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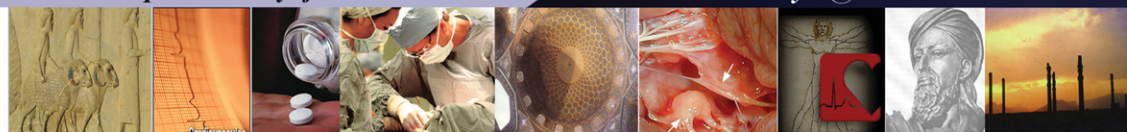

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2. Bonow RO, Mann DL, Zipes DP, Libby P. Braunwald's Heart Disease E-Book: A Textbook of Cardiovascular Medicine. 7th ed. Philadelphia, PA: Elsevier Health Sciences; 2007. p. 1976, 1981, 1982.

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 correlation between educational levels and central obesity in the north of Iran: An epidemiologic study

Gholamreza Veghari[1], Mehdi Sedaghat[2], Siavash Maghsodlo[2], Samieh Banihashem[2], Pooneh Moharloei[2], Abdolhamid Angizeh[2], Ebrahim Tazik[2], Abbas Moghaddami[2]

Original Article

Abstract

BACKGROUND: The main aim of this study was to evaluate the association between educational levels and central obesity in northern Iran in 2010.

METHODS: This was a cross-sectional study carried out on 2428 subjects (1227 men and 1201 women) of 15-65 years of age who were chosen by cluster and stratified sampling methods. Subjects were randomly selected from 125 clusters and each cluster included 20 cases. Interviewers recorded the data using a multidimensional questionnaire comprising socio-demographic indexes.

RESULTS: Central obesity was seen in 34.8% of all subjects (15.9% male and 56.7% female) and in 15% of uneducated people. In the uneducated group, it was 20.0% and 31.1% higher than in the 1-9 years of schooling and high school or college educated groups, respectively (P = 0.001). The risk of central obesity increased in uneducated people (OR = 4.214, P = 0.001) and in people with 1-9 years of schooling (OR = 2.283, P = 0.001) compared with high school or college educated people. The risk of central obesity was higher in urban areas than in rural area (OR = 1.481, P = 0.001), in women than men (OR = 7.039, P = 0.001), in 40-65 year olds than 15-40 year olds (OR = 3.090, P = 0.001), and in the wealthy economic group than poor economic group (OR = 1.360, P = 0.013). The risk of central obesity increased in urban areas (OR = 2.266, P = 0.001) and the wealthy economic group (OR = 1.732, P = 0.001) after it was adjusted for education.

CONCLUSION: Central obesity as a health problem in northern Iran has been supported in this study, and it had an inverse correlation with educational levels. Public health programs that aim to reduce central obesity should mainly focus on the illiterate and low educated people.

Keywords: Education, Northern Iran, Adults, Central Obesity

Date of submission: 11 Nov 2012, ***Date of acceptance:*** 20 Apr 2013

Introduction

The World Health Organization has reported a rise in obesity worldwide reported by World Health Organization.[1] Moreover, it is known that central obesity is a major health problem in Iran, and in northern Iran.[2,3] The rate of central obesity was 9.7%-12.9% and 54.5%-63.7% among Iranian men and women, respectively.[4,5]

Waist circumference (WC) is used for central obesity classification and is associated with cardiovascular disease, stroke, and type 2 diabetes.[6,7]

Education is a multifaceted concept; some social and cognitive skills are learned through formal educational processes; reading and numeracy.[8] Some studies showed a significant correlation between socio-demographic factors and central obesity.[9-12] Some other studies approved the role of literacy skills in health education.[13,14]

Golestan province is located in the north of Iran (south east of the Caspian Sea). There are three ethnic groups of Fars-native, Turkman, and Sisstani in this area. Of the 1.6 million residents of this area, 66.39% are 15-64 years old, and 43.9% and 56.1% are living in urban and rural areas, respectively. Agriculture is the main occupation in rural areas of Golestan.[15]

Since, to our knowledge, no study has been conducted on the correlation between education and central obesity in northern Iran, this study was

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designed and established in this area. The main aim of this study was to evaluate the correlation between educational levels and central obesity in adults in northern Iran in 2010.

Materials and Methods

This was a cross-sectional study established on 2428 participants (1227 men and 1201 women) of 15-65 years of age who were chosen by cluster sampling. Subjects were randomly chosen from 125 clusters, each comprised of 20 cases. Family code of primary health center in villages, and postal code in towns were used to classify the subjects with equal proportion of age and sex. From each district, one team had been trained to complete the questionnaire and measure waist circumference. Interviewers recorded the data using a multidimensional questionnaire including socio-demographic indexes. Pregnant women and unwilling subjects were excluded from this study. This study was approved by the Ethical Research Committee and written consent forms were received from all participants.

Waist circumference was measured to the nearest 0.5 cm at the superior border of the iliac crest. Central obesity was defined based on the WHO classification; WC ≥ 102 cm and WC ≥ 88 cm in men and women, respectively.[16] The subjects were classified, based on their educational level, into three groups; uneducated, 1-9 years of schooling, and high school or college educated.

With regard to the Iranian social-economic circumstances, economic status was categorized based on the six facilities of separate bathroom, separate kitchen, vacuum cleaner, computer, separate freezer, and washing machine. The subjects gained one score for each facility. According to this list, the scoring of the economic status of the subjects in this study was as follows: poor ≤ 2 scores, moderate = 3-4 scores, and wealthy ≥ 5 scores.

Some confounder factors such as location of living, gender, age, and economic status were considered in this study.

SPSS for Windows (version 16; SPSS Inc., Chicago, IL., USA) was used for the statistical analysis, and chi-square was used to compare the frequencies. Logistic regression was applied to estimate the odds ratio (OR) of central obesity considering the educational level at 95% significant level. A P-value of less than 0.05 was considered as statistically significant.

Results

Mean and standard deviation of age and waist circumference were 39.21 ± 14.3 years and 88.7 ± 14.8 cm, respectively.

The characteristics of subjects and waist circumference distributions based on socio-demographic factors are presented in table 1. One in three of the subjects were in the uneducated group, 46.5% were living in urban areas, and 53.7% had a moderate economic status. Central obesity was seen in 34.8% of subjects (15.9% male and 56.7% female) (P = 0.001).

Central obesity was shown in half of the uneducated subjects and in one in three of those with 1-9 years of schooling. In the uneducated group, it was 20.0% and 31.1% higher than in the 1-9 years of schooling and high school or college educated groups, respectively (P = 0.001).

Central obesity had a higher prevalence in urban areas than rural areas (40.9% vs 31.9%) (P = 0.001), in 40-65 year olds than 15-40 year olds (23.6% vs 51%) (P = 0.001), and in the wealthy than other economic groups; while statistical differences were not significant (P = 0.214).

Among the uneducated subjects, the prevalence of central obesity in 40-65 year olds was 13.8% higher than in 15-40 year olds (P = 0.004). Compared with the uneducated group, the prevalence of central obesity was higher in the high school or college educated group (70.2% vs 32.8%). The prevalence of central obesity was higher in men than women in the uneducated group (16.6% vs 12.6%).

There was a direct and significant correlation between central obesity and the three economic status in the uneducated (P = 0.03) and 1-9 years of schooling groups (P = 0.001). However, this correlation was not significant in the high school or college educated group.

Results of logistic regression showed that in comparison with high school or college educated people, the risk of central obesity was higher in uneducated people (OR = 4.214, P = 0.001), and in people with 1-9 years of schooling (OR = 2.283, P = 0.001). The risk of central obesity was higher in urban areas than in rural areas (OR = 1.481, P = 0.001), in women than in men (OR = 7.039, P = 0.001), in 40-65 year olds than in 15-40 year olds (OR = 3.090, P = 0.001), and in the wealthy economic group than the poor economic group (OR = 1.360, P = 0.013). After adjusting education, the risk of central obesity increased in the urban area (OR = 2.266, P = 0.001) and in wealthy economic group (OR = 1.732, P = 0.001) compared with rural area and poor economic group, respectively (Table 2).

Table 1. Comparison of central obesity among three educational levels based on socio-demographic factors

Education level	Characters	Waist circumference (Cm) Mean ± SD	Central obesity (%)	P
Uneducated	Urban (238)	95.5 ± 14.9	153 (64.3)	0.001
	Rural (507)	91.5 ± 13.8	231 (45.6)	
1-9 years of schooling	Urban (396)	93.1 ± 15.3	194 (49.0)	0.001
	Rural (549)	85.6 ± 14.1	150 (27.3)	
High school and college	Urban (495)	86.4 ± 14.1	115 (23.2)	0.001
	Rural (243)	80.5 ± 12.6	33 (13.6)	
Uneducated	Men (259)	88.1 ± 12.5	43 (16.6)	0.001
	Women (486)	95.3 ± 14.5	341 (70.2)	
1-9 years of schooling	Men (501)	87.9 ± 14.5	93 (18.6)	0.001
	Women (444)	89.7 ± 15.7	251 (56.5)	
High school and college	Men (467)	85.8 ± 13.4	59 (12.6)	0.001
	Women (271)	82.3 ± 14.5	89 (32.8)	
Uneducated	15-40 Y (120)	89.4 ± 14.3	48 (40.0)	0.004
	40-65 Y (625)	93.4 ± 14.2	336 (53.8)	
1-9 years of schooling	15-40 Y (570)	84.8 ± 14.7	163 (28.6)	0.001
	40-65 Y (375)	95.0 ± 13.6	181 (48.3)	
High school and college	15-40 Y (547)	81.8 ± 12.7	81 (14.8)	0.001
	40-65 Y (191)	92.6 ± 14.2	67 (35.1)	
Uneducated	Poor (194)	92.1 ± 14.5	93 (43.9)	
	Moderate (429)	92.0 ± 14.3	215 (50.1)	0.030
	Wealthy (122)	96.4 ± 13.3	76 (62.3)	
1-9 years of schooling	Poor (230)	84.8 ± 13.9	65 (28.3)	
	Moderate (505)	89.3 ± 15.2	181 (35.8)	0.001
	Wealthy (210)	91.9 ± 15.2	98 (46.7)	
High school and college	Poor (141)	84.1 ± 14.3	32 (22.7)	
	Moderate (370)	83.1 ± 13.5	62 (16.8)	0.078
	Wealthy (277)	87.0 ± 13.9	54 (23.8)	
Uneducated (745)		92.8 ± 14.3	373 (50.1)	
1-9 years of schooling (945)		88.8 ± 15.1	332 (35.1)	0.001
High school and college (738)		84.5 ± 13.9	140 (19.0)	
Total (2428)		88.7 ± 14.8	845 (34.8)	

Table 2. Odds ratio (OR) of central obesity for educational levels with different socio-demographic factors using logistic regression (CI 95%)

Variables	Crude OR (95% CI)	Education level adjusted OR (95% CI)
Educational level		
High school and college	Ref (1)	-
1-9 years of schooling	2.283 (1.828-2.850)	-
Uneducated	4.214 (3.352-5.269)	-
Location		
Rural	Ref (1)	Ref (1)
Urban	1.481 (1.256-1.747)	2.266 (1.883-2.727)
Gender		
Male	Ref (1)	Ref (1)
Female	7.039 (5.823-8.509)	6.239 (5.144-7.568)
Age groups (Year)		
15-40	Ref (1)	Ref (1)
40-65	3.090 (2.602-3.670)	2.249 (1.857-2.716)
Economic status		
Poor	Ref (1)	Ref (1)
Moderate	1.068 (0.868-1.316)	1.112 (0.896-1.380)
Wealthy	1.360 (1.067-1.733)	1.732 (1.342-2.236)

Ref: Reference

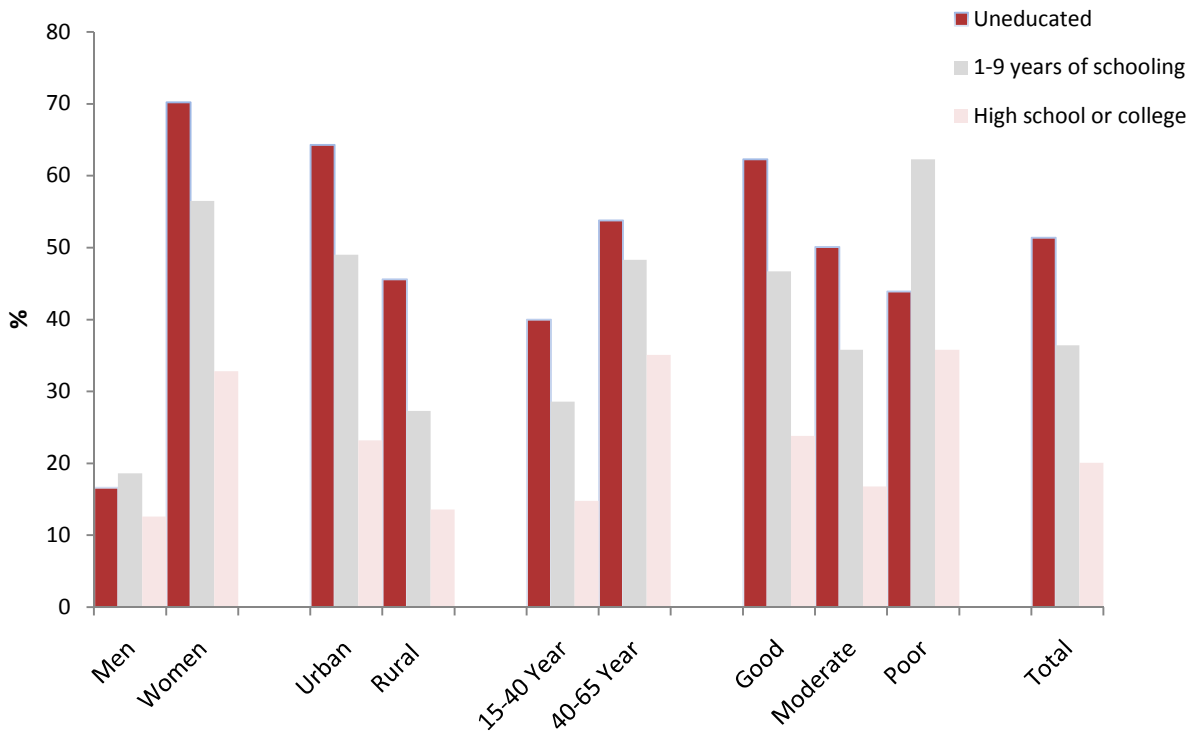

Figure 1. The comparison of central obesity based on three educational levels in adults in Northern Iran

The inverse correlation between central obesity and levels of education was significant (P = 0.001), but this correlation was not significant in men and poor economic status group. The lowest prevalence of central obesity was in the high school or college educated people in all cases (Figure 1).

Discussion

In the current study, central obesity was identified as a health problem in northern Iran, and its risk was higher in uneducated individuals than other groups.

We observed central obesity in 34.8% of adults. The prevalence of central obesity in Gorgan (north of Iran) was 39.1%, and in Ahvaz (south of Iran) 21.2%.[17,18] In the whole of Iran central obesity was reported in 12.9% and 54.5% of adult men and women, respectively.[4] The prevalence of central obesity was 36% in Spanish adults, 24.1% in Egypt, 35% in Canadian adults, and 31.5% and 64.4% in Omanian males and females, respectively.[16,19-21] Compared with other regions, the prevalence of central obesity in our study was high and should be considered as a serious health problem.

In the present study, decrease in the level of education was associated with an increasing prevalence of central obesity. By adjusting confounder factors such as location, gender, age, and economic status this trend remained, except in men and in the wealthy economic status. The correlation between central obesity and socio-economic status was shown in some studies.[9-12] Inverse correlation between educational level and central obesity has been approved in many other studies.[4,22-24] Researchers believed that educational level has a greater effect on central obesity in women than men.[25-30]

In northern Iran, it was not clear why the effect of education on central obesity in men and women was not alike. It is known that northern women are mostly housewives and men, especially the uneducated, are farmers. Therefore, in men physical activity more than education increases abdominal circumference and it is necessary to be considered in further studies. Contrary to the high school or college group, the correlation between central obesity and economic status was significant in uneducated and low educated people. Health knowledge was strongly correlated to the level of education, and cardiovascular disease was controlled well in high educated subjects.[14,31,32] It seems,

literacy and knowledge have a major role in prevention and control of central obesity in adults in northern Iran, and illiteracy is a great risk factor for central obesity.

Iran as a developing country in the Middle East Region is considered to be in the nutrition transition phase.[33] Iran's socio-demographic factors have rapidly changed in the last decade. Non-communicable diseases, especially cardiovascular disease, are the major cause of death in Iran.[34] It is necessary to design a preventive program to control central obesity, especially in uneducated and wealthy people in urban areas in northern Iran.

A limitation of the present study is that we did not evaluate the influence of many socio-demographic factors on the correlation between education and central obesity; including religion, ethnicity, occupation, background disease, physical activity, and food behaviors. Other limitations were that we did not have an exact classification for economic status and educational levels.

Conclusion

This study showed that central obesity is a health problem in adults in northern Iran with an illiteracy risk factor, especially in wealthy families, and women. Public health programs should reduce central obesity by mainly focusing on low educated people.

Acknowledgments

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Conflict of Interests

Authors have no conflict of interests.

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Effects of quince leaf extract on biochemical markers and coronary histopathological changes in rabbits

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Original Article

Abstract

BACKGROUND: Atherosclerosis is the main cause of cardiovascular disease which is caused by a high-fat diet. Many of these patients use boiled quince leaves for their treatment. However, the supporting scientific information is limit. The aim of this study was to evaluate the effect of quince leaf on the progression of atherosclerosis and whether it can be an appropriate alternative to statins.

METHODS: 24 male rabbits were randomly divided into two groups: normal diet (6 n) and high-cholesterol diet (2% cholesterol, 18 n) for 8 weeks. At the end of the 8 weeks, both groups underwent blood sampling and their biochemical markers were measured. Then, all animals in the normal-diet group and three of the high-cholesterol diet group were killed to investigate atheromic plaque in their coronary artery. The 15 remaining rabbits of the high-cholesterol diet group were randomly divided into 3 groups (5 n) after discontinuation of the fatty diet. The first group was not given any treatment, the second received atorvastatin (0.5 mg/kg) orally, and the third received quince leaf extract (50 mg/kg) orally for 12 weeks. At the end of this period, after blood sampling, biopsy of coronary artery was performed for histological study.

RESULTS: The results showed that atorvastatin and quince leaf significantly decreased total cholesterol, triglyceride, LDL, AST, ALT, AP, BUN, and Cr levels compared with the first group of the high-cholesterol diet group ($P < 0.05$). No significant difference was found between atorvastatin and quince leaf extract groups in biochemical markers and atherosclerotic plaque in coronary artery.

CONCLUSION: Atorvastatin and quince leaf extract can effectively prevent the progression of atherosclerosis in coronary arteries. According to the results of this study and also lower toxic effects of herbal medication compared to synthetic medication, leaf extract can be a substitute for statins in treatment and prevention of cardiovascular disease. The anti-atherosclerotic effect of quince leaf is most likely related to its antioxidant components.

Keywords: Hyperlipidemia, Atherosclerosis, Coronary Arteries, Biochemical Markers, Atheromic Plaque, Atorvastatin, Quince Leaf Extract

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Introduction

Studies have illustrated that a high-fat diet causes severe oxidative stress in the vascular tissue.[1] Additionally, it is the cause of mortality and morbidity.[1,2] Many believed that it can be induced from a simple dysfunction of endothelial lining.[1,3-5] Moreover, of the factors causing heart failure life style, fatty regimen, hypertension, and a fatty diet, particularly LDL cholesterol, are mainly responsible for hypercholesterolemia that is related to increased damage in vascular tissue by free radical oxidative stress.[3,6,7] Although cholesterol-lowering drugs such as statins were used for several decades and are effective in preventing cardiovascular disorders, their usage is often limited because of their adverse effects, such as rhabdomyolysis. These effects are very pronounced when a statin is taken with another type of cholesterol-lowering drug, in

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particular fibrate. This resulted in the introduction of plants as a source of natural antioxidants.[8-10] Due to the adverse effects associated with synthetic lipid-lowering drugs, the quest for natural products with lipid-lowering potential and without or minimal side effects is necessary. It has been found that many plants are useful as antioxidant and antimicrobial agents and can be used as forms of herbal medicine.[11-16]Among these plants, quince is a suitable source of antioxidant. It contains appreciable amounts of vitamin E and phenolic compounds (catechins, phenolic acids, and kaempferol-3-o-rutinoside), which also have protective effects. Given the high levels of phenolic compounds in the quince leaves (such as kaempferol-phosphate), they are more effective than the fruit and seeds in the promoting of health and are a useful and inexpensive source of bioactive elements.[11,13,15,16] The quince leaves are widely used to treat diarrhea, heart palpitations, and eye disease.[17] Phenolic compounds from dietary antioxidants are the most natural antioxidants.[18] This study evaluated the effect of the quince leaves on biochemical markers such as lipid profiles, liver enzymes, and kidney function, and compared them to a standard medication called atorvastatin.

Materials and Methods

Drugs and chemicals

All drugs and biochemicals used in this study were purchased from Sigma Co (St, Louis, Mo, USA) and from Merck Company (Darmstadt, Germany). All other chemicals an reagents were of analytical grade.

Atherogenic Food

Pure cholesterol powder was purchased from Farzan Teb Co. (Merck, Germany). Daily food dosage was measured for 3 consecutive days. Intake rate was obtained for calculating the atherogenic diet formula, and the amount of 54 gr was considered for all animals. A high-fat diet with 2% cholesterol was prepared and stored at 4°C.

Preparation of the extract

The quince green dried leaves were purchased from Herbs Chemist (Tabriz, Iran). Methanolic 70% extract was prepared by maceration method. The extracts were filtered three times and concentrated to dryness under vacuum. Then, the percentage of the obtained dry extract (7%) was determined and it was kept at subzero degrees centigrade until administration time. The extract was dissolved in water in order to be given orally by gavage needle.

Methods

24 male New Zealand white rabbits (the least number of animals in each group = 6, with 2500 ± 200 weight, and mean age of 8 weeks) were purchased from the Pasteur Institute of Iran. They were kept at 22°C, and given free access to food (from Sahand Niroo Co., Tabriz, Iran) and water at least 7 days before the experimental study. After adaptation, rabbits were randomly divided into two groups of normal diet (n = 6), and high-cholesterol diet (n = 18). The rabbits with the high-cholesterol diet were fed an atherogenic diet containing 2% cholesterol (54 g/day) for 8 weeks. At the end of week 8, groups underwent blood sampling from marginal ear vein. For histopathological studies, all rabbits of the normal diet group plus three rabbits selected randomly from the high-cholesterol diet group were killed and biopsy was performed from left coronary artery. Then, the remaining rabbits of the high-cholesterol diet group were randomly divided into three groups of five rabbits each after stopping atherogenic diet for 12 weeks. The first group was fed with a normal diet without any treatment and served as control group. The second group was given the same diet as the control group plus atorvastatin at a dose of 0.5 mg/kg once a day orally (atorvastatin group). The third group was fed the same diet as the previous groups plus a supplement of quince leaf extract (5 mg/kg once a day orally). At the end of week 12, the blood samples were taken again, and coronary biopsy was performed on all rabbits after thoracotomy. All animal care and experimental protocols were confirmed by the Medical Ethics Committee of Tabriz and complied with the guidelines of the National Institute of Health (NIH publication 86-23 revised 1985).

Sample collection

Blood samples were collected from all rabbits in two steps that have been mentioned previously. Plasma was prepared by centrifugation at 3000 g for 15 minutes. Serum levels of lipid profiles such as total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, and liver enzymes including aspartate transaminase (AST), alanine transaminase (ALT), and alkaline phosphatase (AP), and other biomarkers for kidney functionality (BUN, Cr) were recorded by an Auto Analyzer.

Histopathological study

For sampling, animals were anesthetized by appropriate doses of ketamine and xylazine by intramuscular injection. Fixation was perfused by saline buffer formaldehyde-cold PBS 4%, PH: 7.2 into heart ventricle. Histological biopsy of the coronary artery was performed after thoracotomy.

After thoracotomy, coronary specimens were immersed in formalin 10% for 48-72 hour. Then, they were embedded in paraffin and cut into thick sections (5µm), subsequently deparaffinized by graded concentrations of ethanol and xylene, and then were stained by specific Weigert's Iron hematoxylin staining. Finally, surfaces of the whole plaques were measured and compared to surfaces of total coronary arteries by Motic Software. The plaque thickness was confirmed by three observers.

Statistical analysis

Results were analyzed by SPSS for Windows (version 16; SPSS Inc., Chicago, IL., USA) and Student's t-test (assuming equal variances), Mann-Whitney test, and Kruskal-wallis test ($P < 0.05$ was considered significant) were performed to determine the statistical significance of data obtained from the two groups and compare them to each other). The diagrams were depicted by Microsoft Excel.

Results

Determination of biochemical markers

Lipid profile levels in the blood plasma of different groups are shown in table 1 and figure 1. In the high-cholesterol diet group TC, TG, and LDL levels increased significantly compared with the normal diet group, and HDL decreased ($P < 0.05$). Moreover, the biomarkers AST, ALT, AP, BUN, and Cr increased significantly in all groups during the two months of using the high-cholesterol diet (Table 1 and Figure 2) ($P < 0.05$). After three months of discontinuing the high-cholesterol diet, all biochemical markers were measured. This showed that the cholesterol level of the control group of the high-cholesterol diet group was lower compared with before stopping. However, it was still significantly high compared with the normal diet group ($P < 0.05$). The 0.5 mg/kg dose of atorvastatin and 50 mg/kg of quince leaf extract significantly decreased TC, TG, LDL, AST, ALT, and Cr levels compared to the control group of the high-cholesterol diet group ($P < 0.05$). However, in both of these groups TC, LDL, and AP levels were significantly higher compared with the normal diet group ($P < 0.05$), but no significant difference was found in TG, HDL, and BUN levels. In both atorvastatin and quince leaf extract groups, the levels of AST, and ALT showed no significant difference to the normal diet group.

Table 1. Comparison of lipid profile, liver enzymes, and plaque thickness in normal and high-cholesterol diet animals (end of 2 months) and after stopping high-cholesterol diet (end of 3 months)

Groups	Lipid profile (mg/dl)				Liver enzymes				Plaque thickness (µm)	
	TC	TG	LDL	HDL	AST	ALT	AP	BUN	Cr	Coronary artery
Normal-diet	76.7 ± 23.2	179.3 ± 14.8	22.8 ± 6.4	68.7 ± 8.5	50.3 ± 6.4	68.0 ± 10.1	56.3 ± 1.9	5.0 ± 2.65	1.46 ± 0.20	-
High-cholesterol diet	467.6 ± 1002.1*	1925.7 ± 2008.2*	2232.8 ± 914.6*	50.6 ± 2.7*	83.0 ± 7.4*	104.6 ± 7.5*	230.0 ± 31.9*	41.14 ± 1.03	2.02 ± 0.31*	0.09 ± 0.04*
Control	1406.0 ± 343.1*	1037.3 ± 228.9*	1073.3 ± 56.8*	42.3 ± 4.8	86.3 ± 10.9	78.0 ± 2.0	145.7 ± 26.0	41.67 ± 0.88	2.03 ± 0.20	0.06 ± 0.01*
Atorvastatin	813.7 ± 427.7*,**	386.7 ± 185.1**	682.3 ± 368.2*,**	54.0 ± 8.1	45.0 ± 4.9**	57.7 ± 6.0**	134.0 ± 15.1*	42.67 ± 1.45	1.44 ± 0.43**	0.06 ± 0.03*
Quince leaf extract	511.7 ± 174.4*,**	138.3 ± 68.3**	534.0 ±52.3*,**	60.0 ± 6.1	45.0 ± 7.0**	68.7 ± 2.7**	121.5 ± 39.5*	41.00±2.08	1.54±0.22**	0.04± 0.01

TC: total cholesterol; TG: triglyceride; LDL: low density lipoprotein; HDL: high density lipoprotein; AST: aspartate transaminase; ALT: alanine transaminase; AP: alkaline phosphatase
*compared with normal diet group ** compared with control group

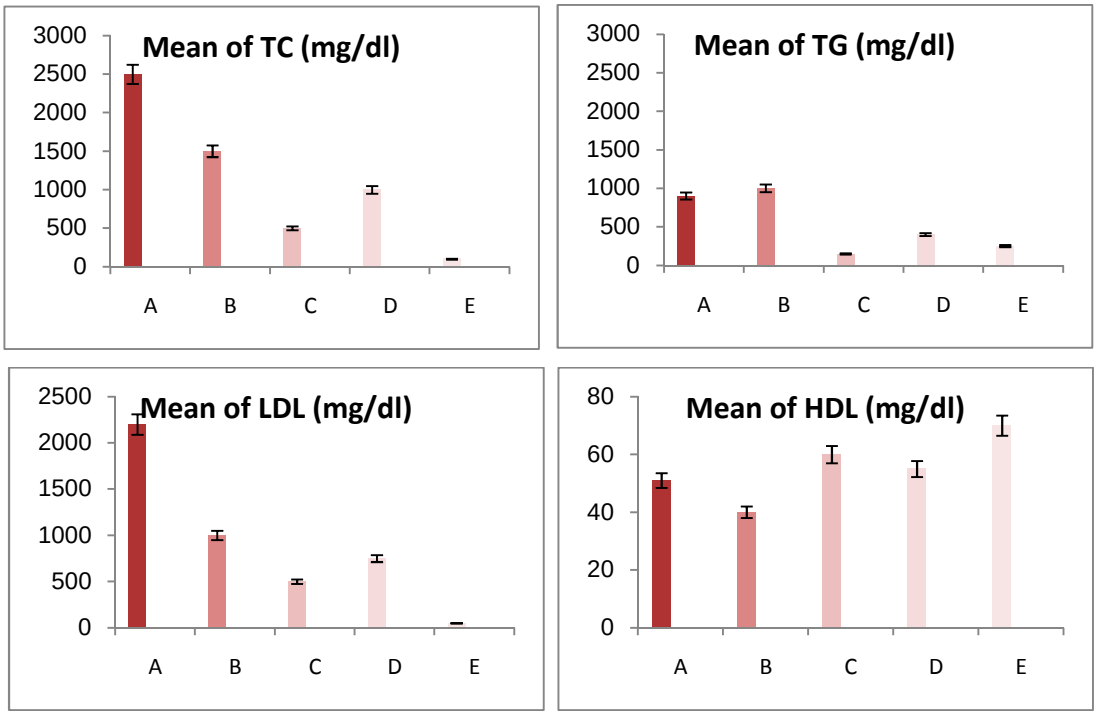


Figure 1. Lipid profile changes in the blood plasma in different groups
A: High-cholesterol diet group; B: Control group after stopping high-cholesterol diet;
C: Quince group; D: Atorvastatin group; E: Normal diet group
TC: Total cholesterol, TG: Triglyceride, LDL: Low density lipoprotein,
HDL: High density lipoprotein

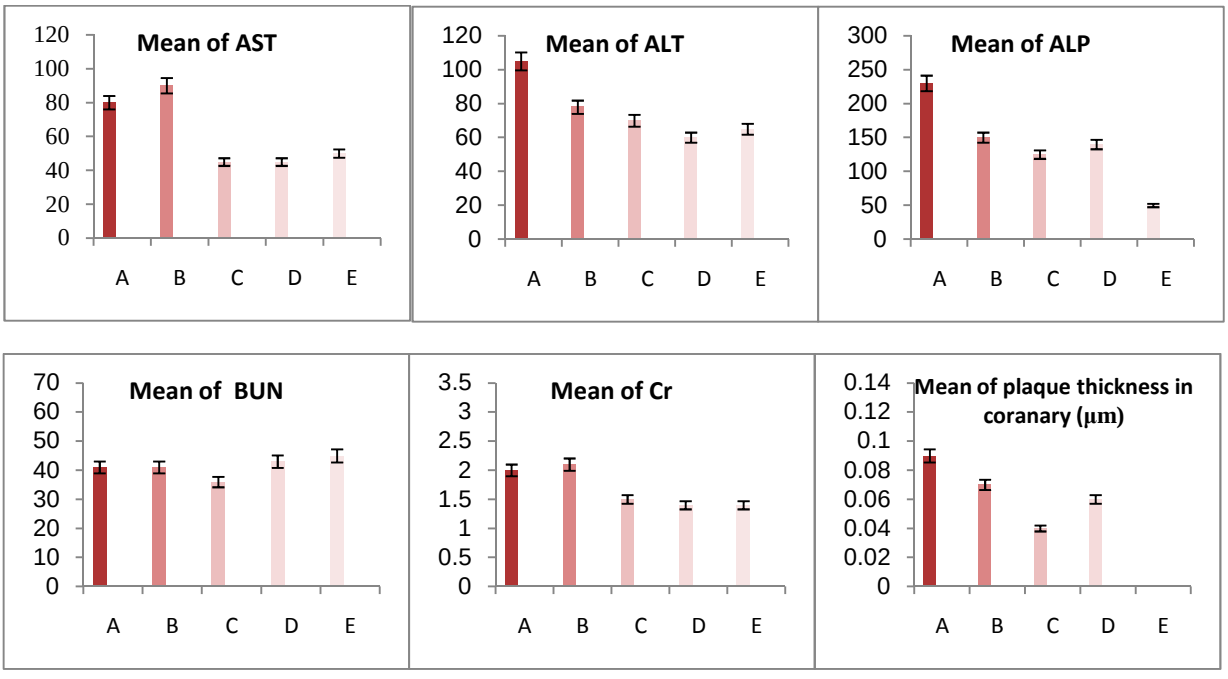
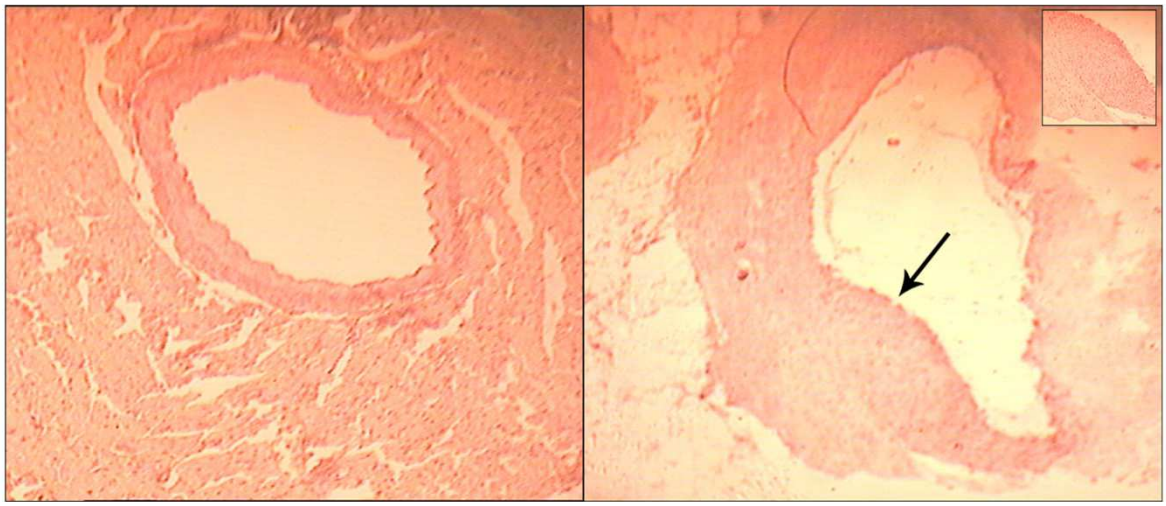
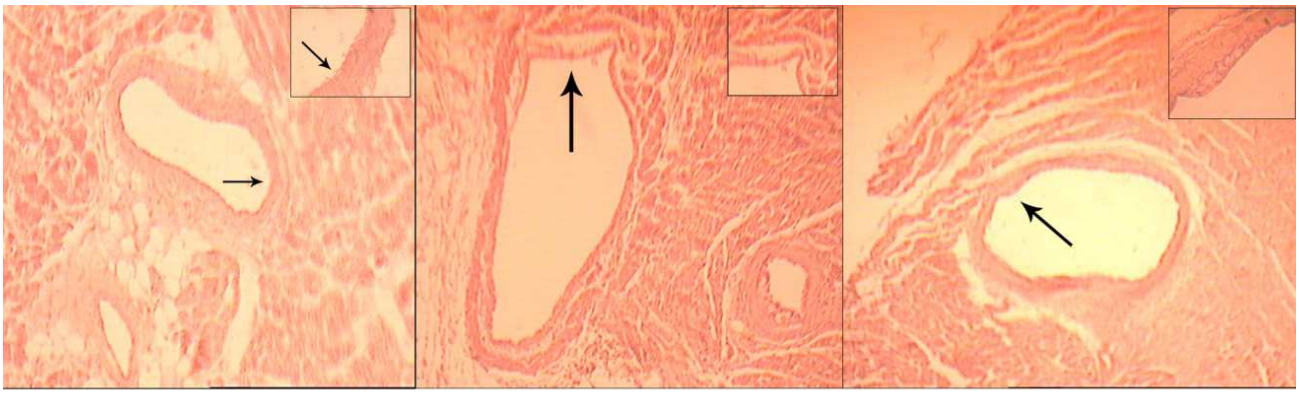


Figure 2. The alternations in biomarkers and coronary plaque thickness in all groups
A: High-cholesterol diet group; B: Control group after stopping high-cholesterol diet;
C: Quince group; D: Atorvastatin group; E: Normal diet group
AST: Aspartate transaminase; ALT: Alanine transaminase; AP: Alkaline phosphatase;
BUN: Blood urea nitrogen, Cr: Creatinine



(a) (b)

Figure 3. Photomicrograph of a section of normal coronary artery (control group) (a) and hyperplasia were seen in media layer along with high infiltration of cells to plaque formation site (b) X40



(a) (b) (c)

Figure 4. Photomicrograph of a coronary artery section of the control group after stopping high-cholesterol diet (a), atorvastatin (b), and quince leaf extract (c) groups

No considerable difference was seen in the extent of atherosclerotic thickness between the atorvastatin and quince leaf extract groups, and control group

Histopathologic findings of coronary arteries

Histological sections of stained coronary arteries and the alternation in coronary plaque thickness from all the groups of rabbits are shown in figures 2, 3, and 4. Atherosclerotic changes were not observed in the normal diet group (Figure 3a). However, in the intimal surface of the coronary arteries from the high-cholesterol diet group, hyperplasia was seen in media layer along with high infiltration of cells to plaque formation site (Figure 3b). The thickness of the plaque had extended in all experimental groups after stopping the high-cholesterol diet. The thickness of plaques in the control group had extended compared with the high-cholesterol diet group. No considerable difference was seen in the extent of atherosclerotic thickness between the atorvastatin and quince leaf extract groups, and the control group (Figure 4a-c).

Discussion

Beyond the shadow of a doubt, hyperlipidemia is the most important risk factor for atherosclerosis.[1,19] Using a daily high-cholesterol diet leads to its accumulation in the plasma membrane that causes membrane damage. This as an atherogenic stimulus increases the production of growth factors and proliferation of smooth muscle cells (SMC).[20]Therefore, any factors that reduce cholesterol levels can affect this process.

In this study, high-cholesterol level in plasma was shown by hypercholesterolemic regimen. Our results were similar to the study by Adaramoye et al. in

which rats received high-cholesterol diets.[21] Additionally, we demonstrated that lipid profiles (TC, TG, LDL, HDL) were returned to nearly normal levels by a standard diet for 12 weeks after stopping the hypercholesterolemic diet in the control group. Salazar et al. also reported that the biochemical parameters of rabbits were returned to normal by returning them to a standard diet. However, the histological parameters were not fully recovered.[22]

In The present study, atorvastatin has been used as a standard drug. This drug is one of the statin family of drugs that reduce cholesterol by inhibiting the HMG-CoAreductase. Furthermore, since atorvastatin was used in this study (oral administration) the results were quite predictable.[23]Until now, this drug has been used with the high-cholesterol diet by the prophylactic method. However, we have used this drug after accumulation of plaque, in order to demonstrate the reduction or returning of plaque and biochemical marker changes. The obtained results indicated that the drug's ability to return the patient to normal condition (normal lipid profiles and biomarkers) has been effective, but it was less than the group receiving quince leaf extract. The early effects of statin therapy have been to lower LDL by 24-63%.[24]

Several studies have indicated that herbal or synthetic medicine decrease mortality of cardiovascular disease (CVD) by cholesterol regulation.[25]Accordingly, many efforts have been made to reduce CVD risk through cholesterol regulation. The health advantages of plant foods have been noted by some studies.[26,27] Plants contain a variety of flavonoids such as flavonols, flavones, anthocyanidins, and quercetin.[28] Moreover, we evaluated the efficacy of quince leaf extract on atheromic plaque. Hayek et al. in their study, showed the reduction in oxidation by flavonoids.[29]In another study, two flavonoids in the form of glucuronide and sulfate compounds were administered orally to rats and their antioxidant capacity increased.

Researches have illustrated that phenolic compounds, typically flavonol derivatives such as kaempferol glycoside and 0-3 kaempferol retinoid, are found inquince leaf and act as a filter protection against UV radiation.[12,13,15]

Flavonoids cause vascular expansion by increasing nitric oxide; this is an antioxidant property against LDL.[30,31] Epidemiological studies have reported the beneficial effect of red wine and foods rich in flavonoids in reducing the risk of high cholesterol.[31-33] Another study compared the protective effect of methanolic quince leaf extract and green tea on erythrocyte hemolysis that is caused by oxidative damage from free radicals.[21] The anti-hemolytic effect in humans was demonstrated by both leaves. This study also revealed that the antioxidant capacity of leaf extract was lower than green tea extract. Moreover, there was no linear correlation between antioxidant activity and free radical reduction. In fact, the antioxidant activity of the leaves could be caused by the antagonistic or synergistic activity of bioactive compounds that are still unknown.[34,35]

In addition, the current study revealed a significant reduction in lipid profile (TC, TG, and LDL) and increase in HDL cholesterol in all experimental groups after stopping the atherogenic diet. These results illustrated that the group receiving quince leaf extract was more similar to the normal diet group, and the atorvastatin group had a better status than the group which was not taking medication. On the other hand, Suk et al. showed that serum levels of rats receiving a high-cholesterol diet were higher compared with rats receiving a standard diet. After receiving a standard diet for 6 weeks, they were able to return to their normal serum cholesterol levels. However, no change was observed in their triglyceride level.[36] In our study, both levels of TC, and TG reduced significantly; the group receiving quince leaf extract was more similar to the group receiving standard regimen in this respect. To confirm, the same results were observed in rabbits fed on apple juice and the group that received high-cholesterol. This result indicates that apple juice has been effective in the adjustment of dyslipidemia caused by a high-cholesterol diet.[37] On the other hand, consumption has been associated with a high-cholesterol diet.

The aqueous quince leaf extract was adminestrated in the three doses of 50, 100, and 200 mg/kg with isoproterenol (ISO) by Rajadurai et al. They administrated them orally, injected, and compared the results to alpha-tocopherol. Our study revealed that quince leaf extract in the dose of 200 mg/kg could regulate lipid profile levels, and reduce CK and LDH enzymes elevated by ISO. The effect of aqueous quince leaf extract 200 mg/kg was found to be equal to the effect of alpha-tocopherolin 60 mg/kg.[17] The investigation method and objective of this study were different to our study; an atherogenic diet was used with quince extract to evaluate the preventive effect of the extract. Furthermore, we investigated the influence of the development or regression process of quince

extract. In this study, we used total extract while previous studies did not mention the component of the leaf extract used.

Our study also showed the reduction of biochemical markers including AST, ALT, ALP, BUN, and Cr by a high-cholesterol diet regimen in the control, atorvastatin, and quince leaf extract groups. These results were consistent with the study by Singanan et al.[35] (they demonstrated the hepatoprotective effect of quince leaf extract), and Suk et al.[36] (they studied on rat for 6 weeks). However, in the histological results, liver damage caused by a high-fat diet did not improve with a standard diet.[36] As expected, an atherogenic diet, as a progression of atheroma catalyst, resulted in an increase of this complication in the aortic and coronary artery in the control group. Increase plaque, in this group, showed that damage to the endothelium caused by a high-cholesterol diet provided a context for further stenosis in blood vessels. In both atorvastatin and leaf extract receiving groups plague formation was considerably higher. In this regard our findings were consistent with the results of other studies.[35,36] Our study indicated that plaque formation in the coronary artery in rabbits receiving atherogenic diet. However, after three months follow-up with quince leaf extract 50mg/kg and atorvastatin 0.5 mg/kg, neither drug were able to inhibit the increase in plaque in the coronary; plaque thickness was higher in the control group, which had not been taking any medication, than the quince leaf extract group. This difference was not significant. Decorde et al. showed that the phenols of grape, black grapes, apple juice, and apple decreased atherosclerotic plaque in hamsters by 93%, 78%, 60%, and 48%, respectively.[38] A survey on red wine showed a significant reduction in plaque in arteries.[39]

Inflammation has an important role in the development of atherosclerosis. The abatement of inflammation in the coronary plaque in the group receiving atorvastatin is due to the anti-inflammatory effects of statins that has already been proven.[40]

In some researches, the activity of some enzymes during the inflammatory process were inhibited.[41-43] Plaque stabilizing effects of statins may also be due to the reduction of some inflammatory cytokine after plasma lipid lowering. The reduced anti-inflammatory cytokine levels, such as CRP, with the lowering in TC and LDL prevented the development of atherosclerosis.[37]

Conclusion

The results of the present study confirmed the correlation between hypercholesterolemia and atherosclerosis, and also that quince leaf extract, like atorvastatin, can effectively reduce a high-fat diet-induced atherosclerosis.

However, according to histological determination, atorvastatin and quince leaf extract were not able to prevent plaque increasing in the coronary after plaque formation for 12 weeks. Both treatments have been able to reduce serum levels to nearly normal level after plaque formation and accumulation; the quince leaf extract was more effective than atorvastatin which may be due to its phenolic components. It seems that the decrease in plaque must be studied for a longer time at least for the dose used in our study.

Further studies are recommended in order to find the exact mechanism of the quince leaf extract in endothelial function improvement. More effective clinical applications of these natural compounds will be determined.

Conflict of Interests

Authors have no conflict of interests.

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Developing an appropriate model for self-care of hypertensive patients: first experience from EMRO

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Original Article

Abstract

BACKGROUND: Cardiovascular diseases (CVDs) constitute 53% of deaths above the age of 30; 54% of these deaths are attributed to high blood pressure. Coronary artery disease (CAD) is the main cause of mortality in the world. Hypertension accounts for 13% of mortalities and 6% of morbidities and is one of the main risk factors that cause loss of healthy life years. Blood pressure is not optimally controlled even among those who are aware of their disease. Previous studies showed that apart from pharmacological treatment, lifestyle improvement can also play a significant role in the prevention of high blood pressure CVDs. Self-care among them has been addressed in several previous studies. There are few self-care programs in Iran, but no study has been conducted on blood pressure.

METHODS: In this study the primary model is designed and then revised, and in the pilot study the feasibility of the project was approved and the final model presented.

RESULTS: The current project proposes a model for self-care of hypertensive patients and their families, and is based on education of health care providers and patients in such a way that patients can control their illness.

CONCLUSION: The model can be implemented at a national scale.

Keywords: Self-Care, Hypertension, Model

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Introduction

Cardiovascular diseases (CVDs) are among the most common causes of mortality and morbidity in both developed and developing countries.[1] Among them, coronary artery diseases (CADs) are the leading cause of premature mortality and morbidity in developed countries.[2]

The main risk factors of CVDs include hypertension, smoking, diabetes, and hypercholesterolemia.

Hypertension accounts for 13% of mortalities and 6% of morbidities and is one of the main risk factors that cause loss of healthy life years.[3,4] It is estimated that one billion people all over the world suffer from hypertension which is projected to afflict 1.56 billion people in 2025.[5]

In individuals who have blood pressures above 115/75 mmHg, with each 20/10 mmHg increase in blood pressure, the risk of CVD will be doubled.[6]

The prevalence of hypertension varies in different regions of the world. However in the current decade, it has shown substantial increase in many countries even in low-income ones.[7-10]

Many studies have demonstrated that a large proportion of patients are not aware of their high blood pressure. Moreover, blood pressure is not optimally controlled, even among those who are aware of their disease; they do not adhere to their treatment regimen. The rate of control for hypertension varies in different countries: 37% in

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Saudi Arabia, 20% in Romania, 12% in China, and 7% in India.[11-14] Results of a multi-national study in 35 countries, show that prevalence, awareness, treatment, and control of hypertension among men are 40.8%, 49.2%, 29.1%, and 10.8% in developed countries and 32.2%, 40.6%, 29.2%, 9.8% in developing countries, respectively. The relevant figures among women are 33.0%, 61.7%, 40.6%, and 17.3% in developed countries and 30.5%, 52.7%, 40.5%, and 16.2% in developing countries, respectively. There was no significant difference in any of the above indicators between developed and developing countries.[15]

As a result, health policy-makers are apt to design new methods for secondary prevention of hypertension. Self-care for chronic diseases has recently been suggested as a plausibly effective method.

Self-care programs are reported to decrease emergency visits by 40% and outpatient visits by 17%.[16] In self-care programs, it is expected that patients become aware of their health status, know when they need care, and gain adequate knowledge regarding the necessity and mode of treatment. Patients should be able to monitor their symptoms and refer in time for routine examinations without needing to refer to their physician.

Hypertension is among the diseases that can be successfully controlled by performing self-care activities.[17] Effectiveness of self-care in hypertension is more significant for the elderly.[18] Different patterns of self-care for hypertension have been observed including knowledge about the disease and its symptoms, adherence to treatment, adopting a healthy lifestyle, and blood pressure monitoring.[19] A study in 2008 in the United Kingdom showed that hypertensive patients used different methods of self-care including blood pressure monitoring at home, complementary treatment, and better adherence to treatment.[20] Home blood pressure monitoring can be even more effective than monitoring by physicians.[17,21] The health personnel including physicians, nurses, nutritionists, and pharmacists play a pivotal role in self-care.[22-25] Cappuccio et al. conducted a meta-analysis of 18 randomized, controlled trials on various patterns of self-care for hypertension. Results showed that both systolic and diastolic blood pressures were lower, and the proportion of patients with controlled hypertension was higher in the intervention group compared to the control group.[26] Blood pressure was controlled better in home monitoring compared to monitoring in clinics.[17] Padfield also reported that home monitoring was the best pattern of self-care for hypertension.[21]

Glynn et al. conducted a meta-analysis on 72 clinical trials. Interventions examined in these trials included: self-monitoring, educational interventions directed at health professionals, nurse- or pharmacist-led care, and a systematic reminder of appointments. Results showed that self blood pressure monitoring can lead to most prominent decreases in systolic and diastolic blood pressures.[27] However, some studies have shown that self-care strategies may not be as effective beyond six months.[28-31] There are a number of controversial reports stating that cost-efficiency of self-care programs may be even less than usual care.[31] Further research is needed to achieve conclusive results on the effectiveness and cost-efficiency of self-care for hypertension.[32-36]

There is not much evidence on self-care in Iran. A study, as a part of the Isfahan Healthy Heart Program (IHHP), investigated the effects of comprehensive self-care programs on improving the knowledge, attitude, and treatment among patients with hypertension. Adherence to treatment significantly increased, especially among obese patients and those above 40 years of age. At the beginning of the study, adherence to treatment varied from 10% to 56%. After 4 years of intervention, adherence to treatment significantly improved, and participants increased their physical activity and lived on a healthy diet.[37] To the best of our knowledge, no other study on self-care in Iran has been published.

The incidence of CAD in Iran is estimated to be approximately 181.4 per 100,000 and CVDs are the cause of 46% of total deaths in Iran and their prevalence is increasing. The Isfahan Cohort Study (ICS) has reported that the relative risk of cardio-vascular events is highest for hypertension.[38] Therefore, improved control of hypertension can significantly prevent cardio-vascular events.

The prevalence of hypertension among men and women has been estimated by Tehran Lipid and Glucose Study to be around 23% and 20%, respectively.[39] The prevalence of hypertension has been reported about 26.6% by the Third National Surveillance of Risk Factors.[40] The IHHP showed that the knowledge, adherence to treatment, and percentage of hypertension control were 49.9%, 43.8%, and 15.8%, respectively. The rate of control has increased from 7.1% in 2001 to 15.8% in 2007.[41] Still, it is less than the majority of developed countries, where coverage is over 30%, and just slightly higher than India and China.

Based on the existing data, no project has been conducted in Iran regarding self-care for hypertension until today. Regarding the high prevalence of hypertension and inadequate control level, the current protocol is presented for the design of a self-care model for hypertension. The current proposal is developed to design a model for self-care of hypertensive patients and to examine its feasibility.

Materials and Methods

As a first step, a steering committee was formed in 2011 in order to determine the priorities and devise an action plan for preparing a model for hypertension self-care. This committee encompassed a wide range of experts of self-care and hypertension including director general of Health Education and Promotion of the Ministry of Health of Iran, some of the academic members and prominent experts of Health Education and Promotion, two cardiologists, and the Head of the Isfahan Cardiovascular Research Institute (ICRI). Moreover, the executives of the program arranged interviews with some of the experienced experts in this field to take advantage of their knowledge and experience. It was determined that the project be designed and examined exclusively in urban areas, as the health system in urban areas in spite of having high proportion of population and high prevalence of hypertension, is not comprehensive enough.

After gathering the related data and considering viewpoints of consultant experts a primary model was designed based on the education of care providers, patients, and their families. The suggested model was tested in some of the care delivering units as follows: 1) The Khaneh Isfahan Health Center, an urban health center for controlling NCDs, mainly diabetes. 2) The Khajoo Health Center, a traditional urban health center 3) some Private offices and 4) The Ghahjavarestan Health Center, a rural health center near Isfahan city, Iran.

Information was given to patients through lectures, questions and answers, face to face training, and follow-up. Due to a large number of patients who refer to private offices, the private sector is the important part of the project. Physicians believe in the effectiveness of self-care. As for pharmacies and laboratories, leaflets were utilized but were not as effective as face-to-face consultation.

In rural areas the project can be quite successful if health workers in Health Houses (Behvarzan) are trained and capable of controlling blood pressure.

Overall, in all of the four aforementioned units, patients were significantly satisfied of the program and many of them expressed in interviews that they have learned points of which they were never aware. Patients demanded further and earlier additional sessions.

As for health care providers, the level of satisfaction was also significant as said in their interviews. The main barriers declared by health personnel were large number of patients, lack of suitable physical space, and inadequate equipment and time for visits that reduced the quality of consultation and led to long waiting time.

Overall, the results of the pilot demonstrated the feasibility and necessity of integrating self-care programs in the health system, which requires providing the needed infrastructure. It can be planned based on mandatory periodical education settings to empower health personnel.

An important part of this project is providing self-care education in aforementioned units. Parts of the project are focused on empowerment of health care providers. Although the researchers tried to cover all domains of self-care, the project has certain defects, which will hopefully be corrected in future.

Stakeholders' Analysis

As shown in table 1, there are different stakeholders who can be involved in the project. This analysis helps to do efficient advocacy with these stakeholders to have their collaboration in the project.

In general, it seems apart from secondary beneficiaries and some of the partners; others do not have adequate knowledge of and attitude toward self-care. For each subgroup, a relevant and appropriate message was devised. Techniques of encouragements of stakeholders were also developed.

Results

The suggested model

The practical goals of the study included: 1) to present an appropriate model of self-care for similar studies; 2) to present the methodology and results of the project to legislators and policy-makers; 3) to improve the lifestyle of participants if the model be implemented; and 4) the project could be generalized to large provincial or national scales.

Inclusion criteria were 30 to 60 year-old patients residing in Isfahan, Iran, with approved cardiovascular diseases (Atrial fibrillation, hypertension, ischemic heart disease, or chronic heart failure).

Exclusion criteria were refusing to participate and change of address. Convenience sampling was conducted in two health centers (Khaneh Isfahan, and Khajoo Urban Health Centers). The

Table 1. Stakeholders' Analysis

	Stakeholder categories		Subgroups	Barriers to make contact
1	Beneficiaries	Primary	Individuals at risk, Hypertensive patients, and their families	Large group, Moderate access, Relatively difficult message development
		Secondary	Medical universities and the relevant offices in MOHME, Insurance companies, Pharmaceutical companies, Private sector	Large group, Inadequate access, Relatively difficult message development
2	Decision-makers	Legislators	Members of Islamic Parliament, Members of city councils	Small group, Difficult access, Difficult message development
		Policy-makers	MOHME and all the subordinates, the Mayor, Heads of mass media	Small group, Easy access, Easy message development
		Executers	Provincial and district health centers in Isfahan	Moderate group, Easy access, Difficult message development
3	Partners		Public and private health centers, Hospitals, Pharmacies, Private Clinics, Physicians of Private sector	Large group, Relatively easy access, Relatively easy message development
4	Opponents		Unhealthy food industries and Tobacco companies	Large group, Difficult access, Difficult message development

MOHME: Ministry of Health and Medical Education

methodology included development of educational contents, conducting pilot, stakeholders' analysis, comprehensive advocacy for stakeholders, and development of techniques for encouragement.

The operational model for self-care in hypertensive patients

In the beginning, it should be determined where hypertensive patients should be referred: public, or private sections, or non-governmental organizations. The health care providers who should be educated include: physicians, nurses, nutritionists, and consultants for physical activity and mental health. They should be capable of diagnosing hypertension, examining complications, providing pharmaceutical and non-pharmaceutical treatment, correct blood pressure measurement, and appropriate referral of patients in need. Skills for providing education, treatment, and follow-up will be taught based on the approved curriculum.

In the next step, hypertensive patients will be invited to participate in the project through public announcements, general practitioners, and health centers. History taking, physical examination, and diagnosis of patients should be carried out by the physician. Thereafter, the physician should teach the patient the correct method of blood pressure measurement and inform him/her that the disease is asymptomatic and may end in inevitable complications if left untreated, lasts till the end of life, and it should be controlled by pharmaceutical and non-pharmaceutical treatment. Other non-pharmaceutical advices are provided by nurses, nutritionists, and consultants of physical activity and mental health. A file should be filled out for the patient including the contact information, the date of the next appointment, and if necessary referral of the patient to specialists such as cardiologist, nephrologist, endocrinologist, hospitals, or consultants for cessation of addiction, nutrition, mental health, or rehabilitation.

The following resources are needed for the implementation of this project: 1) human resources: the least is a physician capable of follow-up, treatment, and consulting for nutrition, life-style, and quitting smoking; 2) appropriate physical space: for physical examination, education, and follow-up; and 3) equipment: manual or electronic file for patients, sphygmomanometer, and etcetera.

The project can be integrated in other programs such as diabetes control.

The importance of situation analysis lies in the feasibility of integrating the project into the family physician program.

In the final model, two educational packages have been developed:

1) Improving the capabilities of health care providers for controlling hypertension.

2) Educating hypertensive patients, their families, and people who are high risk for hypertension.

The education requirements that care providers should meet include: 1) access to information; 2)

acceptance and participation; 3) responsiveness; and 4) developing local structural capacity.

The educational curriculum for health care providers consists of two parts:

1) Curriculum to increase capabilities in teaching (30-40 hours) including:

a) Mandatory skills: education planning, needs assessment, communication skills, overall view of behavioral models, and general principles of behavioral change

b) General training: general concepts of health, self-empowerment, quality of life, life skills, and supportive laws and systems

2) Curriculum for capabilities in fields specific to hypertension (30-40 hours) including:

a) Goals, strategies, and activities in the project

b) Duties of health personnel in various levels of the health system

c) Rights of patients

d) Symptoms of hypertension

e) The necessary diagnostic measures, and the importance of preventing hypertension and its acute and chronic complications

f) Diagnosis of disease, and guidelines for completion of files for patients

g) Methods of preventing hypertension

h) Correct measurement of blood pressure

i) The principles of controlling hypertension

j) Method for monitoring and self-care for hypertensive patients and their families, and the correct usage of sphygmomanometers

k) Pharmacological treatment

l) Non-pharmacological treatment

m) The characteristics of the disease

n) Methods to cope with the disease

o) Social support

p) Referral in necessary cases

q) Guidelines for follow-up and care for patients

r) Methods for saving and delivering the information

s) Prevention and control of hypertension in specific groups of patients such as the elderly and children

The educational curriculum for patients and their family members:

Education is the basis of care for hypertension. The first step is to understand the situation of the patient and his family members and friends, to assess their knowledge, attitude, beliefs, and skills. Each patient has unique needs and capacity for learning and patients should be considered independently.

The self-care program takes place in many settings such as offices of general physicians, health care organizations, health centers, health houses, hospitals, pharmacies, state and private institutes, and etcetera. For all of these settings a specific chart of delivering service is prepared. One of these charts is given in table 2.

Educational methods

Face to face consultation and group education and for non-attending classes: leaflets, books, pamphlets, electronic books, CD, and etcetera.

The self-care project for hypertension in family physician program

Considering the implementation of the family physician program in rural areas and its extension to urban areas, the self-care model has been developed to be integrated into the family physician program.

Duties of non-physician health care providers such as nurses, health workers and nutritionists, for controlling hypertension

1) Filling out the form for hypertensive patients who are approved by the physician

2) History taking

3) Physical examination and measurements

4) Referral of the patient to physician based on symptoms

5) Educating the patient: disease description, its complications and dangers, the necessity of controlling blood pressure and complications of hypertension, change of lifestyle

6) Non-pharmacological treatment and follow-up

7) Follow-up: monthly visits

8) Documenting of measures taken in the file

9) Non-pharmacological treatment, follow-up and education of specific groups of patients such as the elderly, children, and their families

Treatment and follow up of hypertension in specific groups of patients such as the elderly and children

1) Consultation and referral to a specialist

2) Supervising other personnel of the team

3) Completing tasks that have not been done by other personnel

4) Documenting of measures taken in the house-hold

The system for monitoring and evaluation of the self-care project

The program is evaluated based on the satisfaction of patients and health care providers, the number of referrals, the method of distributing information, the coverage of the program, and the overall rate of hypertension in the area.

Evaluation includes the three categories of process, effect, and result.

Table 2. Providing the service expected by physicians in private offices (including general or specialized, and family physicians) regarding hypertension (HTN) self-care training

Service recipient	Methods of training	The place of service	Content of the curriculum	Assessment
• Patient	-Face to face training -Pamphlets and brochures designed in simple language -Patients' index card -Training CDs -SMS -Follow-up by phone calls	-Physicians' office -Service provider: physicians or their trained secretaries	-The importance and necessity of treating HTN -Complications of HTN -The importance of non-medical therapy and suitable lifestyle -The significance of salt consumption incidence and exacerbation of HTN -Medical therapy and correct administration of drugs including type of drug, dose of drug, and the way of storing drugs -Familiarity with important side effects of the drugs -Normal blood pressure does not mean stopping administration of drugs -Control of other cardiovascular factors -Follow-up with the required tests in time according to the relevant physician -Training correct measurement of blood pressure at home -The necessity to know symptoms of HTN that require visiting a physician -The importance of going to the service providing unit regularly -Requesting the physicians or nurses to measure blood pressure in every visit to an office or a hospital	-Number of patients covered by self-care program -Number of distributed training printed aids -Study of patients' KAP -Counting the pills remaining at the end of each period -Patients' satisfaction -Number of files related to HTN self-care in the office -Physician's satisfaction -Number of referrals by physicians -Number of regular visits of patients -Number of patients under care that suffer complications -Number of patients under care with controlled HTN -Number of patients referred to higher levels of service providers
• Patients' family members	-Face to face training -Pamphlets and brochures -Training CDs	-Physicians' office -Service provider: physicians or their trained secretaries	-The importance and necessity of treating HTN -Complications of HTN -The existence of family history in incidence of HTN -The importance of non-medical therapy and suitable lifestyle -Encouraging the patients to follow the physicians' instructions -The importance of measuring blood pressure of patients' families -The importance and how to measure blood pressure of the patients -Knowing the patients' drugs -The importance of appropriate support by family -Being in touch with the patients to follow up their process of treatment -Being in touch with the therapists to follow up the process of treatment	-Performing the non-medical therapeutic recommendations at home -Satisfaction of the patients' families of the training -Number of patients covered by self-care program -Number of distributed training aids -Study of KAP of patients' families
• People at high risk (including those with obesity, diabetes, a sedentary lifestyle or any other factor causing HTN)	-Face to face training -Pamphlets and brochures designed in simple language -Patients' index card -Training CDs -SMS -Follow-up by phone calls	-Physicians' office -Service provider: physicians or their trained secretaries	-The importance of preventing HTN -Risk factors of HTN -A suitable lifestyle including appropriate nutrition, suitable physical activity, control of stress, smoking cessation -Requesting the physicians to measure blood pressure in every appointment with a physician for other reasons -Training the use of appropriate social support -Doing necessary tests periodically -Measurement of blood pressure at home	-Examining the visits done at the appointed time -Smoking cessation and controlling obesity -Number of people covered by self-care program -Number of distributed training aids -Study of people s' KAP -Performing the non-medical therapeutic recommendations at home -Satisfaction of the people under training -Rate of controlling other diseases -Number of people affected with HTN

*Execution of this program does not need superordinates; HTN: Hypertension; KAP: Knowledge, Attitudes, Practice

A) Process evaluation:

1) Evaluation of planning
2) Evaluation of pilot study
3) Evaluation of the executive phases of the project
4) Evaluation of information distribution
5) Evaluation of needs assessment of participants

B) Effect Evaluation:

1) KAP study on participants, before and after, regarding concepts and importance of self-care and the levels of health care system
2) Assessment of clients who referred to specialized health centers
3) Assessment of clients who referred to consulting centers
4) Assessment of clients who joined self-help groups
5) Assessment the various costs of care among clients
6) Assessment of the number of referrals
7) Assessment of the treatment results in clients
8) Assessment of the satisfaction of clients
9) Assessment of the satisfaction of health care providers

C) Result Evaluation:

1) The percentage of patients with controlled blood pressure
2) The percentage of patients who were afflicted by ultimate complications of hypertension including stroke, renal failure, or visual defects
3) Assessment of the change in the quality of life among clients
4) Assessment of cost-efficiency of the project

Each of these evaluations consists of three main components of tool, standards, and protocol.

Discussion

The model of self-care could be implemented and generalized to large provincial or national scales in Iran to improve the lifestyle of participants. The program should be implemented in different settings based on resources and capabilities present in different areas. Though government sector plays a major role in this program, the potential role of the private health sector cannot be ignored.

Full report of this project is available in http://www.icrc.ir/images_/selfcare.pdf

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Conflict of Interests

Authors have no conflict of interests.

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Factors affecting outcome of primary percutaneous coronary intervention for acute myocardial infarction

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Original Article

Abstract

BACKGROUND: Primary percutaneous coronary intervention (PCI) is the main treatment for patients with ST-segment elevation myocardial infarction (STEMI). We investigated factors affecting the major complications of this procedure.

METHODS: This case-control study assessed 200 patients receiving primary PCI for STEMI. Effects of some factors including age, sex, coronary artery risk factors, left ventricular function, thrombolysis in myocardial infarction (TIMI) flow, and number of involved vessels on major adverse cardiac events (MACE) were studied.

RESULTS: Two thirds of patients were male but sex had no significant effect on MACE. Similarly, age, hypertension, and hyperlipidemia did not significantly affect the incidence of MACE. However, Killip class, left ventricular ejection fraction, diabetes, TIMI flow, and type of involved vessels had significant relations with the incidence of MACE.

CONCLUSION: According to our findings, factors such as diabetes, left ventricular function, left anterior descending artery involvement, and low TIMI flow are risk factors of MACE.

Keywords: Primary Percutaneous Coronary Intervention, ST-Segment Elevation Myocardial Infarction, Major Adverse Cardiac Events

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Introduction

Myocardial infarction is one of the main causes of mortality in the world which is mainly treated with fibrinolytic drugs and percutaneous coronary intervention (PCI).[1] While one third of patients undergoing primary PCI are women, mortality rates are higher among women than in men.[2] Moreover, some studies have identified high age as a predictor of major adverse cardiac events (MACE) after primary PCI for myocardial infarction.[3,4] Patients with diabetes who receive primary PCI for ST-segment elevation myocardial infarction (STEMI) are also at higher risk of mortality especially during hospitalization and the first year following the procedure.[5-7] On the other hand, some studies have demonstrated better reperfusion after PCI in smokers compared to nonsmokers.[8]

Arterial hypertension is a poor prognostic risk factor in patients with acute coronary syndrome.[9,10] In patients with myocardial infarction, high lipoprotein (a) levels have been found to be associated with adverse long-term results.[11] In addition, many studies have suggested thrombolysis in myocardial infarction (TIMI) flow grade 3 to improve survival rates and reduce complications.[12-14] Patients undergoing primary PCI will also have an increased risk of MACE in presence of multivessel coronary artery disease.[15,16] Another risk factor of MACE in patients receiving primary PCI is lower left ventricular ejection fraction (LVEF).[17,18] Finally, shorter interval between the onset of myocardial infarction

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symptoms and primary PCI will lead to better results. The most favorable interval has been determined as 90 minutes.[19,20] The present study was conducted to determine factors that influence the outcome of patients who underwent primary PCI due to myocardial infarction.

Materials and Methods

This case-control study was performed in Chmaran Hospital (Esfahan, Iran) in 2011-2012. Considering alpha = 0.05, β = 0.2, and d = 0.5, the number of participants in each group was determined as 100. Patients admitted with acute chest pain within 6 hours and ST elevation in two leads on one surface of 12-lead EKG or patient with STEMI without response to streptokinase who were suitable for primary PCI were included in this study. Patients with contraindications to PCI, e.g. left main coronary artery involvement or not knowing the responsible vessel, were excluded from the study. During hospital stay, patients who died or had complication including serious arrhythmias (ventricular fibrillation and ventricular tachycardia), heart failure, bleeding of the artery that needed blood transmission, or needed a second PCI of the same vessel were allocated to the case group and other patients that had not this complications were allocated to the control group.

At admission, the patients' demographic information (age, sex, and occupation) and risk factors including diabetes, smoking, hypertension, hyperlipidemia, and family history were obtained. Left ventricular function was assessed using echocardiography before coronary angiography or left ventricular angiography. During angiography, TIMI flow and number of involved vessels were determined. The intervals between the onset of symptoms and hospital admission and between hospital admission and PCI were also recorded. Qualitative items were obtained by check list. Blood pressure was assessed using mercury barometer and adult cuff. LV function in patient without LV angiogram was assessed using two-dimension echocardiography in three planes by a colleague. Severity of coronary stenosis and TIMI flow were assessed by interventionist and then reevaluated by investigator for prevention of operator biases.

During the hospital stay, patients were examined daily to find any major complications following PCI (as mentioned for definition of case group). We defined heart failure as the simultaneous occurrence of low LVEF with dyspnea, orthopnea, and pulmonary rale, or the third heart sound.

Informed consents were obtained from all patients to participate in the study. The study protocol was also approved by the research ethics committee of Isfahan University of Medical Sciences (Isfahan, Iran). The confidentiality of information was ensured. The collected data was analyzed with Student's t-test and chi-square test in SPSS software (SPSS Inc., Chicago, IL, USA). Ethical approval code was 391372 obtained in 17 January 2012.

Results

In this study, 200 patients [46 (23%) females] with STEMI who underwent primary PCI were evaluated in two groups of case and control. Although two thirds of the patients in both groups were men, sex had no significant effect on patients' outcome. The mean age of the subjects in the case and control groups was 60.2 and 59.3, respectively (P = 0.669) (Table 1).

The mean diastolic and systolic blood pressure of the case group was 80.7 and 113.5 mmHg, respectively. The corresponding values were 83.1 and 120.3 mmHg in the control group. Despite the lower values in the case group, the two groups were not significantly different in terms of diastolic or systolic blood pressure (Table 1).

On the other hand, the majority of patients with Killip class 2 or 3 were in the case group and the two groups were significantly different in this regard (P < 0.001). In contrast, no significant associations were found between hyperlipidemia or family history and outcome of patients who received primary PCI (P = 0.747). Smoking was slightly more frequent in the case group but the difference between groups was not statistically significant (P = 0.5). Diabetes was detected in 34 patients in the case group and 13 patients in the control group (P < 0.05) (Table 1).

The average time interval between symptoms onset and hospital admission was 10.5 hours in the case group and 7.6 hours in the control group (P = 0.391). The average time interval between hospital admission and PCI was 3.4 hours in the case group and 3.6 hours in the control group (P = 0.241). However, the mean time from the onset of symptoms until PCI was 13.5 minutes in the case group and 11.2 minutes in the control group (P = 0.046) (Table 1).

Furthermore, the cases and controls were not significantly different in terms of the number of vessels with stenosis. While the two groups had significant differences in left anterior descending

artery (LAD) involvement or absolute obstruction, no significant differences were observed in other coronary arteries. The number of patients who underwent PCI for two or three vessels simultaneously was higher in the case group but this difference was not statistically significant (Table 2).

The mean TIMI flow grade was 2.49 in the case group and 2.80 in the control group ($P < 0.05$). The mean LVEF in the case and control groups was 35.5% and 41.0%, respectively ($P < 0.05$).

Table 1. Demographic characteristics of patients undergoing percutaneous coronary intervention (PCI) for myocardial infarction

Variables	Groups		P
	Case (n = 100)	Control (n = 100)	
Gender (female)	24	22	1.000
Age (years)	60.20 ± 14.20	59.30 ± 10.70	0.669
Interval between symptoms onset and hospital admission (hours)	10.50 ± 19.00	7.85 ± 14.30	0.048
Interval between hospital admission and PCI (hours)	2.45 ± 2.05	3.58 ± 7.19	
Hyperlipidemia	21	24	0.703
Diabetes	34	13	0.005
Hypertension	31	33	0.747
Smoking	29	22	0.383

Values are mean ± SD or numbers (as both group included 100 subjects, percentages are not provided)
PCI: Percutaneous coronary intervention

Table 2. Vascular status and left ventricular function of patients undergoing percutaneous coronary intervention for myocardial infarction

Variable		Group		P
		Case (n = 100)	Control (n = 100)	
Number of involved vessels	1	86	91	
	2	12	9	0.248
	3	2	0	
Number of vessels receiving PCI	1	34	43	
	2	51	36	0.505
	3	15	21	
Left main coronary artery status	Normal	87	95	
	Non-significant	11	5	0.244
	Significant	0	0	
	Cut-off	2	0	
Left anterior descending artery status	Normal	9	13	
	Non-significant	8	3	0.046
	Significant	37	57	
	Cut-off	46	27	
Left circumflex artery status	Normal	56	56	
	Non-significant	11	3	0.271
	Significant	22	32	
	Cut-off	11	9	
Right coronary artery status	Normal	33	35	
	Non-significant	10	2	0.275
	Significant	32	33	
	Cut-off	25	30	
Ramus circumflexus status	Normal	92	98	
	Non-significant	1	0	0.013
	Significant	5	2	
	Cut-off	2	0	
Thrombolysis in myocardial infarction flow		2.49 ± 0.80	2.80 ± 0.53	0.010
Left ventricular function		35.5 ± 12.1	41.0 ± 11.00	0.013

Values are mean ± SD or numbers (as both group included 100 subjects, percentages are not provided)
PCI: Percutaneous coronary intervention

Discussion

This study sought to identify factors affecting MACE in patients who underwent primary PCI for STMEI. Although two thirds of patients were men, sex had no significant effect on MACE. However, some studies have found higher mortality rates in women than in men.[2] The absence of such a higher risk among our female participants emphasizes the benefits of primary PCI in women.

While according to our findings the incidence of MACE was not related with age, increased age generally increases the risk of mortality in patients with myocardial infarction.[3,4] Since very old patients with STEMI did not undergo primary PCI and were prescribed with pharmacological treatment instead, this difference is justifiable.

We found diabetes to increase the risk of MACE in patients who received primary PCI for STEMI. In other words, diabetes was significantly more prevalent in the group with complications than in the control group. Various studies have also highlighted the short-term (during hospitalization and the first year after the disease) and long-term effects of diabetes on the MACE.[5-7] Diabetes can thus be considered as a risk factor for MACE after primary PCI.

Smoking is another major risk factor for coronary artery disease. The importance of smoking in the incidence of MACE after primary PCI is a matter of concern. In this study, smoking did not have any negative effects on MACE. However, a previous research reported better reperfusion rate after PCI in smokers.[8]

High arterial blood pressure is a risk factor for coronary artery disease and increases the risk of complications after acute coronary syndrome.[9,10] However, we not find significant differences in level of blood pressure between the two groups.

Despite the fact that hyperlipidemia is a risk factor for coronary artery disease, it had no significant effects on the incidence of MACE in this study. Some studies have identified high levels of lipoprotein (a) to be associated with poor outcome in patients with acute myocardial infarction.[11]

TIMI flow is one of the important factors in determining the outcome of PCI in patients with STEMI. Good TIMI flow at the time of angiography and PCI is a determinant of MACE in patients undergoing primary PCI. Patients with TIMI flow grade 3 are expected to have higher survival rates and fewer complications following primary PCI.[12-14] In the present study, TIMI flow grade 3 was associated with reduced MACE in patients receiving primary PCI for STEMI.

A major determinant of patients' survival and the incidence of MACE after primary PCI is left ventricular function. Better left ventricular function is associated with improved survival. On the other hand, low LVEF leads to higher incidence of MACE.[17,18] In the current study, low LVEF had statistically significant effect on MACE in patients undergoing primary PCI.

We also observed a significant relation between higher Killip class and increased incidence of MACE. Killip class is a kind of classification for heart failure rate after a myocardial infarction based on clinical symptoms. Higher Killip classes are usually associated with lower LVEF.

There was no significant relationship between the number of involved vessels in patients and MACE. However, LAD involvement was significantly more prevalent in patients who developed complications following STEMI than in the controls. This finding confirms the importance of LAD involvement in patients with myocardial infarction. Some studies have also introduced multivessel involvement in patients to increase the risk of primary PCI complications.[15,16]

In the present study, the mean interval between the onset of symptoms and hospital admission was too long. Similarly, the interval between entrance to emergency department and PCI was much longer than the recommended time (90 minutes from door to PCI).[19,20] As such long delays increase patients' mortality and risk of MACE, their reasons need to be investigated.

Conclusion

In this study, factors with effect on outcome in patiatn under primary PCI included diabetes mellitus, low left ventricular function, left anterior descending artery involvement, and low TIMI flow.

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Conflict of Interests

Authors have no conflict of interests.

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The relationship between inflammatory markers, angiogenesis, and obesity

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Review Article

Abstract

Obesity is recognized as a chronic low grade and systemic inflammatory disease. Angiogenesis is critical for adipose tissue expansion. Several evidences have demonstrated that angiogenesis sustains inflammation by preparing oxygen and nutrients for inflammatory cells and inflammation in turn can cause insulin resistance, type 2 diabetes, and cardiovascular disease. The understanding of mechanisms of obesity especially main roles of inflammation and angiogenesis in fat mass expansion can lead to therapeutic approaches in growing field of obesity and its related disorders. In this review, we studied the relationship between obesity, angiogenesis, and inflammation.

Keywords: Obesity, Angiogenesis, Inflammation

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Introduction

Inflammation is an intricate network of chemical signals, cell types and factor interactions in response to tissue damage against pathogenic, traumatic or toxic injury. The inflammatory process is the result of balance between pro- and anti-inflammatory molecules[1-3] such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), leptin, resistin, monocyte chemoattractant protein-1 (MCP-1), C-reactive protein (CRP) and anti-inflammatory molecule of Adiponectin.[4] These molecules involve in regulation of cell chemotaxis, migration and proliferation. Although inflammation participates in healing process but imbalance between pro- and anti-inflammatory molecules lead to sustained inflammation (chronic inflammation) and in turn it mediates a wide spectrum of diseases such as psoriasis, rheumatoid arthritis, osteoarthritis, metabolic syndrome-associated disorders including type 2 diabetes and atherosclerosis, ocular disorders, Crohn disease, and cancer.[5,6]

Obesity is a complex metabolic disorder that is one of the most prevalent public health problems. Based on the World Health Organization (WHO) definition, obesity is considered as body mass index (BMI) of 30 kg/m^2 or higher. Obesity is associated with the development of most common and severe human diseases such as type 2 diabetes mellitus, coronary heart disease (CHD), hypertension, increased incidence of certain cancers, respiratory complications (obstructive sleep apnea), and osteoarthritis.[7,8]

Angiogenesis is a process of growth and remodeling of an initial vascular system which is modified to create an intricate branching network and matured vasculature.[9] It is a multistep process that consists of extracellular matrix (ECM) degradation, endothelial cell proliferation and migration, tubal formation and anastomosis.[10,11] Physiological angiogenesis is essential for the wound healing, growth and action of female reproductive organs, such as ovary and endometrium during menstrual cycle and pregnancy.[12] In addition, disturbance of the mechanisms involving in physiological angiogenesis can lead to a growing list of diseases either in the form of overproliferation of blood vessels such as cancer, psoriasis, arthritis, retinopathies, obesity, diabetes, asthma, and atherosclerosis or inadequate angiogenesis including heart and brain ischemia, neurodegeneration, hypertension, osteoporosis, respiratory distress, preeclampsia, endometriosis, postpartum cardiomyopathy, and ovarian hyper stimulation syndrome.[13-16]

Chronic low grade inflammation during obesity

Obesity was identified as a chronic low grade

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inflammation especially in white adipose tissue (WAT) nearly a decade ago when increase in the cytokine (TNF-α) and progress of insulin resistance with diet-induced obesity were demonstrated in rodents.[17] Numerous studies have demonstrated the increase in plasma levels of MCP-1 after 4 weeks high-fat diet.[18]

In relation to the origin of the inflammatory response that leads to insulin resistance in obesity, an initial mechanism is the inhibition of signaling downstream of the insulin receptor. For example, exposure of cells with TNF-α leads to inhibitory phosphorylation of serine residues of insulin receptor substrate-1 (IRS-1).[19,20] Another mechanism is that nutrient overload in adipocytes induces endoplasmic reticulum (ER) stress that leads to activation of inflammatory cascades.[21] ER is an organelle specialized in the cell for protein folding, maturation, storage and transport of nutrients. Following nutrient surplus, misfold or unfolded proteins aggregate in the ER and create unfolded protein response.[22] It leads to increased activity of c-Jun NH_2-terminal kinase C (JNK), IκB Kinase (IKK-ß), IRS-1 and nuclear factor kappa-B (NF-κB) pathways that in turn cause to increase expression of pro-inflammatory cytokines such as TNF-α, IL-6, CRP, and disruption of insulin signaling.[23,24] Moreover, rapid and dynamic expansion of fat tissue in obesity leads to adipose tissue hypoxia.[25,26] Finally, the ER responds to this cellular stress in the form of increased activation of inflammatory pathways.[27,28]

There are at least two different states of macrophage infiltrations in obese adipose tissue. M_1 or inflammatory macrophages that are induced by pro-inflammatory mediators such as lipopolysaccharide (LPS) and interferon (IFN-γ) and anti-inflammatory M_2 macrophages normally exist in adipose tissue that are produced by cytokines such as IL-4, IL-13, and IL-10.[29,30] Several evidences have shown that high fat diet changes phenotype of macrophages in adipose tissue from M_2 to M_1 that in turn accelerate adipose tissue inflammation.[31]

Furthermore, surplus glucose metabolism also can cause to increase in mitochondrial production of reactive oxygen species (ROS).[32,33] ROS production in obesity causes activation of inflammatory pathways and in turn participates in inhibition of insulin signaling including JNK, IKK (NF-κB kinase)[34] and the activation of these kinases in obesity show the overlap of metabolic and immune pathways. The IKKB, one of the inflammatory kinases, can affect insulin signaling by at least two ways;[35] first, direct phosphorylation of IRS-1 on serine residues and the second is the phosphorylation of inhibitor of NF-κB (IκB). Thus, activation of transcription factor can stimulate generation of several inflammatory mediators such as TNF-α and IL-6.[36] In addition, other mechanism that participates in inflammation-induced insulin resistance is at least 3 members of the suppressor of cytokine signaling (SOCS) family[37] with inhibition of insulin signaling through IRS-1 and IRS-2 tyrosine phosphorylation or by targeting IRS-1, IRS-2 proteosomal degradation.[38]

Adipose tissue expansion and angiogenesis

Adipose tissue has a large vascularity and each adipocyte is enclosed by one or more capillaries.[39] Reciprocal interplay between endothelial cells and adipocytes is nicely shown, as dysfunction of each compartment can has a substantial effect on the other system.[40] Functional vascular system is critical for adipose tissue expansion by several mechanisms including, supplying oxygen and nutrients, waste products removal, and trigger of growth and survival signals for physiological function of adipocytes by growth factors and cytokines available in plasma.[41] During expansion of adipose tissue, hypoxia is an important factor for vascular growth and remodeling.[42] Likewise, increased adipocyte size leads to over longer distance for diffusion of oxygen and nutrients to adipocytes and results in a decrease of partial oxygen pressure to 20 mmHg against 40 mmHg in obese versus lean mice, respectively. Adipose tissue in response to hypoxia generates hypoxia inducible factor 1-α (HIF1-α),[27,43] a heterodimer consisting of the oxygen regulated HIF1-α subunit and the constitutively expressed HIF1-β.[44] In normoxic condition, HIF1-α is degraded by an oxygen-dependent hydroxylation of two proline residues. In contrast, in hypoxic conditions the level of prolyl hydroxylation decreases and protein translocates into the nucleus, and binds to hypoxia response elements (HRE) of target genes such as VEGF-A and angiopoietin-2 and thus, induces an angiogenic response that can participate in better oxygenated and nutritionally-enriched microenvironment of tumors.[45]

Adipose tissue generates several angiogenic and angiostatic factors including placental growth factor (PLGF), FGF2, angiopoietin-2, angiostatin, endostatin, leptin, thrombospondin (TSP-1), resistin, IGF (insulin growth factor), HGF, etc.,[46,47] but most of the angiogenic activity is attributed to vascular endothelial growth factor

(VEGF/VEGFR).[48] The plasticity of adipose vasculature is the result of a net balance between angiogenic factors and inhibitors. Adipose tissue produces multiple angiogenic inhibitors such as adiponectin[49] that significantly decrease in obese animals and humans and their blood levels have inverse correlation with their BMI. In addition, a number of studies have demonstrated that it inhibits angiogenesis in mouse corneal, CAM in vivo model and tumor angiogenesis.[50,51]

Accumulating these evidences demonstrated that the relationship between capillary endothelial cells and adipocytes can be created through paracrine signaling pathways and direct cell-cell interactions.[52,53] For example, expression of $\alpha_v\beta_3$ integrin and plasminogen activator inhibitor 1 in human pre-adipocytes and capillary endothelial cells direct preadipocyte migration toward developing networks to coordination of the development of both tissues at the same location.[54]

Relationship between obesity, inflammation and angiogenesis

Angiogenesis maintains inflammation by supplying oxygen and nutrients for the cells of inflammatory region. In chronic inflammatory condition such as obesity, nitric oxide (NO), an inflammatory cytokine, is produced by inducible NO synthase (iNOS). NO dilates vessels and stimulates its permeability that leads to immune cell extravasation. Adhesion of immune cells to the endothelium is one of the most important steps in inflammatory process.[55] Adhesion molecules such as E-selectin play a communication role in inflammatory process and can have a role in immune cell extravasation.[56] There are similar roles for adhesion molecules, intracellular adhesion molecule (ICAM-1), vascular cellular adhesion molecule (VCAM-1), and integrins.[57]

Inflammatory cells also release angiogenic factors including: VEGF, Angiopoietins, fibroblast growth factor (bFGF), Hepatocyte growth factor (HGF), platelet-derived growth factor (PDGF), transforming growth factor (TGF-ß), etc that have mitogenic and migratory effects on endothelium.[58-60] A common stimulus for both chronic inflammation and angiogenesis is hypoxia[61] that induces HIFs expression; it in turn increases transcription of angiogenic genes such as, VEGF and Ang-2.[5,62]

Activation of transcription factor NF-ϰB is considered as the primary event in inflammation.[63,64] Several studies have demonstrated interplay between NF-ϰB and Ang-Tie2 signaling pathway.[65] Ang-2 is an angiogenic factor that upregulates several pro-inflammatory pathways that can be led to leukocyte recruitment and infiltration through NF-ϰB signaling interaction.[66]

Adipose tissue remodeling is the changes in turnover of the adipocytes, angiogenesis and rebuild of the extra cellular matrix in response to factors such as growth factors and expansion of adipose tissue, variations of hormonal concentrations, aging and diseases such as cancer and cachexia.[67] Some studies have shown that high fat diet (60% calories of fat) approximately stimulates complete remodeling of epididymal fat tissue of male mice.[68]

During adipose tissue expansion, blood flow per unit adipocyte surface and delivery rate of oxygen and nutrients to the adipocyte becomes suboptimal.[69] On the other hand, PO_2 is inversely correlated with pro-inflammatory markers. Therefore, hypoxic condition of adipose tissue during obesity leads to inflammation, fibrosis and adipocyte dysfunction.[70,71] Adipocyte dysfunction may participate in the cycle of adipose tissue remodeling.[72] Hypoxia in adipose tissue leads to increase of transcription factor of HIF that in turn causes angiogenic response by binding to the HRE of target genes such as VEGFA, angiopoietin-2[73,74] and lysyl oxidase (LOX), one enzyme with cross-link between elastins and collagens in the extracellular matrix that increases extracellular tensile strength and leads to HIF-1α mediated fibrosis.[75] Furthermore, adipose tissue macrophages in obesity shift to an M_1 inflammatory phenotype and the increase in the number of M_1 macrophages and the M_1/M_2 ratio can lead to systemic inflammation and induction of insulin resistance that have been shown in figure 1.[76,77]

In conclusion, obesity is identified as a chronic low grade inflammation state and macrophages possibly play a critical role in inflammation. Hypoxia is considered as a common stimulus for inflammation and angiogenesis. Thus, there is a reciprocal interplay between inflammation and angiogenesis and both are involved in pathophysiology of obesity. Close relationship between inflammatory cells, angiogenesis and adipose tissue expansion should be considered in prevention and/or treatment of obesity.

Conflict of Interests

Authors have no conflict of interests.

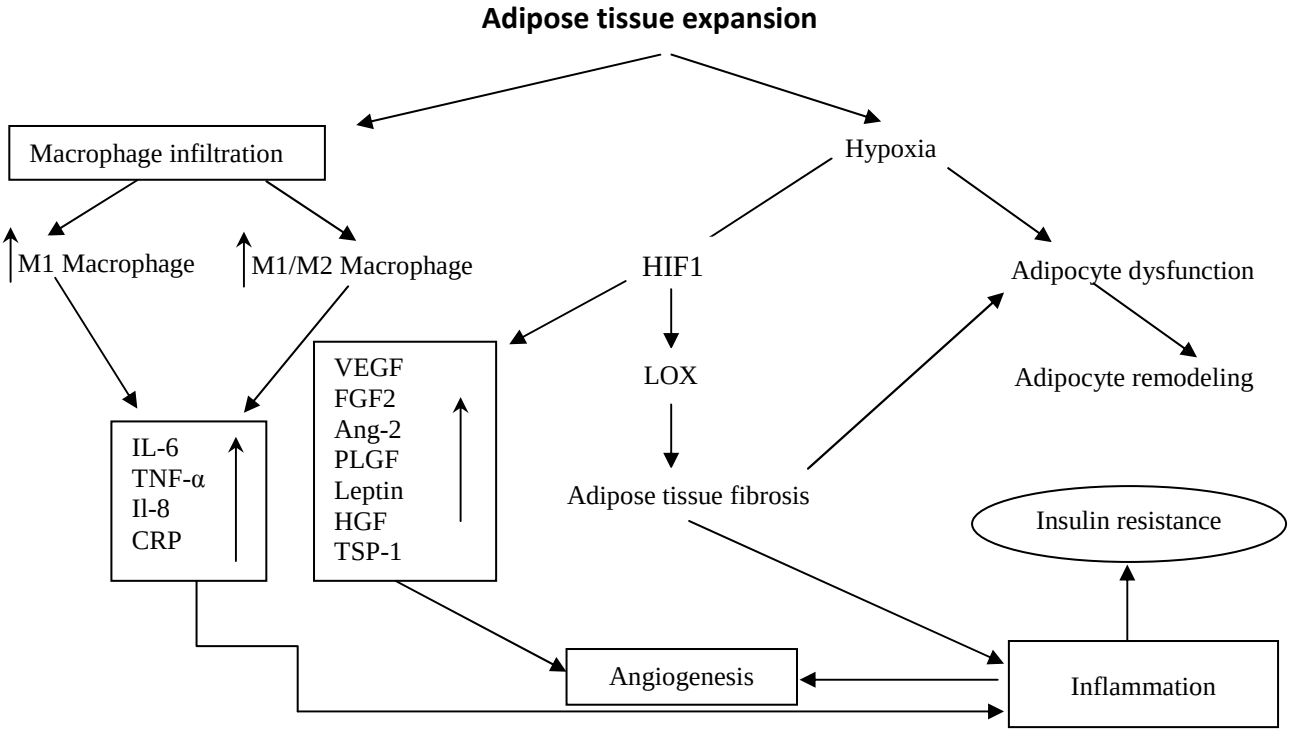

Figure 1. Relationship between adipose tissue expansion, angiogenesis and inflammation

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A case report of truncus arteriosus communis and genetic counseling

Gholamreza Nourzad[(1)], Mahnaz Baghershiroodi[(2)]

Case Report

Abstract

BACKGROUND: Truncus arteriosus communis (TAC) is a rare heart disorder with the prevalence of approximately 1%, mostly in male newborns. In this disease, aorta and pulmonary artery have not been separated during fetus development and both originate jointly from left ventricle. In addition, various disorders are reported like ventricular septal defect (VSD), mitral and tricuspid valves defects, aortic septal defect (ASD), reduction of lung and lung vessels' resistance, pulmonary hypertension, increase in heart rate, high perspiration, bad digestion, and tetralogy of Fallot.

CASR REPORT: Parents of deceased patient were referred for genetic counseling after the death of third girl due to severe cardiac disorder. Cardiologist declared the disease in deceased girl as TAC based on findings along with VSD, ASD and hypoplastic aortic arch which resulted to death in the first day of birth.

CONCLUSION: There was no chromosomal disorder in chromosome analysis of patient' skin. Parents were interested to have another child, so they were referred to university's Genetic Counseling Center to become aware of their next child's condition. This disorder is genetically heterogeneous and multifactorial and because all external factors are not recognized, the accurate estimation of risk is not possible and the probability of risk for the next child is about 10% to 20%.

Keywords: Heart Disorder, Truncus Arteriosus Communis, Genetic Counseling

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Introduction

Congenital cardiac disorders are one of the most common congenital disorders with the prevalence of 1-5% in every 100 newborns.[1] Among them, truncus arteriosus communis (TAC) is a rare cardiac disorder,[2-4] in which aorta and pulmonary artery were not separated completely during fetus development and both originate jointly from left ventricle. In addition, various disorders like ventricular septal defect (VSD), mitral and tricuspid valves defect, aortic septal defect (ASD), reduction of lungs and lungs' vessels resistance, pulmonary hypertension, increase in heart rate, high perspiration, and bad food digestion along with tetralogy of Fallot are some of reported disorders.[5-8] Prevalence of this disease is low and in males is higher than females.[8,9] During past 20 years, diagnostic and therapeutic methods along with immediate intervention for surgery in infancy with complete reparation of VSD lead to evident improvement and less morbidity in newborns.

Along with genetic role including microdeletion of 22q11.2 in 30% of isolated conotruncal disorders, the effect of external factors has been considered in these disorders.[2,3,10] Because of diversity in disease demonstration, its causes had been classified by Collet and Edwards in 4 different types in 1949.[11] Because of later reported deviances,[12,13] another classification was introduced by van Praaghs in 1965 with modifications in 4 initial types,[14] but it seems that none of classifications are ideal because there are cases which does not belong to any of classifications,[4,11,15-17] defined as unpredictable differences.[18-20]

In order to diagnose before birth, procedures like ultrasound, echocardiography and measurement of alpha-fetoprotein of maternal serum (Quadric test) were used and methods like X-ray angiography,

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contrast enhanced magnetic resonance angiography (CEMR) and other imaging techniques were used after birth.[9,21,22]

Case Report

Parents were not relatives and were 34 years old at the birth of their first daughter. At the time of this study, this girl was 10 years old (Figure 1 IV/1), she was healthy with natural growth. The second pregnancy was a boy who was aborted before third month of pregnancy (Figure 1 IV/2). Forth pregnancy resulted in early abortion without determining the gender of fetus (Figure 1 IV/4). Proband in this study was the fifth pregnancy which died in the evening of the first birth day with TAC diagnosis (Figure 1 IV/5). Then parents were seeking consultation for sixth pregnancy. Father had natural karyotype (Figure 1 III/1). Father's younger brother had the same cardiac disorder (Figure 1 III/3), his disease was diagnosed by cardiologists of Munich University and was operated in US, now he has good physical health (Table 1). One of the father's cousin of patient (Figure 1 III/6) died after Hiatus hernia operation because of a sub-diaphragm abscess. She suffered from tetralogy Fallot (defect of ventricle septum, high discharge of right ventricle pulmonary artery stenosis, and aortic defect or ductus Botalli). It was reported that 3 paternal brother had died in childhood. One of the brothers had died because of diphtheria (Figure 1 II/2). Death reasons of other brothers (Figure 1 II/5,7) were not clear. Among 9 sisters and brothers of mother, two girls had died early; one in 5 months old because of diarrhea (Figure 1 II/12) and the other because of septicemia (Figure 1 II/16).

Even mother (Figure 2 III/8) had natural karyotype in chromosome analysis. One cousin of mother had died in 3 months old due to convulsion caused by teeth fever. Other family members were healthy. The dead patient is shown with an arrow (Figure 1 IV/5).

Pregnancy, birth and newborn

In the 9th and 10th weeks of pregnancy, patient's mother had suffered from intestinal infection and diarrhea without fever. She had been weak with pain in her abdomen and back like her second pregnancy but this time did not result in abortion. Monographic examinations had not shown cardiac or ventricle disorder. Until the moment of birth, the patient was placed in the seat position, but then turned to head position. Delivery was in 40th week of pregnancy without any problem. Amniotic fluid

Table 1. Patients' status

Patient III/3	TAC with VSD	Had surgery
Patient III/6	VSD	Died after hiatus hernia surgery
Patient IV/5	Suspected to TAC with VSD and ASD	Died

TAC: Truncus arteriosus communis; VSD: Ventricular septal defect; ASD: Aortic septal defect

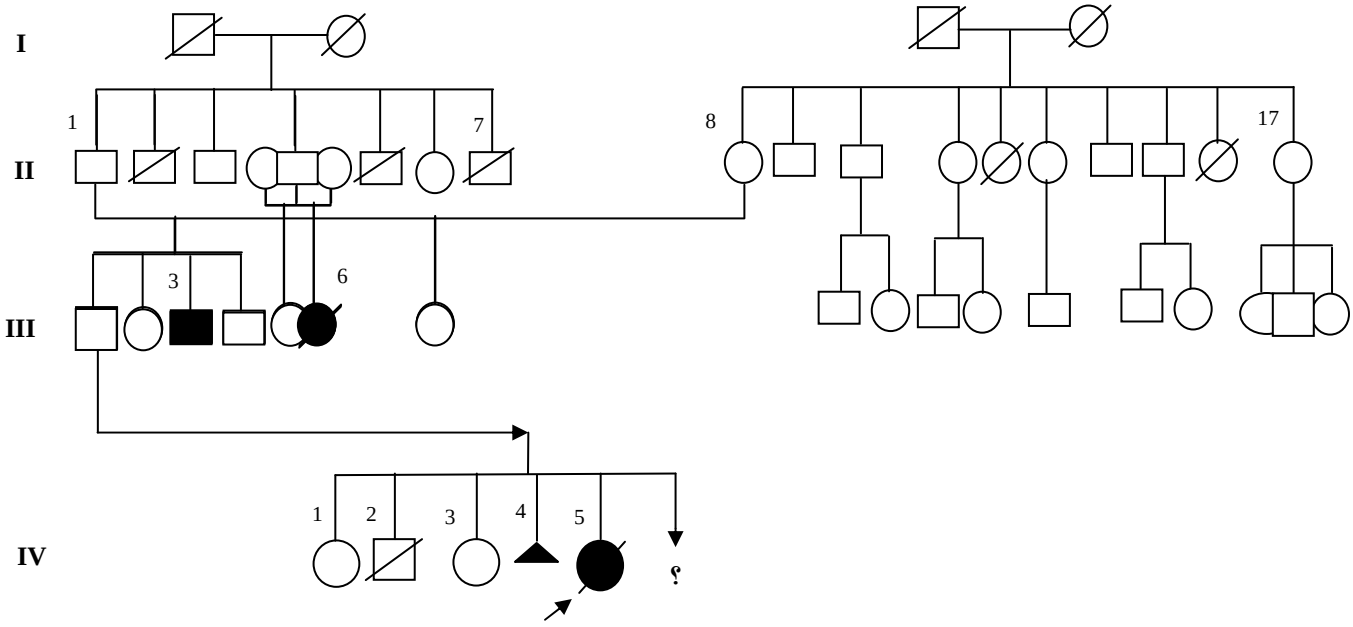

Figure 1. Paternal pedigree

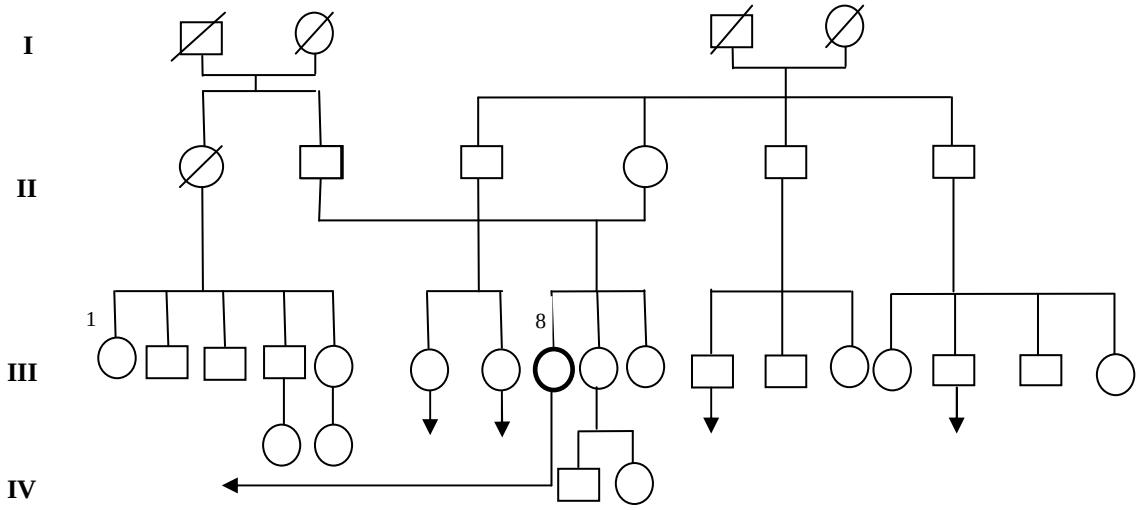

Figure 2. Maternal pedigree

was green. Length of body was 52 cm at birth which was up normal (< p90) for birth week. Apgar scores (10/10/90), birth weight (3150 g), and head diameter (33.5 cm) were normal. The patient had no apparent difference with her sisters. According to reports of her parents, she shortly cried after birth. She smiled in first 15 minutes of her life, moved her eyes and month, even she was curious in physical examinations. Cardiac sound was diagnosed in initial examinations. Infusion was conducted because of cyanosis and reduction in saturated oxygen pressure. Then she was transmitted to pediatric clinic and was not seen alive by her parents again. Echocardiography results in pediatric ward showed TAC with VSD, ASD, and hypoplastic aortic arch. Therefore, patient was transmitted to cardiac center by giving prostaglandin and artificial respiration to continue treatment. After establishing relatively stable condition in pediatric clinic, patient's condition was serious during echocardiography. The patient died in the evening of her first birth day. There was no chromosomal disorder or microdeletion of 22q11 in skin sampling. Despite interpretation of echocardiography, the reason of death was not clear.

Genetic counseling

We talked about psychological aspects of this death in the first day of birth and newborn's severe cardiac disorder, which was known from paternal pedigree. We reflected the mental condition of parents using a model image. In consultation time, they were in emotionally difficult situations (5 weeks after newborn's death) and asked themselves why this disaster had happened for them. They remembered that they had lost 2 children and must have coped with the fact that only two children were left for them from 5 pregnancies. Mother was more eager for third child. We talked about this issue with the father that they must end their mourning before a new pregnancy, because with remembering grief of lost child, it is impossible to improve their health. This was the first condition for health and stability of family. After mourning, parents succeed in planning for new baby. This was the first step to accept the destiny of next child.

Probability of recurrence risk

Paternal pedigree showed the risk of cardiac conotruncal defect in two generations and 3 family members (Figure 3 IV/5, III/6, III/3) which were relative via their healthy fathers (Figure 3 III/1, II/4, II/1).

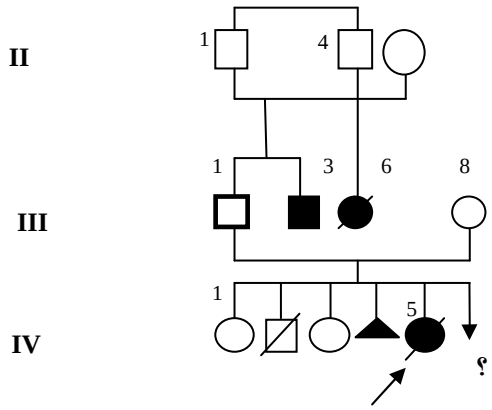

Figure 3. Pedigree of inheritance of the disease in two generations

Inherited pattern conforms with conotruncal cardiac defects reports which are not related to a

monogenic inheritance, but it is a multifactorial pathology. Accumulation inherited and various external factors' effect is shown in the figure 4. The accumulation of different external and hereditary factors is illustrated in figure 4, which explains that the different genes (polygeny) in father's family genome is responsible for conotruncal defect. However, their expression was influenced by some external factors which have not been recognized completely. Therefore, the result of this accumulation is above the fetus tolerance threshold.

Epidemiologic studies about inheritance of conotruncal cardiac disorders in scientific literature are limited.[1,10,16,23-26] Because all factors have not been identified, accurate statistical calculations are not possible. Probability of risk was estimated 10-20%, because the illness of brother and sister was similar. Karyotype study and microdeletion of 22q11 which is reported in 30% of TAC was rejected for deceased patient and her parents by Munich University Genetic Center and there were no other genetic examinations.[10]

Diagnosis before birth

Regarding parents age, we can consider a chromosome analysis although it imposes high costs in the absence of insurance. The probability of a new chromosome mutation for parents between 35-40 years old in the first and second pregnancies is about 1-2%. It is not possible to reject or prove conotruncal defects with these laboratory studies. Early sonography and echocardiography by experts will be promising for early diagnosis. We talked with parents about consequences of prenatal diagnosis which will result in abortion and they feared it because of their past experiences. It is important to know that there is no impulsion to receive more information about child before pregnancy, because it has no medical result for them.

Discussion

TAC is a rare congenital cardiac disorder with the prevalence of 0.056 to 0.03 in every 1000 births.[2-4,8,17,21] In most reported cases there is not an even and similar picture among ill children.[27-29] Attempts to prepare a clear detailed pattern or classification have partially failed. In most cases, TAC has genetic origin[1] with the effect of teratogens (virus, metabolic imbalance, industrial and pharmaceutical factors) and caused by concurrent effect of both factors.[30] In more than 30-50% of cases, consistency is shown with 22q11 chromosome microdeletion and Di George syndrome; even in this case the picture of disease is not the same.[8,10,16,30,31]

Disorder in human embryo neural crest, where first neural cells of heart and aortic pulmonary are formed, is reported as a factor for the conotruncal disorders.[6,7,13,30] Some disorders in embryos with cardiac neural crest defect are related to growth factors [fibroblast growth factor (FGF8) and bone morphogenetic proteins (BMP)] and transcription factors (T-box, Pax, NKX2-9, ANF, GATA-C)[21,24] and cell membrane gap protein (connexin 40).[25] Cardiac-neural crest plays a role in forming smooth muscle of great vessels.[30,32]

In some studies, markers of cell proliferation, apoptosis, and fibronectin were significantly higher in the right ventricular myocardium of patients with hypoplastic left heart syndrome (HLHs) compared to truncus arteriosus. Type I collagen content and NKX2.5 expression were significantly lower in HLHS than the truncus group.[12] Regarding this and various reported mutations relating to TAC disorders including mutation in CFC1 (De George syndrome) with dysmorphic face or Velo-cardio-facial syndrome (VSFS) in 90% of cases, mutation in NKx2.6,[24,25] deletion in chromosome 22 (22q11)[6,10,16,30,31] and chromosomes 8, 16, 18, and 19,[1,30]

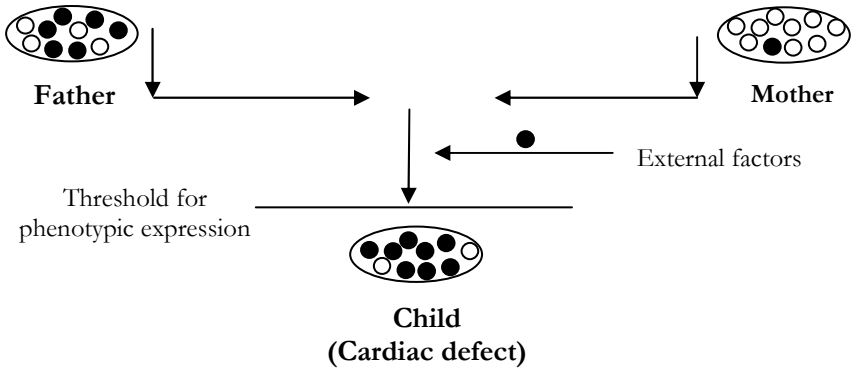

Figure 4. An illustration of external and inherited factors accumulation

mutation in cardiac homeobox containing CSX gene (5q34) which has been expressed in heart cells in fetus.[33] Homeobox containing Msk2 gene,[23] Tbx1-gene,[26] and even disorder in diabetic mother's child dependent on insulin,[31,33] which shows the polygenic and multifactorial nature of these disorders has been reported. In the absence of these various mutations, it could be imagined an autosomal dominant inheritance with reduced penetrance and variable expressivity.

In our study, there was no chromosomal disorder in infant and her parents. In terms of genetic counseling, regarding multifactorial nature of congenital TAC and its diverse epidemiologic and anatomic picture, different diagnostic tests such as ultrasound, echocardiography and quadruple test are recommended for prenatal diagnosis. Amniocentesis and chorionic villus sampling can also be used to check the relevant genes.[9,21] In the case of birth and diagnosis, immediate intervention with diagnostic methods for treatment, surgery and reparation of cardiac defects give an acceptable survival chance to child. Even with selecting newborn gender due to high resistance, we can increase the chance of healthy child.[25] Using stem cells as an alternative treatment showed that during activity of these cells, 32000 various transcripts (gene expression products) were constructed which help to improve some disorders.[2,34]

Conflict of Interests

Authors have no conflict of interests.

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Global coronary arteries spasm in a young patient

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Case Report

Abstract

BACKGROUND: Coronary artery spasm is a transient narrowing of coronary arteries that slows or stops blood flow through the artery.

CASE REPORT: We present a 42-year-smoker man without any medical problem who developed syncope. Coronary angiography revealed diffuse significant narrowing of proximal left anterior descending artery (LAD), 90% osteal stenosis of large obtuse marginal (OM), 90% diffuse narrowing of proximal right coronary artery (RCA), which was relieved by intracoronary administration of nitrate. He was discharged on calcium channel blockers and nitrates but one month later developed syncope again and died.

CONCLUSION: Multivessel coronary artery spasm should be considered in young smoker patients without any other coronary risk factors who present with syncope.

Keywords: Syncope, Implantable Cardiac Defibrillators, Variant Angina

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Introduction

Coronary artery spasm is a transient narrowing of coronary arteries that slows or stops blood flow through the artery.[1] About 2% of patients with angina have coronary artery spasm. It occurs most commonly in smokers.[1,2] If the spasm lasts long enough, it may even cause acute myocardial infarction, ventricular arrhythmias, and sudden cardiac death. Long-term prognosis of treated patients is excellent but is dependent on the severity of vasospastic episodes and the degree of underlying coronary artery disease and symptoms of patients.

We reported a case of severe multivessel coronary vasospasm in a 42 years old smoker man who had negative T wave in anterior leads and one episode syncope. He was referred to our cardiology clinic for work-up.

Case Report

A 42-year-old smoker man without history of cardiac problem and no other cardiac risk factors presented with one episode syncope and was referred to our cardiology clinic for work-up. His syncope was sudden, with no triggered factor, tongue biting, abnormal movement, lower limb weakness and blurred vision and chest pain. He had negative T inversion in anterior leads, therefore we admitted him in our ward.

On admission, heart rate was 56 beats/min, blood pressure was 110/70 mmHg, and he was breathing at a rate of 12 per minute, with oxygen saturations around 95% on room air. Cardiovascular examination was normal. There was not orthostatic change. Blood chemistry was normal including cholesterol levels. Asymptomatic episodes of ST-segment elevation were revealed in the 24-hour Holter monitoring and we decided to perform coronary angiography. Echocardiogram was normal. His coronary angiogram showed diffuse significant narrowing of proximal left anterior descending artery (LAD), 90% osteal stenosis of large obtuse marginal (OM), 90% diffuse narrowing of proximal right coronary artery (RCA) (Figures 1 and 2).

We decided to perform multivessel percutaneous coronary intervention (PCI) for him, but after intra-coronary injection of nitrate, amazingly his angiogram became completely normal (Figures 3 and 4). There

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was no organic coronary stenosis. Patient symptoms were completely resolved and he discharged on diltiazem and nitroglycerine, one month later he presented with sudden cardiac death.

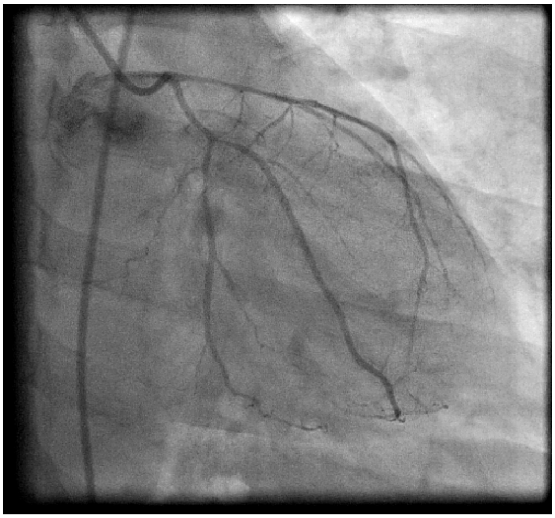

Figure 1. Diffuse significant narrowing of proximal left anterior descending artery

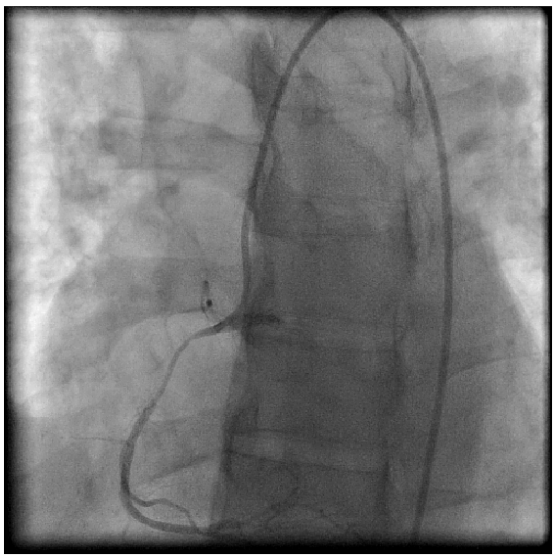

Figure 2. 90% diffuse narrowing of proximal right coronary artery

Discussion

Prinzmetal or variant angina, is due to focal coronary artery spasm and may be associated with myocardial infarction, ventricular arrhythmias, and sudden cardiac death. Factors found to adversely affect long-term prognosis in variant angina include extent and severity of coronary artery disease, diffuse ST-segment elevation without myocardial infarction and left ventricular dysfunction.[2,3] Our patient had multivessel coronary spasm and had not experienced chest pain or myocardial infarction. In fact, the incidence of silent myocardial ischemia caused by coronary artery spasm is even three times more than symptomatic ischemia.[3,4]

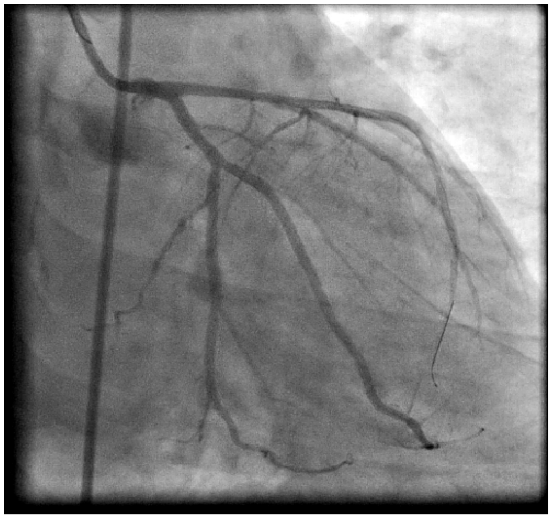

Figure 3. After intra coronary injection of nitrate in left anterior descending artery

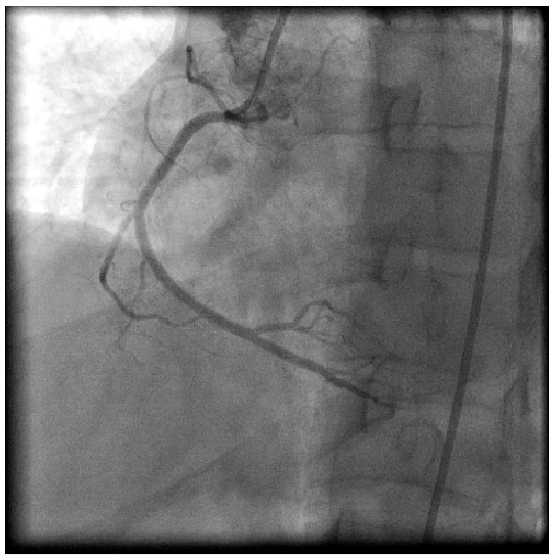

Figure 4. After intra coronary injection of nitrate in right coronary artery

The spasm in the whole arterial system involving the whole length of arteries including the branches is rare. It is anticipated that their prognosis is not well, but it is not well known that are these patients good candidate for intra cardiac defibrillator (ICD) insertion?[4]

ICD insertion indication is controversial and clinical randomized trial must respond to this debate but according to this case study, we think that in groups of patients who present with

multivessel and silent coronary artery spasm, implantation of ICD should be considered. In addition, optimal medical therapy with calcium channel blockers and nitrates reduce the incidence of episodes but do not guarantee the absence of recurrences of coronary spasm.

Global coronary arteries spasm has to be suspected in smoker young patients without any other coronary risk factors who present with syncope. It should be included in the differential diagnosis of syncope and have to be investigated with coronary angiography and treated with vasodilators.

Conflict of Interests

Authors have no conflict of interests.

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The correlation between early complications of percutaneous coronary intervention and high sensitive C-reactive protein

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Short Communication

Abstract

BACKGROUND: Increased incidence of cardiovascular diseases, especially coronary artery disease (CAD), during recent decades shows this disease entity to be the leading cause of death in the world. On the other hand many successes were achieved in the treatment of these diseases with new technology, which has its own side effects and threats for the patient. Among these new strategies is percutaneous coronary intervention (PCI), especially with stent implantation. Although coronary stents are effective in the treatment of dissection and prevention of restenosis, many side effects and even death have been observed, from 5-10% per year. Some studies showed that there is a relation between high sensitivity C-reactive protein (hs-CRP), as a laboratory marker for early detection of thrombosis and/or restenosis, and early complications of percutaneous coronary intervention. The aim of this study is to evaluate hs-CRP level in patients after PCI and to investigate if this can be a prognostic value for detection of early complication.

METHODS: This is a descriptive, analytical study done in Shahid Chamran Hospital (Isfahan, Iran) in 2011–2012. 87 patients who had undergone PCI were studied. Their hs-CRP level was measured before and after the study. Moreover, early stent complications were detected during the first 24 hours after insertion. The data was recorded in a researcher-constructed checklist and analyzed by SPSS for Windows 20.

RESULTS: The mean ± SD of hs-CRP level in patients with and without complication were 1.36 ± 0.97 and 3.09 ± 1.8, respectively. According to Student's t-test, the hs-CRP level in patients with early complications was higher than patients without early complications of stent implantation; the difference was statistically significant ($P < 0.001$).

CONCLUSION: The hs-CRP serum concentrations of patients with, and without early stent complications were significantly different. According to the control diseases center (CDC) guideline, patients with a high level of hs-CRP need special care and attention.

Keywords: High Sensitivity C-reactive Protein (hs-CRP), Percutaneous Coronary Intervention (PCI) Complication

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Introduction

Cardiovascular diseases remain the biggest cause of deaths worldwide. Although over the last two decades cardiovascular mortality rates have declined in many high-income countries, they have increased at an astonishingly fast rate in low- and middle-income countries.[1,2] Due to the high incidence of cardiovascular diseases, their treatment methods and techniques were improved in recent decades. One of the most important treatment methods is stent implantation; but unfortunately this new technique and instrument has some side effects and may lead to death or serious complications. For example stent thrombosis is a complication associated with stents implantation, and continues to be a risk for several months after the procedure.[1-6] According to other studies the total of stent insertion complications is 5-10%. The most important early complications of stents are death, myocardial infarction (MI), urgent target vessel revascularization, stroke, acute thrombosis resulting from stent, and angiographic complications

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including coronary perforation and coronary dissection. In-stent restenosis (ISR) is still a serious complication associated with stent insertion in percutaneous coronary intervention (PCI), even in the drug-eluting stent (DES) era.[1-5]

High sensitivity C-reactive protein (hs-CRP) is a sensitive inflammatory marker. Increased hs-CRP level is related to cardiovascular events such as stent restenosis in the patients.[6-8] The association of hs-CRP with PCI for ISR, especially in the DES era, is still a controversial issue. Current optimal medications such as statins, which exert anti-inflammatory effects, can modulate plasma hs-CRP level by decreasing coronary events.[8] Few studies have assessed the association of hs-CRP with ISR at both admission and follow-up in a large group of patients, especially in the Iranian population. We summarized the results of 87 consecutive stable angina (SA) patients who underwent coronary DES implantation. The aim of this study was the comparison of serum level of hs-CRP in patients with and without early complications.

Materials and Methods

a) Study design

This is a descriptive analytical study done in Shahid Chamran Hospital during 2011-2012.

The inclusion criteria were patients with chronic stable angina who had undergone stent implantation. Patients who died within 24 hours after the procedure were excluded.

b) Methodology

A total of 87 consecutive patients with chronic stable angina who had undergone PCI were selected and followed for 24 hours after stent implantation for early stent complication. We obtained a sample of blood within 24 hours after PCI and sent it to the laboratory in order to determine hs-CRP level. According to the CDC guideline, hs-CRP should be checked twice in two weeks, the patients' average hs-CRP should be considered, and the patients should be in a fixed position. If hs-CRP is more than 10 mg/l, the test is repeated to exclude possibility of inflammatory disease. Plasma hs-CRP level was measured with an immunoturbidimetric method (Beckmann Assay 360, Bera, California, USA) as previously described.[9] Ethylenediaminetetraacetic acid (EDTA) anticoagulated peripheral blood was taken after a 12-hour fasting upon the patients' admission. Plasma was obtained with a centrifugation of 3000 r/min at 4°C for 15 minutes, and the resulting sample was immediately stored at −80°C until further analysis. The lower detection limit of hs-CRP was 0.2 mg/L, the upper limit was 500 mg/L, and the median normal value was 0.8 mg/L. Other major biochemical indicators were examined at the same time in our clinical laboratory center. All patients were followed for 24 hours after stent implantation for early complications of PCI. The data included hs-CRP level (reported by the laboratory), demographic data, and early complication (recorded in special check lists).

c) Statistical analysis

Finally the data were entered into the computer and analyzed by SPSS for Windows (version 20; SPSS Inc., Chicago, IL., USA). The chi-square, one way ANOVA, Fisher's exact and student's t-test were used for data analysis.

Results

Of 87 patients 62 (71.3%) were male and 25 (28.7%) were female. The mean of patients age was 57 ± 7.2 years (range of 44-76); 16 (18.4%) were under 50, 29 (33.3%) were 50-59 and 42 (48.3%) were 60 and above. The mean ± SD of age were 54.7 ± 6.9 and 62.8 ± 3.8, respectively, for men and women. According to the student's independent t-test the difference between male and female was statistically significant ($P < 0.001$).

Any death, urgent target vessel revascularization, and stroke were seen until 24 hours after stent implantation. Other early complications included MI in 2 (2.3%) cases, coronary dissection in 3 (3.4%), and coronary perforation in 1 (1.1%) and were seen within 24 hours after stent implantation.

The mean ± SD of age of patients without early complication, with MI, coronary dissection, and coronary perforation was shown in table 1. According to one way ANOVA there was no statistical difference between the 4 groups ($P = 0.98$). Moreover, frequency distribution of early complications by sex was shown in figure 1 and according to Fisher's exact test there was no statistical difference between male and female ($P = 0.84$).

The mean ± SD of hs-CRP level was 1.48 ± 0.36 (range of 0.2–5.6) in all patients. Furthermore, hs-CRP level was higher than 1mg/l in 52 (59.8%) patients, between 1-3 mg/l in 24 (27.6%), and 3mg/l and higher in 11 (12.6%) patients. The mean ± SD level of hs-CRP in patients with and without complications was 1.36 ± 0.49 and 3.09 ± 0.83, respectively; according to Student's independent t-test, there is a statistical difference between the two groups ($P < 0.001$). The distribution of hs-CRP level based on early

complications was shown in figure 2.

The level of hs-CRP in patients with and without early complication was shown in table 2. According to one way ANOVA there was significant difference between the hs-CRP levels of the above groups (P < 0.001). Moreover, the hs-CRP level based on age groups was shown in this table, and according to one way ANOVA test the difference between age groups was statistically significant (P = 0.013). The hs-CRP level in male and female were 1.43 ± 0.54 and 1.6 ± 0.48, respectively, and according to Student's independent t-test, no statistical difference was seen between males and females (P = 0.52).

Table 1. Number and age based on early complications in patients who had undergone PCI

Early complication	Number of patients	Mean age	SD
No complication	81	57.00	7.2
MI	2	56.50	9.2
Dissection	3	57.00	7.8
Perforation	1	54.00	0.0
Total	87	57.02	7.2

(P = 0.84)

PCI: Percutaneous coronary intervention; MI: Myocardial infarction

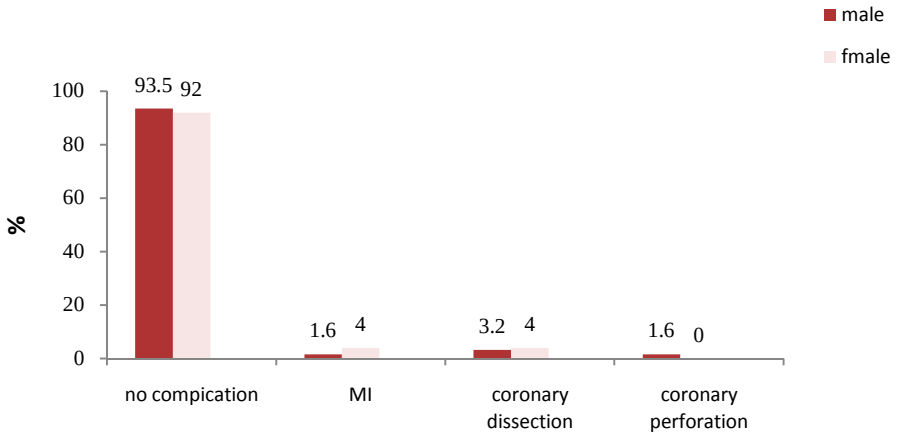

Figure 1. Frequency distribution of early complications based on sex in patients who had undergone PCI

(PCI: Percutaneous coronary intervention; MI: Myocardial infarction)

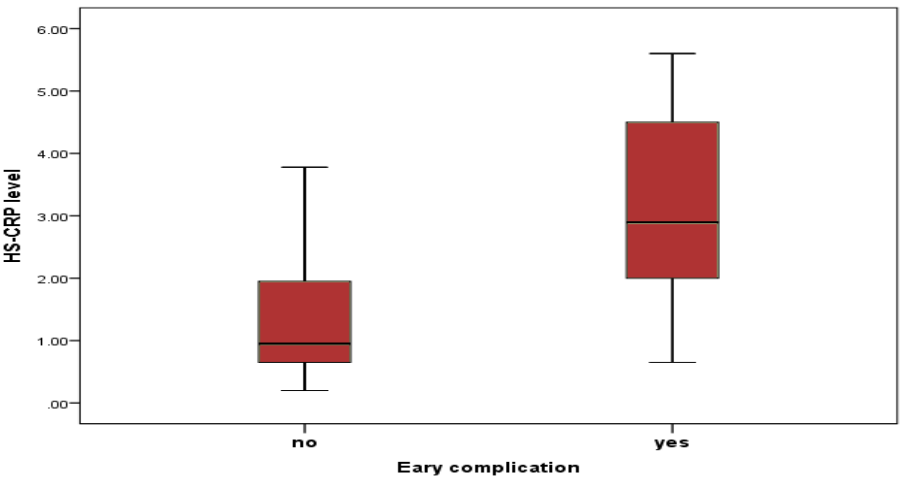

Figure 2. Distribution of hs-CRP level based on early complications in patients who had undergone PCI

(hs-CRP: High sensitivity C-reactive protein; PCI: Percutaneous coronary intervention)

Table 2. level of hs-CRP based on age, sex, and early complications in patients who had undergone PCI

Variables		Number of patients	Mean of hs-CRP	SD	P
Early complication	No complication	81	1.36	0.97	< 0.001
	MI	2	1.33	0.95	
	dissection	3	3.80	1.67	
	perforation	1	4.50	0.00	
Age groups	< 50	16	0.74	0.49	0.013
	50-59	29	1.70	1.20	
	≥ 60	42	1.60	1.15	
Sex	Male	62	1.43	1.14	0.520
	Female	25	1.48	1.09	

hs-CRP: High sensitivity C-reactive protein; PCI: Percutaneous coronary intervention; MI: Myocardial infarction

Discussion

The aim of this study was to determine the relationship between hs-CRP level and early complications of PCI. Since the first human percutaneous transluminal coronary angioplasty (PTCA) procedure was performed in 1977, the use of percutaneous coronary intervention (PCI) has increased dramatically, becoming one of the most common medical interventions performed. However, some researchers believe that this operation may lead to reinflammation and restenosis in the coronary artery. In the next decades many cardiologists and surgeons encountered a new problem; restenosis and other serious complication that may lead to death. Thus many cardiologists searched for a way to predict these complications and these studies have continued to the present day. Now, we wish to find a biomarker that can predict life threatening complications. Recent advances in guide wires, stents, and devices to cross chronically occluded arteries are evolving, so that more patients with chronic total occlusions (CTOs) are now being successfully treated percutaneously.

Our study showed that plasma hs-CRP level may independently predict early complications of PCI. This finding is similar to the findings of a study conducted by Xu et al. in china.[2] This shows that a chronic, sustained, systemic inflammatory response might be involved in early complications of PCI. Inflammation plays an important role in complications of percutaneous coronary intervention; multiple inflammatory factors such as cytokines and chemokines are involved in the neointimal tissue response at the site of coronary stenting, and the inflammatory responses are related to arterial injury.[9] On the other hand, hs-CRP, an acute phase reactant and a strong marker of inflammation, has been found repeatedly to be a strong predictor of future cardiovascular events after treatment by PCI.

In their study Dibra et al. used CRP as a unique inflammatory marker to investigate the impact of rosuvastatin treatment on cardiovascular events. The study enrolled healthy men and women with low-density lipoprotein cholesterol levels of less than 130 mg/dl and high-sensitivity (hs) CRP levels of 2.0 mg/l or higher. Rosuvastatin reduced low-density lipoprotein cholesterol levels by 50% and hs-CRP levels by 37%. Importantly, the decrease in CRP levels was accompanied by a significant reduction in the incidence of major cardiovascular events.[10] Moreover, in another study done by Hong et al. a significant positive correlation was found between pre-interventional CRP level and stent complications.[11]

Conclusion

Due to the considerable role of inflammation in cardiovascular disease and the prognostic value of CRP, preprocedural measurement of CRP level has been considered to be a tool in identifying patients at higher risk for restenosis and recurrent cardiovascular events.[12,13] However, the association between CRP levels and cardiovascular events occurring after percutaneous coronary intervention (PCI) remains uncertain and is still under investigation.

Conflict of Interests

Authors have no conflict of interests.

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