Relation of Opium Addiction with the Severity and Extension of Myocardial Infarction and Its Related Mortality

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Original Article

Abstract

Background: Despite some evidences about protective or triggering role of opium use in patients with coronary artery disease, the exact role of opium is still under question. The current study aimed to address the relation of opium dependence on the severity and extension of myocardial infarction (MI) and its related mortality.

Methods: The study population consisted of 460 consecutive patients (239 opium addicts and 221 non-addicts) with first acute MI. Study information was extracted from hospital recorded files as well as face to face interview.

Findings: In-hospital mortality in opium addicted patients was numerically lower than another group (5.4% versus 8.2%), but this difference was not statistically significant. Regarding types of MI, anterior wall MI was higher in non-addicted patients than addicts (36.4% versus 26.4%). Among patients with anterior wall MI, early mortality was significantly higher in non-addicted compared to addicted subjects (20.0% versus 7.9% P = 0.043). The main associated factors of in-hospital mortality due to acute MI in addicts were advanced age and family history of coronary artery disease and in non-addicts were advanced age and hypertension.

Conclusion: In current study total in-hospital mortality was not different between opium addicted and non-addicted groups but opium may reduce the occurrence of anterior wall MI and its related early mortality.

Keywords: Opium, Myocardial infarction, Mortality

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Introduction

Although opium use is considered to have a declining trend in most societies, recent data have shown notable attendance to opium usage in some developing countries such as Iran.[1-3] The incidence of opium addiction is especially higher in some diseases subgroups. The prevalence of opium addiction is about 2-2.8 percent among Iranian general population; whereas it was estimated about 9.9-19 percent in the group with acute myocardial infarction (MI).[4,5] The most important reason for this high prevalence is the misconception in our population that opiates can prevent and control risk factors for coronary artery disease such as hypertension and diabetes mellitus and also has an ameliorating effect in the process of these factors.[4] This belief about protective cardiovascular effects of opium has been extended even among a few physicians that some of them believe alternative treatment role of opium for some of cardiovascular risk factors specially diabetes.[6,7]

However, this belief has not been supported by some recent basic and clinical investigations. In some of them, serum levels of biochemical risk factors for coronary artery disease such as lipoprotein (a) and C-reactive protein were significantly higher in opium addicted patients and these factors were major determinants of risk factor for premature atherosclerosis.[8,9] Masoomi et al. reported that opium was an independent risk factor for coronary artery disease (CAD).[10] Furthermore, some basic trials have confirmed that opioid peptides are involved in ischemic preconditioning via K+-ATP channel in cardiac mitochondria that play a pivotal role in a number of pathological conditions in cardiovascular system.[11,12] However, some other studies could find some evidences about protective role of opium use. Marmor et al. indicated that long-term exposure to opiates could be associated with decreased severity of coronary artery disease, and hence with decreased incidence of fatal MIs.[13]

Furthermore, Najafi et al. revealed that the different domains of quality of life in opium-addicted and non-addicted patients with coronary artery disease were not statistically different.[14] There is controversy among clinicians about the effects of opium on the cardiovascular system. In addition, these effects on outcome of different subgroups of acute MI have been unclear. The present study aimed to address the differences in clinical outcome of acute MI between opium addicted and non-addicted patients in different subgroups. Moreover, we determined the relationships between in-hospital mortality and opium dependence in different subgroups of MI. Finally, we tried to determine main predictors of short-term mortality in addicted and non-addicted patients with MI.

Methods

The study population consisted of 460 consecutive patients with first acute MI admitted within 6 hours of the onset of chest pain to coronary care units (CCU) in the city of Kerman. Patients had the following criteria: 1) typical chest pain lasting ≥ 30 minutes; 2) ST-segment elevation ≥ 0.2 mV in ≥ 2 contiguous precordial leads (for the diagnosis of anterior wall MI) or in leads V_1–V_3 (for the diagnosis of anteroseptal wall MI) as well as ≥ 0.1 mV in II, III, and aVF leads (for the diagnosis of inferior wall MI) on the admission's ECG; 3) increase in serum creatine kinase (CK) level more than twice the normal value; 4) no previous MI; 5) no other heart or lung disease.

Participants were classified into two groups: 1) opium addicted patients (n = 239) and non-addicted patients (n = 221). Opium addiction was defined on the basis of the DSM-IV criteria for substance dependence as regularly consumption of inhalatory opium more than three times per week and/or oral opium daily.[15] Demographic characteristics and clinical criteria of these patients were extracted from hospital recorded files as well as face to face interview if required, and were entered into a computerized database form. The patients were given self-administered questionnaires about their medical history and early complications after MI including general characteristics, Killip class and coronary artery disease risk factors: Current smoking history (patients regularly smoke a tobacco product/products one or more times per day or have smoked in the 30 days prior to admission),[16] hypercholesterolemia (total cholesterol ≥ 5.0 mmol/l, HDL-cholesterol ≥ 1.0 mmol/l in men, or ≥ 1.1 mmol/l in women, and triglycerides ≥ 2.0 mmol/l),[17] family history of CAD (first-degree relatives before the age of 55 in men and 65 years in women),[18] hypertension (systolic blood

pressure ≥ 140 mmHg and/or diastolic ≥ 90 mmHg and/or on antihypertensive treatment),[18] diabetes mellitus (symptoms of diabetes plus at least one of the following: plasma glucose concentration ≥ 11.1 mmol/l, fasting plasma glucose ≥ 7.0 mmol/l, and 2-hpp ≥ 11.1 mmol/l).[20] We considered in-hospital MI as criteria for in-hospital outcome.

Results were reported as mean ± standard deviation (SD) for the quantitative variables and percentages for the categorical variables. The groups were compared using the Student's t-test for the continuous variables and the chi-square test (or Fisher's exact test if required) for the categorical variables. Predictors exhibiting a statistically significant relation with mortality in the two groups in univariate analyses were taken for multivariate logistic regression analysis to investigate their independence as predictors. Odds ratio (OR) and 95% confidence intervals (CI) were calculated. This study was done with the power of 90%. P-values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 13.0 (SPSS Inc., Chicago, IL, USA) and SAS version 9.1 for Windows (SAS Institute Inc., Cary, NC, USA).

Results

As presented in table 1, opium addicted and non-addicted patients were similar in terms of Killip class, left ventricular ejection fraction as well as lipid profiles. However, male to female ratio was higher in opium addicted patients and these participants were younger than the non-addicted ones. Among general risk factors for coronary artery disease, only family history of heart disease was not different between the addicted and non-addicted patients. The overall prevalence of hypertension and diabetes mellitus were higher in non-addicted participants, whereas history of current cigarette smoking was more in opium addicted individuals. There was no significant difference with respect to in-hospital mortality between too groups (P = 0.242).

Regarding types of MI, anterior wall MI was found to be higher in non-addicted patients than addicts (36.4% versus 26.4%, P = 0.021); however, the incidence of inferior wall MI was similar in the two groups (43.0% versus 41.6%, P = 0.761). Among patients with anterior wall MI, early mortality was significantly higher in non- addicted

Table 1. Baseline characteristics and clinical data of study patients

Characteristics	Total (n = 460)	Opium addicted (n = 239)	Non-addicted (n = 221)	P
Male gender	348 (75.8)	207 (86.6)	141 (64.1)	< 0.001
Age (year)	58.1 ± 12.0	55.5 ± 11.4	60.8 ± 12.1	< 0.001
Current smoking	169 (39.9)	135 (64.0)	34 (16.0)	< 0.001
Diabetes mellitus	132 (28.8)	55 (23.1)	77 (35.0)	0.005
Hypertension	143 (31.2)	64 (26.8)	79 (35.9)	0.033
Family history of CAD	96 (20.9)	46 (19.2)	50 (22.7)	0.360
Killip class				
I	314 (72.2)	169 (74.4)	145 (69.7)	
II	85 (19.5)	42 (18.5)	43 (20.7)	0.625
III	23 (5.3)	11 (4.8)	12 (5.8)	
IV	13 (3.0)	5 (2.2)	8 (3.8)	
Ejection fraction (%)	44.0 ± 9.9	44.7 ± 9.4	43.2 ± 10.4	0.126
Myocardial infarction:				
Anteroseptal wall	119 (25.9)	71 (29.7)	48 (21.8)	0.053
Anterior wall	143 (31.2)	63 (26.4)	80 (36.4)	0.021
Inferior wall	197 (42.9)	105 (43.9)	92 (41.8)	0.649
Laboratory parameters:				
Fasting blood sugar	145.3 ± 71.0	136.2 ± 65.1	155.0 ± 75.8	0.007
Triglyceride	148.8 ± 97.9	137.3 ± 80.9	160.9 ± 112.0	0.012
Cholesterol	202.9 ± 54.4	198.8 ± 55.3	207.3 ± 53.2	0.104
HDL	43.1 ± 12.2	43.3 ± 14.2	42.9 ± 9.8	0.848
LDL	116.6 ± 52.0	116.5 ± 44.8	116.7 ± 58.8	0.979

Data are presented as mean ± SD or n (%)
CAD: Coronary artery disease   HDL: High density lipoprotein   LDL: Low density lipoprotein

compared to addicted subjects (20.0% versus 7.9%). Regarding types of MI, anterior wall MI was more appeared in non-addicted patients and inferior MI was similar between the two groups. With regard to in-hospital mortality following acute MI (Table 2), among patients with anterior wall MI, the rate of mortality was significantly higher in non-addicted compared to addicted subjects (20.0% versus 7.9%, P = 0.043). However, in other types of MI, mortality rates were not different between the two study groups. Although in opium-addicted group, short-term mortality rates were comparable between the different types of MI, mortality was occurred more in those with anterior wall MI in non-addicted group.

Multivariable regression analysis revealed that the main associated factors of in-hospital mortality due to acute MI in opium-addicted patients were advanced age [odds ratio (OR): 1.121, P = 0.002] and family history of coronary artery disease (OR: 4.407, P = 0.040) (Table 3). In non-addicted patients, advanced age (OR: 1.076, P = 0.003) and hypertension (OR: 4.776, P = 0.004)

could effectively predict short-term mortality following acute MI (Table 4).

Discussion

Current study tried to identify the role of opium dependence as a trigger for short-term mortality due to MI. Furthermore, relationship between the type of infarction and mortality in the two groups of patients who were addicted to opium and non-addicted ones was determined. The prevalence of opium addiction in our study group was estimated as 52.0% that was considerably high. In a study by Ziaaddini et al.[1] it was suggested that the prevalence of substance abuse in rural area in Kerman was 22.5% with addiction rate of 6%. Their study mainly focused on general population. However, regarding the prevalence of opium addiction among patients with coronary artery disease, some other studies on Iranian population confirmed significantly high prevalence of opium dependence in those with early onset coronary artery disease in comparison with normal subjects.[21] It seems that cultural

Table 2. In-hospital mortality following acute myocardial infarction in opium addicted and non-addicted patients

Type of myocardial infarction	Total (n = 460)	Opium addicted (n = 239)	Non-addicted (n = 221)	P
Anteroseptal wall	2 (1.7)	2 (2.8)	0 (0)	0.515
Anterior wall	21 (14.7)	5 (7.9)	16 (20.0)	0.043
Inferior wall	9 (4.5)	6 (5.7)	3 (3.2)	0.284
P	< 0.001	0.421	< 0.001	

Table 3. Determinants of in-hospital mortality following acute myocardial infarction in opium addicted patients in the presence of cofounders

Item	Multivariable P	Odds ratio	95% Confidence intervals	
			Lower limit	Upper limit
Female gender	0.335	0.521	0.138	1.961
Advanced age	0.002	1.121	1.042	1.207
Diabetes mellitus	0.165	0.418	0.122	1.433
Family history of CAD	0.040	4.407	1.073	18.094
Hypertension	0.541	1.487	0.416	5.316

Hosmer- Lemeshow goodness of fit: $\chi^2 = 13.949$, P = 0.083   CAD: Coronary artery disease

Table 4. Determinants of in-hospital mortality following acute myocardial infarction in non-addicted patients in the presence of cofounders

Item	Multivariable P	Odds ratio	95% Confidence intervals	
			Lower limit	Upper limit
Female gender	0.106	2.671	0.810	8.800
Advanced age	0.003	1.076	1.025	1.130
Diabetes mellitus	0.135	0.435	0.146	1.297
Family history of CAD	0.799	1.187	0.318	4.429
Hypertension	0.004	4.776	1.664	13.874

Hosmer- Lemeshow goodness of fit: $\chi^2 = 8.730$, P = 0.366   CAD: Coronary artery disease

factors and socioeconomic status are the most important reasons for high opium dependence among Kerman's population. These effective factors have been identified on the basis of population-based studies so that the positive attitudes towards drug consumption and faulty knowledge of therapeutic use of opium were recognized as affecting factors on addiction tendency in Kerman.[22]

Effect of opium use on the physiopathological processes of myocardial ischemia and infarction has been under question. Some studies showed that the opiates could be a potential risk factor for the severity of cardiac ischemia. In a study by Sadeghian et al.[21] relationship between the presence of coronary artery disease and opium addiction was confirmed only in men especially in those with the history of current smoking. Furthermore, it has been indicated that the influence of opium addiction on progression of atherosclerosis might be restricted to presence of hypercholesterolemia. In fact, in normocholesterolemic animal models, opium could not change the atherogenic processes.[3] Moreover, some researches confirmed the deleterious effects of opium on traditional risk factors including hemoglobin A1c, high-density lipoprotein, lipoprotein (a), factor VII, fibrinogen and C-reactive protein. However, they also showed that these deleterious effects were dependant to the period of addiction and their levels were increased following long-term opium addiction.[7] In addition, some other studies hypothesized the protective effects of opium on the severity and extension of coronary artery disease. Marmor et al.[13] indicated a significant protective effect against adjusting for age and a history of hypertension.

In the present study, non-addicted patients suffered from anterior wall MI more than addicts and opium use could affect the severity and extension of atherosclerosis by reducing the occurrence of anterior wall MI. One possible explanation for this finding is that narcotics may decrease inflammation, which is directly associated with atherogenesis and plaque disruption.[23-26] Recent biological studies were also provided some evidences for a protective function

of opioids via K-ATP channels in the heart.[11,12] Furthermore, stimulating some opioid receptor agonists such as TAN-67 reduces infarct size via activation of those channels.[27-29] Moreover, Masoomi et al. showed that the response of addicts to the streptokinase was more prominent in comparison with non-addicts.[30] Therefore, long-term use of opiates may be associated with decreased severity of CAD, hence, with a decreased incidence of fatal anterior wall MI.

In current study, although total in-hospital mortality in opium addicted patients was numerically higher than another group (5.4% versus 8.2%), but this difference was not statistically significant. However, with regard to death following different types of MI, mortality rate in non-addicts was significantly higher in anterior wall group, whereas this rate was similar in the types of MI among addicted ones. Similarly, in Davoodi et al. study,[31] no significant difference was observed in specifications, short term outcome and prognosis of acute MI between opium dependents and non-dependents except for duration of hospitalization. We think that the dependence to opiates not only may reduce the incidence of anterior wall infarction, but also decrease the mortality caused by this type of infarction in opium users. However, we strongly emphasize that the direct use of opiates should not be programmed for improving outcome of MI because of their other harmful physical, psychological and social effects. Therefore, the use of these compounds should be limited to the administration of opioid drugs in high risk groups especially under consideration of specialists.

Conclusion

In current study, total in-hospital mortality was not significantly different between opium addicted and non-addicted groups but opium may reduce the appearance of anterior wall MI and its related early mortality. However, in administration of drugs originated from opiates, their harmful side effects should be considered.

Conflict of Interest

The Authors have no conflict of interest.

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رابطه اعتیاد به تریاک با میزان مرگ و میر و شدت انفارکتوس حاد میوکارد

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مقاله پژوهشی

چکیده

مقدمه: رابطه اعتیاد به تریاک و بیماری عروق کرونر به طور دقیق مشخص نمی‌باشد و نتایج بررسی‌ها متناقض است. مطالعه حاضر با هدف، بررسی رابطه اعتیاد به تریاک با میزان مرگ و میر و شدت انفارکتوس حاد میوکارد انجام شد.

روش‌ها: جمعیت مورد مطالعه را ۴۶۰ بیمار با انفارکتوس حاد میوکارد تشکیل می‌دادند که ۲۳۹ نفر معتاد به تریاک و ۲۲۱ نفر غیر معتاد بودند. اطلاعات مورد نظر با پرسش و پاسخ از بیماران و پرونده آنان کسب گردید.

یافته‌ها: میزان مرگ و میر بیمارستانی افراد معتاد به تریاک نسبت به گروه غیر معتاد کمتر بود، اما این اختلاف از نظر آماری معنی‌دار نبود. در رابطه با نوع انفارکتوس حاد میوکارد، انفارکتوس قدامی در افراد غیر معتاد (۳۶/۴ درصد) نسبت به افراد معتاد بیشتر بود (۲۶/۴ درصد) و میزان مرگ و میر بیمارستانی گروه غیر معتاد به طور معنی‌داری بیشتر از گروه معتاد بود (۰/۰۴۳ = P). سن بالا و سابقه فامیلی بیماری عروق کرونر از عوامل اصلی مرتبط با مرگ و میر بیمارستانی در گروه معتاد و سن بالا و پرفشاری خون علت اصلی در گروه غیر معتاد بود.

نتیجه‌گیری: در مطالعه حاضر، میزان مرگ و میر کلی بیمارستانی ناشی از انفارکتوس حاد میوکارد در بیماران معتاد به تریاک و غیر معتاد، تفاوت معنی‌داری نداشت؛ اما وقوع انفارکتوس قدامی و میزان مرگ و میر ناشی از آن در گروه بیماران معتاد به تریاک کمتر بود.

واژگان کلیدی: تریاک، انفارکتوس میوکارد، مرگ و میر

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