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Comparison of Specifications, Short-Term Outcome and Prognosis of Acute Myocardial Infarction in Opium Dependent Patients and Non-dependents

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Abstract

Background: The effects of opium dependence on prognosis and short term outcome of patients with acute myocardial infarction (AMI) are not clear yet. Methods: From March 2004 to August 2004 all male patients admitted with diagnosis of AMI were enrolled. Patients who fulfilled DSM-IV-TR criteria were chosen as opium dependent patients (ODP).Demographic data, risk factors, peak enzyme levels, location of MI, mortality and ejection fraction were collected and analyzed. In short term follow up (184 ± 37 days) we studied; mortality, readmission, functional class, performed revascularizations and coronary angiogram results. Results: A total number of 160 patients were enrolled, of which 45 (28.1%) were opium dependent. In 137 patients 6 months follow up was completed. Duration of admission was higher in ODP (11.3 days versus 8.7, P= 0.03) There was no significant difference in age, EF, location of MI, peak enzymes levels, angiographic findings, risk factors (except for cigarette smoking and triglyceride level), in-hospital mortality, need for readmission, 6 months mortality, functional class, and the need for revascularization. Conclusion: In an unselected cohort of patients admitted with AMI, there was no significant difference in specifications, short term outcome and prognosis of AMI between ODP and non-dependents except for duration of hospitalization (German J Psychiatry 2005; 8:33-37).

Keywords: Opium dependence, acute myocardial infarction, mortality, prognosis, angiographic findings

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Introduction

Opium dependence is a major public health problem in some parts of the world including our country Iran. Opium has always been the most widely abused substance in Iran. Unlike the pure opioids such as morphine, opium is a complex and variable mixture of substances. Daily amount used both by smoking and by mouth vary from less than 1 gram to more than 30 grams equivalent to 75-3000 mg of morphine. The effects of opium are essentially those of morphine. The major effects of opium are on central and autonomic nervous systems and the bowels, while it has certain influences on other organ systems including respiratory and cardiovascular systems (Kalant, 1997). Orthostatic hypotension has been reported after opium consumption. Several investigations about the effects of opioid peptides on cardiovascular system have also been performed. They show that hypotension, bradycardia, peripheral vasodilatation or sometimes hypertension and tachycardia are among the cardiovascular effects of opioids (Ventura et al., 1992) which are produced mainly through their effects on K and Ca channels as well as adenylate cyclase (Brink et al., 2003). Opioid peptides of myocardial origin have also recently been shown to play a key role in local regulation of the heart. Ischemic preconditioning which

reduces the infarct size is abolished in human and rat by blocking opioid peptide receptors with naloxone (Tomai et al., 1999; Karch et al., 2001). Rats treated with morphine or selective delta agonist before ischemia, produced significant and similar reduction in infarct size when compared with vehicle (Gross et al., 2004). Induction of hypertrophy may also be associated with increased enkephalin production in the heart (Hao et al., 1997). There may be also effects on age-associated reduction in ß-adrenergic responsiveness (Xiao et al., 1991). A study in Iranian drivers showed significant lower cholesterol level, as well as lower diastolic blood pressure, which in combination with other effects of opium can influence the outcome of cardiovascular disease (Rajabizade et al., 2004). Considering the above mentioned data there are beliefs among some people (including some medical staff) that opium consumption has protective effects in cardiovascular disease, while others disagree and yet others believe that opium has harmful effects. There is no sufficient and reliable data regarding the influences of opium dependence on the patient's outcome after myocardial infarction which is the most important heart disease. Therefore, we decided to perform this study to evaluate the probable effects. The aim of the present study was to compare the specifications, short term outcome, complications and prognosis of acute myocardial infarction in opium dependent patients and nondependent patients.

Material and Methods

From March 2004 to August 2004 all male admitted patients with diagnosis of Acute Coronary Syndrome (ACS) in Tehran Heart Center (THC) were registered. Serial ECGs for the first 72 hours were recorded and compared with previous ECG recordings (if available). Creatinin kinase (MB) level, and troponin I levels were checked 3 times during this first 72 hours. Patients were examined by our cardiologists and a complete history including the specifications and quality of their chest pain was obtained. Meanwhile they were asked about their history of opium dependence criteria. Those who fulfilled the ESC/ACC criteria for acute MI (The Joint Committee 2000) were identified.

Patients who died prior to a possible enzyme rise who had typical symptoms and ECG changes of AMI were also selected only if there was enough time to ask for the history of opium dependence.

Due to the low prevalence of opium dependence in our female patients (compared to male patients), they were excluded from this study. Patients admitted with AMI who had a history of PCI or CABG were also excluded from the study.

Patients who fulfilled the DSM-IV-TR criteria for substance (opium) dependence (by smoking or oral intake) were enrolled as Opium Dependent Patients (ODP).

The management strategy including indications for thrombolytic therapy, and the guidelines for use of beta-blockers, ACE inhibitors, anti-platelets, statins and nitrates were identical for both ODP and non-dependents.

The following variables were collected: age-history of hypertension; history of cigarette smoking; history of diabetes-lipid profile (cholesterol, triglyceride, HDL and LDL by sampling in the first 24 hours of MI); peak enzyme level (CK-MB and troponin I within the first 72 hours); ejection fraction (by echocardiography); location of MI (based on ECG changes as diagnosed by cardiologists and categorized as inferior, anterior and non ST elevation MI); duration of hospital admission and in-hospital mortality.

The patients were followed for an average of 6 months and in the follow up performed by the cardiologist in charge, the following data were collected: mortality in the follow up period; readmission rate; the performed cases of CABG or PCI; the results of selective coronary angiography (SCA) including the location of involvement (with more than 50% stenosis) and the number of involved vessels (single, two or three vessels); functional class of patient after 6 months (categorized and classified as asymptomatic or F.C=1, mildly to moderately symptomatic (F.C=2 and F.C=3) and severely symptomatic (F.C=4) respectively).

Statistical analysis

For continuous variables including age, lipid profile, enzyme levels, ejection fraction and number of involved vessels the values are expressed as mean ± standard deviation and in those marked by * as mean ± standard error mean. For discrete variables, values are expressed as percentages. This was a prospective study in which patients were followed for an average of 6 months. The calculated power of study based on ejection fraction and mortality was more than 85%. For continuous variables t-Test was used to assess the differences between two groups and for qualitative variables, chi-square test was used. For small sizes we used Fisher's exact test. In order to determine the effects of confounder variables we used Mantel-Haenszel test. All statistical analyses were performed using SPSS for Windows 11.5.

Results

A total number of 160 patients were enrolled in this study of which 45 patients (28%) were opium dependent (ODP) and 115 patients (72%) were not dependent to opium. Demographic data showed no significant difference in age and frequency of risk factors except for cigarette smoking which was significantly more common in ODP and triglyceride level which was significantly lower (Table I).
Comparisons between in- hospital mortality, location of MI, duration of hospital admission peak enzyme levels and ejection fraction between ODP and non dependents shown in Table 2 indicates no significant difference except in the duration of admission which was significantly higher in ODP (Table 2).

In the follow-up study, which was performed for a mean of 184±37 days after MI, 137 patients (85.6%) were followed of which 37 (82.2% of 45) were ODP and 199 (86.9% of 115)

were non dependents. 23 patients did not complete the follow up. Mortality in the follow up period, readmission rate, the performed cases of CABG or PCI and the functional class of patients at the end of follow up were compared (Table 3). They show no significant difference between ODP and non-dependents.

Selective coronary angiogram was performed in 103 patients (75%), of which 30 patients were ODP (81% of ODP) and 73 were not (73% of non-dependents) and the results of angiograms (the location of involvement and the average number of involved vessels) are compared in Table 4, which shows no significant difference in any of the above mentioned items.

Discussion

The aim of this study was to compare the short-term outcome, complications and mortality of AMI between ODP and non-dependents. Opium addiction is a common habit and health problem in many eastern countries. There are beliefs about protective cardiovascular effects of opium consumption in some societies or in some papers, while others mention it as an aggravating factor or even a probable risk factor for CAD. There is no definite answer to many of the questions regarding the cardiovascular effects of opium dependence.

First we had to identify ODP. Since some of these patients may deny their dependence, there was a probability of under estimation of ODP. On the other hand relying on urine test for opium would give a large number of false-positive results because most of our patients received narcotics among their drugs. Therefore we decided to directly ask the patients, through their cardiologist, about opium dependence in their first visit. Patients were informed that the data will be used only for this study and would not be mentioned elsewhere. In order to have an estimate of reliability of the answers, we performed urine test for opium in 18 patients who denied OD and did not receive narcotics (selected randomly), and all these tests were negative. This was a strong clue for reliability of patients' answers to our question about OD

We used DSM-IV-TR criteria for diagnosis of OD. Therefore some patients who used opium infrequently were not enrolled as ODP. We did not separate patients who used opium by oral route or by smoking because of the similar pathologic or physiologic effects. On the other hand there is much cross-over between ODP using each of these two methods of opium consumption. By this definition, 28% of our patients were OD, which is significantly higher than the prevalence of opium dependence in our country mentioned in official reports. Also some studies in our country have reported dependence rate between 2.1% to 20% in different social groups (Ahmadi et al., 2003). This may have some explanations; first; underestimation of opium dependence rates in the official reports which is probable. Second; opium dependence may be a risk factor or a predisposing factor for CAD or AMI. Finally; the most important factor seems to be the demographic specifications of our study group which is quite different from the whole population of our country and the study is performed only in men. Since this study was designed only for evaluation of effects of opium dependence on patients' outcome after AMI, we can not give comments regarding these items.

The mortality, complications and outcome of patients with prior history of CABG or PCI who experience AMI is influenced by several other variables; therefore we excluded such patients from our study.

In-hospital mortality in ODP was 4.4% and in non addicts was 3.4% which is close to mortality rates reported in Global Registry of Acute Coronary Events (GRACE) (Step et al., 2002) and the Euro Heart Survey of Acute Coronary Syndrome (EHS-ACS) (Hasdai et al., 2002).

The results of selective coronary angiography (SCA) in our patients were also similar to the above mentioned studies and a newer study comparing mortality rates in patients with ST elevation versus non-ST elevation acute MI (Terkelsen et al., 2005).There was no significant difference between ODP and non-dependents in angiographic results.

Table 1: Demographic Data and Risk Factors

	Opium dependents	Non-dependents	df	Statistic	P-Value
Age	55.87±9.7	59.50±12.42	158	t = -1.95	0.054
Diabetes	28.9%	29.6%	1	X^2 = 0.007	0.93
Hypertension	30%	29.2%	1	X^2 = 0.009	0.92
Cigarette smoking	84.4%	43.5%	1	X^2 = 21	0.002**
Triglyceride	142±8.8*	190±12.1*	153	t = -3.20	0.002**
Total cholesterol	190±7*	197±3.2*	157	t = -0.96	0.33
HDL	43±1.8*	42±1*	157	t = 0.15	0.91
LDL	118±6.3*	117±3.2*	154	t = 0.12	0.89

***Standard error mean **Significant**

Table 2: In-Hospital Findings

		Opium dependents	Non dependents	P-Value	df	Statistic
CK-MB		147±15.4*	130±8.2*	0.30	158	t = 1.03
Troponin-I		19±4.8*	14±2.2*	0.41	74	t = 0.82
EF		44%±1.9*	42%±1.1*	0.21	142	t = 1.2
In-hospital mortality		4.4%	3.4%	0.78	-	-
Duration of hospitalization (days)		11.3±1.4*	8.7±0.5*	0.03**	158	t = 1.68
MI location	**Inferior Inferolateral Posterior Inferior & RV**	33.3%	36%	0.75	1	X^2= 0.09
	Anterior Anteroseptal Anterolateral	48.9%	50.9%	0.82	1	X^2 = 0.05
	Non ST elevation	17.8%	13.2%	0.45	1	X^2 = 0.55

***Standard error mean **Significant**

ODP were cigarette smokers in 84.4% of cases but non dependents mentioned cigarette smoking (C.S) in 43.5%. This is not surprising because most of the ODP are smokers as well. We analyzed the probable effect of different CS frequency in the two groups and corrected it by Mantel–Haenszel statistics which revealed that the findings were still valid after correction for different levels of CS. Fortunately the prevalence of diabetes and hypertension was similar in the two groups so the results of our study were not confounded by these factors. Mortality during 6 months follow up was 2.7% versus 2.9% and the differences were not significant. Our results resembled other large study results. Peak enzyme levels (CK-MB and troponin I) which are reliable predictors of outcome and size of MI were compared in the two groups and were not significantly different.

Table 3: Follow-up Findings

	Opium dependents	Non dependents	P-Value	df	X^2
Readmission rate	14.3%	26.7%	0.13	1	2.2
CABG performed	33.3%	26.5%	0.39	1	0.72
PCI performed	11.1%	17%	0.35	1	1.1
Mortality in follow-up	2.7%	2.9%	0.94	-	-
Function Class	70.5%	59.6%	0.21	1	1.5
Symptom free or FC-1	22.7%	33%	0.20	1	1.5
FC-2 or FC-3	6.8%	7.3%	0.91	1	0.01
FC-4					

Study limitations

As discussed above, although we tried to identify the OAP precisely, there may still be some under estimations. The other limitation of our study is inclusion of male patients only. The prevalence of opium addiction among our female patients was low and since there are demographic differences as well as differences in risk factors and prognosis between men and women after AMI, we excluded female patients in order to get more reliable results with a smaller sample size. The next limitation of this study is silent MI which is supposed to be more frequent in OAP (because of narcotic effects and pain relief). Since this study was performed only on patients admitted with ACS (and the final diagnosis of AMI) we can not give advices on this item either.

Conclusion

In an unselected cohort of patients admitted with AMI; specifications, location, prognosis and complications of AMI were similar in ODP and non-dependents (both during their hospitalization, and after 6 months follow-up) except the longer duration of admission in OAP. Cigarette smoking was much more frequent in ODP while their Triglyceride level was significantly lower. Angiographic findings were also similar in the two groups. Therefore we did not find any protective effect of opium in ODP after AMI.

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Table 4: Angiographic Findings

	Opium dependents	Non dependents	p-Value	df	Static
Number of vessels	2.2±0.1*	2.3±0.09*	0.54	101	t= -0.6
LAD territory	82.8%	87.7%	0.51	1	X^2= 0.42
LCX territory	62.1%	60.3%	0.86	1	X^2= 0.02
RCA territory	58.6%	61.6%	0.77	1	X^2= 0.08

*** Standard error mean**

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