hand some echogenic mass presented in those veins (Figure 1). DVT in the left lower limb was thus confirmed. Baseline platelet count was 173,000/μL but dropped to 32,000/μL two weeks after the initiation of enoxaparin (Figure 2).

Based on clinical history and laboratory findings, the diagnosis of thrombosis associated with HIT was made. Enoxaparin was therefore discontinued

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immediately and oral dabigatran was administered (110 mg twice a day). A few days later, platelet count increased to the normal range (236,000/µL) and the patient declared improvement in symptoms (Figure 2). On the tenth day of treatment with dabigatran, Doppler ultrasound was repeated which indicated the recanalization of the thrombosis (Figure 3).

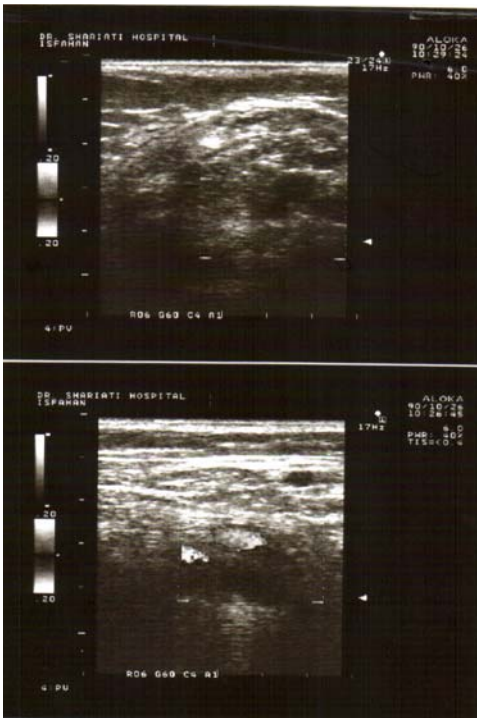

Figure 1. Ultrasound before dabigatran administration (1/15/2012)

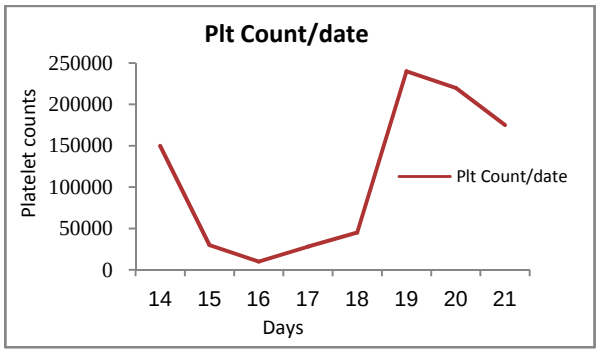

Figure 2. Platelet (Plt) counts before and after treatment whit dabigatran

Discussion

HIT with thrombosis, or the "white clot syndrome", is a rare but well recognized fatal complication of heparin therapy. The syndrome is idiosyncratic, immune-mediated, and not dose-dependent. It is therefore equally likely to occur with prophylactic and therapeutic heparin dosage regimens. HIT with thrombosis is associated with significant incidence of morbidity and mortality. The frequency of HIT in orthopedic patients is about 0.5% for low molecular weight heparin (LMWH) and 3% for unfractionated heparin (UFH).[9] Prompt recognition of this complication and immediate withdrawal of heparin therapy are imperative.

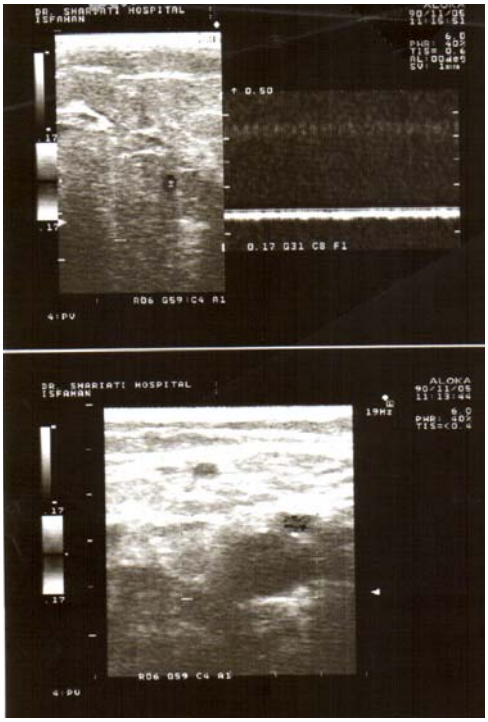

Figure 3. Ultrasound ten days after initiation of dabigatran (1/25/2012)

Since HIT and thrombosis are mainly clinical diagnoses, one should not wait for objective test confirmation before stopping heparin treatment. On the other hand, LMWH should not be used to treat HIT because most HIT antibodies exhibit cross-reactivity with LMWH.[10] In addition, due to the consumption of protein C in this condition, administration of warfarin can trigger skin necrosis.[11]

The agents most frequently used in such conditions are parenteral direct thrombin-inhibitors such as lepirudin, argatroban, and bivalirudin, or factor Xa inhibitors such as fondaparinux.[10] However, we used dabigatran which is an oral direct thrombin inhibitor. It has been approved in the USA for prevention of stroke in patients with atrial fibrillation and is licensed in Europe and Canada for short-term thromboprophylaxis after elective hip and knee replacement surgery. Moreover, it has limited drug interactions, does not require monitoring, and has rapid peak blood level. Therefore, administration of dabigatran can be

helpful in the prevention and treatment of HIT. Nevertheless, dabigatran is contraindicated in patients with renal dysfunction since it may cause potentially catastrophic results. In this case, dabigatran was administered with no complications.

Conclusion

All physicians who use heparin in the course of their practice need to be aware of life threatening HIT and the spectrum of its clinical presentations and management. In case of HIT, replacing UFH or LMWH with dabigatran is one of the life-saving strategies. Dabigatran is more convenient for patients and health care providers and has the potential to improve clinical outcomes. Although the use of dabigatran may result in major changes in thrombosis management and prevention, drug contraindications should not be forgotten.

Conflict of Interests

Authors have no conflict of interests.

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Non-administration of thrombolytic agents in acute myocardial infarction patients in Hajar hospital, Shahrekord, Iran: prevalence rate and causes

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Short Communication

Abstract

BACKGROUND: Cardiovascular diseases are the major causes of mortality worldwide and acute myocardial infarction (AMI) is the leading cause of mortality among cardiovascular diseases. Thrombolytic therapies, especially during the first few hours after the disease onset, can significantly reduce AMI-related mortality.

METHODS: The current study aimed to determine the prevalence and causes of non-administration of thrombolytic therapy for AMI patients admitted to Hajar Hospital, Shahrekord, Iran, from May until November 2000. Non-probability convenient sampling method was used to select 106 subjects with Q-wave AMI. Data was collected by completing a questionnaire, reviewing medical records, and interviewing with patients. $SPSS_{7.5}$ was for data analysis.

RESULTS: A total number of 106 AMI patients were studied among whom 62 (59%) individuals received thrombolytic therapy. Delayed referral to the hospital was the major cause of failure to provide thrombolytic therapy. The cause of non-treatment could not be identified in 15 (19.5%) subjects eligible to receive therapy.

CONCLUSION: Training general practitioners and individuals involved in this regard along with accelerating the process of patient referral to hospitals can reduce AMI-related mortality.

Keywords: Acute Myocardial Infarction, Thrombolytic, Therapy

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Introduction

Cardiovascular diseases (CVDs) are the leading causes of mortality in the world. In fact, they cause 50% of mortalities in developed countries and 25% of mortalities in developing countries.[1] Acute myocardial infarction (AMI) is responsible for most mortalities due to CVDs. In the U.S., more than one million people diagnosed with AMI are annually admitted in hospitals. Almost one-third of these patients die.[2]

Like many other countries, CVDs are the main cause of mortality in Iran and heart attacks occur during the 4th and 5th decades of patients' lives.[3] In recent years, thrombolytic therapies could reduce the MI-related mortalities from 15% to approximately 6.5%. In addition to mortality reduction, thrombolytic therapies can also lessen disease symptoms and complications such as interventricular septal rupture and cardiogenic shock.[4]

In order to be effective on mortality, thrombolytic therapies are suggested to be administered until 12 hours after the onset of AMI.[5] In addition to the time limit, patients should not have the contraindication prescription. The most important thrombolytic drug contraindications are active internal bleeding, cerebrovascular events in the past one year, possibility of aortic dissection, and history of intracerebral hemorrhage.[5] Despite the approved role of thrombolytic therapy in AMI, it is still not administrated in many hospitals for all the patients. Venturini et al. collected information

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from ten countries and found that 37.3% of patients with AMI did not undergo thrombolytic therapy mainly due to delayed referral.[5] In another study, race was shown to have influenced the percentage of thrombolytic therapy administration, i.e. while 75% of Caucasians admitted with AMI volunteered and received thrombolytic therapy, only 62% of black patients underwent treatment.[6] Furthermore, some studies have suggested the administration rate of thrombolytic therapy to be lower in women than men with AMI. The reason might be delayed referral of women to hospitals, higher age among women with AMI, the existence of comorbidities which did not make women as appropriate volunteers for thrombolytic therapies, or differences in quality of services provided to female and male patients.[6-8] In another study, the rate of thrombolytic therapy was higher in patients treated by a cardiologist than by a general practitioner or internist which indicates the impact of specialty of physicians on administration rate of thrombolytic drugs.[9]

The administration rate of thrombolytic therapy to candidates with AMI might indicate the quality of the provided services to patients. Therefore, all health care centers should pay utmost attention to administer such drugs to AMI patients. However, no previous report has been published about the frequency of non-administration of thrombolytic therapies in the province of Chaharmahal-e-Bakhtiari (Iran). Due to the high value of thrombolytic drugs as major pharmacological therapies in patients with AMI, this study aimed to determine the prevalence rate and causes of non-administration of thrombolytic therapies.

Materials and Methods

This was a prospective, descriptive, cross-sectional study. The study population included all the patients with MI admitted in coronary care unit (CCU) of Hajar Hospital, Shaherkord, Iran during May-November 2000. AMI was diagnosed by a cardiologist based on indicators of the World Health Organization including history of chest pain, echocardiographic changes, and increased cardiac enzymes.[4] Non-probability convenient sampling method was used to select subjects. Overall, 106 patients diagnosed with Q-wave AMI were examined in terms of administration or non-administration of thrombolytic therapies. Data was collected by completing a questionnaire, reviewing medical records, and interviewing with patients. Data was extracted, categorized and analyzed by proportions difference test in $SPSS_{7.5}$. In order to compare the findings, P less than 0.05 were considered as significant.

Results

As indicated in table 1, the numbers of male patients were more than females. Among the 106 studied patients 62 (59%), including 54 males (87.1%) and 8 females (22.9%), received thrombolytic therapy.

Out of 44 patients who did not receive streptokinase, 18 (41%; 11 males and 7 females) referred late, 11 (25%; 6 males and 5 females) had contraindications, and 15 (34%; 9 males and 6 females) did not mention any special reasons while they were candidates for thrombolytic therapy.

Although a total number of 77 patients were candidates to receive thrombolytic therapy, only 62 (80.5%) received the treatment. To be more precise, 89% of men and 62% of women underwent thrombolytic therapy.

Discussion

As indicated in the results of the study, AMI was more prevalent in men, i.e. the number of men was three times more than women. Sex-dependent differences have also been indicated in other studies. In a large study on more than 3600 AMI patients, only 26% of the patients were female.[10] Therefore, being male is known as a risk factor for the incidence

Table 1. Demographic characteristics of patients and summarized results in male and female patients

Number of patients	Males 80 (75.5%)	Females 26 (24.5%)
Mean age (year)	60.5	64.7
Those who did not received thrombolytic therapy	26 (32.5%)	18 (69.2%)
Candidates of receiving thrombolytic therapy	63 (78.8%)	14 (53.9%)
Candidates for thrombolytic therapy who did not receive it	9 (14.3%)	6 (42.9%)
Patients who did not receive thrombolytic therapy due to delayed referral	11 (13.8%)	7 (26.9%)
Patients who did not receive thrombolytic therapy due to contraindications	6 (7.5%)	5 (19.2%)

Males and females were significantly different in all groups ($P < 0.05$).

of coronary artery diseases and AMI. In this study, mean age of women was higher than men. In most previous studies, females aged higher than males.[8,10]

According to our findings, 59% of all AMI patients were treated with streptokinase while 41% did not receive any thrombolytic drug. Male and female patients were significantly different in terms of receiving thrombolytic drugs (67.5% vs. 30.5%; $P < 0.05$). A study in Spain reported 23.9% of women and 41.3% of men with first AMI to have received thrombolytic therapy. Although we found higher percentages, the two studies found a higher prevalence among men.[10]

In addition, 80.5% of patients eligible to receive thrombolytic therapy did not receive it. Since the rates were 90% in men and 32% in women, a significant difference was observed between the two sexes ($P < 0.05$), which can be justified by the lower prevalence of AMI among women due to delayed diagnosis and treatment. Another reason for lower frequency of thrombolytic therapies administration in women might have been their older age compared to men. On the other hand, the percentage of women who did not receive thrombolytic drug due to contraindications was significantly higher than men. Differences in the frequency of thrombolytic therapy administration between men and women have also been mentioned in previous studies.[8,10]

The overall rate of thrombolytic therapy administration to the eligible patients seems to be lower in this study compared to some other research. For instance, a study reported 93% of patients treated by a cardiologist to have received thrombolytic drugs.[9]

In this study, the most prevalent cause of non-administration of thrombolytic therapy was delayed referral. There was no significant difference between men and women in this regard. It can be justifiable given that Chaharmahal-e-Bakhtiari is a mountainous province and sometimes it takes patients hours to get to the hospital. Moreover, such therapies are currently accessible only in hospitals and administration of the drugs is not possible in emergency stations and ambulances. Previous studies have also indicated the most prevalent cause of non-administration of thrombolytic therapy as delayed referral.[11-13]

Therefore, in order to provide better health care services and treatment to patients with AMI, all the emergency physicians, who are somehow involved in treatment of such patients, are recommended to be trained with the required educations about pharmacological therapy. Moreover, providing emergency centers with necessary facilities for early diagnosis of AMI and administration of thrombolytic therapies can prevent the mentioned delays. Furthermore, public educations of AMI symptoms, particularly to those at risk including elderly people, smokers and diabetics, can lead to earlier referral of patients to hospitals.

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Conflict of Interests

Authors have no conflict of interests.

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