ST SEGMENT RESOLUTION IN OPIUM ADDICT PATIENTS AFTER THROMBOLYTIC THERAPY FOR ACUTE MYOCARDIAL INFARCTION

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Abstract

BACKGROUND: The aim of this study was to assess resolution of ST segment elevation after streptokinase therapy in opium-addict patients with acute myocardial infarction (AMI).

METHOD AND MATERIALS: The studied population consisted of AMI patients who have criteria for thrombolytic therapy. Three groups of ST segment resolution were defined: complete resolution (≥ 70%), partial resolution (70% to 30%) and no resolution (< 30%).

RESULTS: A total number of 240 patients were studied (126 opium addicts and 114 non-addicts). Overall, 52.5% of addicts and 38.7% of non-addicts had complete ST segment resolution (P = 0.06). The odds of ST elevation resolution in addicts was 1.8 (95%, CI: 1.09-2.95) compared to non-addicts. When it was adjusted for other variables, it reduced to 1.03 (95%, CI: 0.54-1.97).

CONCLUSION: There was not any significant relationship between opium addiction and response to thrombolytic therapy among patients with acute MI.

Keywords: Acute myocardial infarction, opium, streptokinase, substance abuse.

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Introduction

Cardiovascular diseases cause 12 million death throughout the world each year,[1] which represents 29% of all deaths.[2] Acute myocardial infarction (AMI) and sudden death are common occurrences of coronary atherosclerosis.[3] Most such events are related to thrombotic occlusion at the site of atherosclerotic plaques in epicardial coronary arteries.[4] Streptokinase is a bacterial protein, widely used as a thrombolytic agent in the treatment of ST segment elevation AMI. Several studies have shown that early resolution of ST segment elevation is a simple and useful predictor of infarct size, left ventricular function and clinical outcomes after thrombolytic therapy.[5-6] It has been shown that a lower mortality risk in younger patients and in smokers coincides with better early reperfusion rates and is associated with better ST elevation recovery.[7-8] Opium addiction is a common habit and health problem worldwide. Opium has always been the most widely abuse substance in Iran.[9] Although, thromoblytic therapy may be most effective in current smokers,[10] there is no survey about the response of opium user to thrombolytic therapy. The aim of this study was to assess resolution of ST segment elevation after streptokinase therapy in opium addict patients with AMI. We also studied most important cardiovascular risk factors among this group of patients.

Materials and Methods

A cross sectional study was designed in Kerman University of Medical Sciences. The studied population consisted of consecutive patients with first AMI admition to coronary care units in Shafa and Afzalipour hospitals in the city of Kerman, from

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March 2006 to October 2007. Diagnosis of AMI was confirmed based on history, serial ECG charges and enzyme analysis.

A 12-lead ECG was recorded before and 180 minutes after the start of the streptokinase infusion. Opium addiction was assessed according to DSM-IV-TR criteria. Inclusion criteria were AMI patients treated with streptokinase within six hours from onset of chest pain. Patients with left bundle branch block or pacemaker and those missing ECG were excluded. ST segment analysis was performed in blinded manner by a cardiologist. The sum of the ST segment elevation and resolution was measured 20 ms after the end of the ORS complex from leads 1, avl and v_1-v_6 for anterior AMI and leads II, III, avf, v_5 and v6 for inferior AMI. In addition, subgroups of patients who had a reciprocal ST segment depression ≥ 0.1 mv were also evaluated. Consistent with previous studies,[11] three categories of ST segment elevation resolution were applied: complete resolution defined as ST segment elevation resolution ≥ 70%, partial resolution defined as ST segment elevation resolution < 70% to 30%, no resolution defined as ST segment elevation resolution < 30%.

Statistical analysis

The data were analyzed using Stata version 9. In the first step, we compared the differences between addicts and non-addicts using simple statistical tests (pooled t test and chi-square). In the next step, we treated the response to the streptokinase (dependent variable) as an ordinal variable: reversing ST elevation less than 30%, between 30% and 70%, and more than 70%. In ordered logit model, an underlying score is estimated as a linear function of the independent variables and a set of cut-points. Using "ologit" command, we estimated ORs by the ordinal logistic regression model. In our models, we estimated the crude and adjusted ORs for those variables which showed differences in addicts and non-addicts by simple statistical tests.

Results

We recruited 126 addicts and 114 non-addicts. As we expected, the frequency of addiction in females were lower than males (10.3% versus 28.1%; P < 0.0001). Also the frequency of current smokers in addict group was around four times ex-smokers (68.3% of addicts were current smoker) (Table 1).

The two groups of addicts and non-addicts were more or less comparable in medical records and lab tests except in age, triglyceride, WBC and blood sugar. The mean age of non-addicts and addicts were 57.5 ± 12.2 and 53.5 ± 10.3 years respectively (P = 0.007). Around 37% of non-addicts and 21% of addicts had diabetes (P = 0.01). Also, FBS and BS of non-addicts were around 27 and 39 g/dl greater, respectively (Table 2). Similarly triglyceride in non-addicts was around 40 mg/dl greater (P = 0.007), while the number of WBCs was lower (10500 vs. 12700; P = 0.05).

Overall, 52.5% of addicts and 38.7% of non-addicts responded to the injection of streptokinase and more than 70% of their ST elevations reversed (P = 0.06). The crude OR between addiction and ST response was 1.8 (95% CI: 1.09-2.95), showing that the response of addicts to the streptokinase was more prominent (P = 0.02). However, adjusted OR for other influential variables was 1.03 (95% CI: 0.54-1.97). To check which variable(s) had prominent effects on the relationship between addiction and response to the injection of streptokinase, we added the variables in the model one by one. The OR changed less than 10% by adding sex, age, the gap between the onset of symptoms and injection of streptokinase, FBS and WBC. While, adding diabetes in the model dropped the OR from 1.8 to 1.45. Also, we found similar results by adding smoking (OR = 1.47). Therefore, most of the observed difference between the crude and adjusted ORs was due to the impacts of diabetes and smoking, adding both of these two variables in the model dropped the OR to 1.27 (95%, CI: 0.71-2.28).In addition, we checked the associations between other variables and response to the injection of streptokinase. The crude and adjusted OR between current smoking and the response to the injection of streptokinase was 1.88 and 1.34 respectively (Table 3). The crude OR showed that the response of smokers was significantly more prominent while the adjusted OR showed a weaker association and was not statistically significant (95%, CI: 0.66-2.73).

Females responded less to the streptokinase. The crude and adjusted ORs were 0.45 (95% CI: 0.24-0.84) and 0.51 (95% CI: 0.24-1.07) respectively. Although the confidence interval of the adjusted OR included one and its p-value was borderline (P = 0.07), the OR was very far from one, which implies that females' responses were not obvious compared to males'.

Moreover, our results showed that age, FBS, WBC and diabetes on their own did not have significant associations with the response to the streptokinase. The crude ORs between diabetes and FBS with the response to the streptokinase were less than one and significant, but their adjusted ORs were not significant. Both crude and adjusted ORs for age and WBC were insignificant (Table 3).

Table 1: Demographic and clinical variables in addicts and non-addicts

Variable	Non-addicts Mean (SD)	Addicts Mean (SD)	p-value
Sex			
Male	82(71.9)	113(89.7)	< 0.0001
Female	32(28.1)	13(10.3)	
Smoking			
No	91(79.8)	40(31.7)	< 0.0001
Yes	23(20.2)	86(68.3)	
Ex-smoking			
No	111(97.4)	114(90.5)	0.028
Yes	3(2.6)	12(9.5)	
Diabetes			
No	65(63.1)	86(78.9)	0.011
Yes	38(36.9)	23(21.1)	
Hypertension			
No	70(70.0)	83(76.9)	0.263
Yes	30(30.0)	25(23.1)	
Family history of IHD			
No	57(74.0)	73(76.0)	0.760
Yes	20(26.0)	23(24.0)	
ST response			
Less than 30%	17(15.3)	10(8.2)	
30-70%	51(45.9)	48(39.3)	
More than 70%	43(38.7)	64(52.5)	

Table 2: Comparison of age and laboratory variables in addicts and non-addicts

Variable (mean/SD)	Non-addicts (%)	Addicts (%)	p-value
Age	57.5(12.2)	53.5(10.3)	0.007
Fasting blood sugar	157.8(86.0)	130.0(54.8)	0.005
Blood sugar	213.3(96.4)	174.4(66.6)	0.013
Cholesterol	206.0(51.2)	199.6(57.1)	0.377
LDL	109.6(39.7)	115.1(34.6)	0.505
HDL	43.3(9.5)	45.9(21.0)	0.467
TG	182.9(135.3)	142.7(87.1)	0.007
WBC	10.5(6.4)	12.7(10.1)	0.051
RBC	5.7(4.8)	6.2(5.6)	0.465
HB	15.8(4.3)	17.0(6.8)	0.107
HCT	46.8(15.9)	46.2(9.6)	0.762
Platelet	227.2(88.9)	213.8(74.3)	0.210
The gap between the onset of symptoms and injection of streptokinase in hour	2.9(2.6)	2.8(2.4)	0.627

Table 3: crude and adjusted odds ratios between addiction and other influential variables following streptokinase

	Crude Analysis		Adjusted Analysis	
	OR	**95% CI**	**OR**	**95% CI**
Addiction				
No	1	-	1	-
Yes	1.80	1.09-2.95	1.03	0.54-1.97
Smoking				
No	1	-	1	-
Yes	1.88	1.14-3.10	1.34	0.66-2.73
Sex				
Male	1	-	1	-
Female	0.45	0.24-0.84	0.51	0.24-1.07
Age (year)	0.99	0.97-1.02	1.004	0.98-1.03
Diabetes				
No	1	-	1	-
Yes	0.48	0.27-0.87	0.81	0.33-1.97
Fasting blood sugar (g/dl)	0.995	0.992-0.999	0.998	0.992-1.003
WBC	1.02	0.99-1.06	1.03	0.99-1.08
The gap between the onset of symptoms and injection of streptokinase in hour	0.83	0.72-0.97	0.83	0.70-1.00

As we expected, the gap between the onset of symptoms and the injection of streptokinase was significant. Both crude and adjusted ORs showed that delay in the injection deteriorated the response to the streptokinase (crude and adjusted ORs were 0.83, $P < 0.05$).

Discussion

Our findings showed that the response of addicts to the streptokinase was better. But, after adjusting for other variables, the difference was not significant. We also found that the responses in females were lower, and the gap between the onset of symptoms and the injection of the streptokinase was very important. We also noticed that the response of smokers to streptokinase therapy was more prominent and it was significant in univariate analysis. The hypercoagulable state of smokers due to increased fibrinogen and thrombin generation has been invoked to explain this difference between smokers and non smokers.[12,13]

There are also some evidence about the hypercoagulable state in opium users, and we previously reported that plasma fibrinogen level was elevated in opium addicts.[14] Another study also showed that fibrinogen level was high in heroin users.[15] Besides, Ceriello et al reported that antithrombin III activity was significantly decreased in opiate addicts.[16] Therefore, there is an important hypothesis that more active thrombogenic mechanisms may be operative in opium users leading to a larger thrombus component that is more susceptible to lyric therapy. However, more studies are needed to clarify the pathophysiologic mechanisms. The main demographic characteristics of opium users in this study population included lower age and high prevalence of cigarette smoking, along with the lower prevalence of diabetes mellitus in females. These characteristics are similar to risk factors for young patients with AMI1.[7,18].

We tried to identify the opium users via patients' history; there may still be some under estimations. But, the prevalence of opium users in this study was high. Also, we used only ST segment resolutions for assessing the efficacy of reperfusion therapy.

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