Opium dependency and in-hospital outcome of acute myocardial infarction

Hamid Reza Javadi[1], Abbas Allami[2], Navid Mohammadi[3], Rezvan Alauddin[4]

Abstract

  Background: Impact of substance abuse on outcome of hospitalized patients with acute myocardial infarction (MI) is a frequent question. Available studies show disagreements over its impact, thus we performed this study to find a clear answer.

  Methods: In a cross sectional study, 304 patients (include 152 consecutive opium dependents and equal number of independents) with acute MI admitted to coronary care units (CCU) in Bou-Ali Sina Hospital of Qazvin University of Medical Science were enrolled. Data on demographics (e.g. age, sex and education), identified MI risk factor (smoking and diabetes), clinical findings (e.g. Killip class and in-hospital mortality), ECG findings (e.g. localization of infarction and arrhythmia), echocardiographic examinations (e.g. ejection fraction and regional wall motion abnormality) and laboratory findings (lipid profile, glycemic situation) were gathered.

  Results: The mean age was 63.01 ± 12 years for opium users and 64.3 ± 10 for non-users. Educational level was higher in patients who used opium. No significant differences were found between opium users and non-users in rate of hypertension, diabetes mellitus, hyperlipidemia, and cigarette smoking. The mean duration of experienced chest pain in hospital stay was significantly higher in non-opium users compared to opium users (1.78 ± 0.63 vs.1.52 ± 0.54) ($p< 0.001$). Higher Killip class and arrhythmia have been identified as the most important independent predictors of early in-hospital mortality (in both groups).

  Conclusion: The higher Killip class and age identified as the most important independent predictors of early in-hospital mortality and addiction do not act as a major risk or protecting factor in this context. Nevertheless, we believe that a more comprehensive study with follow up of patients should be carried out for evaluation of opium addicted patients, their outcome after MI, and a better decision making for their treatment.

  Keywords: Opium dependence, Myocardial infarction, Outcome.

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Introduction

The 10th revision of the International Classification of Diseases and Health Problems (ICD-10) has defined the dependence syndrome as "being a cluster of physiological, behavioral, and cognitive phenomena in which use of a substance or a class of substances takes on a much higher priority for a given individual than other behaviors that once had greater value" (1). The main components of opioid dependence include: strong desire or sense of compulsion to take opioids; difficulties in controlling opioid-taking behavior; a withdrawal state when opioid use has ceased or been reduced; evidence of tolerance, such that increased doses are required to achieve effects originally produced by lower doses; progressive neglect of alternative pleasures or interests; and persistence with opioid use despite clear evidence of overtly harmful consequences (2). Opium abuse is a social prob-

1. Associate Professor, Department of Cardiology, Faculty of Medicine, Qazvin University of Medical Sciences, Qazvin, Iran.
javadi.hr@gmail.com
2. (**Corresponding author**) Associate Professor, Department of Infectious Diseases, Faculty of Medicine, Qazvin University of Medical Sciences, Qazvin, Iran. allami9@yahoo.com
3. Associate Professor, Department of Community Medicine, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran.
nvmohammadi@iums.ac.ir
4. General Practitioner, Qazvin University of Medical Sciences, Qazvin, Iran.

lem and it is estimated that prevalence of opium addiction has grown up by three folds for the past 20 years and now has been estimated about 2-2.8% according to official reports in Iranian (3) A rapid situational analysis in 2007 showed a prevalence of 3.32 for men and 0.55 for women (more than 15 years old). Estimated number of drug dependent people is about 1.2 million in Iran (4).

Myocardial Infarction (MI) is one of the most common diseases with high mortality and morbidity. There are well-known risk factors for coronary artery disease (CAD) including old age, male gender, cigarette smoking, hypertension, diabetes mellitus and hyperlipidemia (5). Theoretically, substance abuse could be a risk factor for the appearance of complication in ischemic heart disease (IHD) due to coincidence of smoking. On the other hand, presence of risk factors such as diabetes and history of heart disease, probably make people prone to opium use. Behind the great occurrence of opium addiction in Iran, especially among older age people, is a general traditional belief of inhibitory effects of opium on the progression of diabetes mellitus (DM), hypertension, and cardiovascular disease (6). Though, few studies have investigated the effect of opium addiction on CAD. Some studies reported harmful effects of opium on the cardiovascular system (7-9). Although intravenous morphine sulfate was recommended for the relief of chest pain or anxiety in patients with acute MI for many years, recent studies have indicated that use of morphine either alone or in combination with nitroglycerin has been associated with higher mortality for patients with non–ST-segment elevation acute coronary syndromes (10). Some other studies did not find any association between opium and CAD (11-13). Hence, we performed this study to compare in-hospital outcome and characteristics of MI patients in two groups of opium users and non-users.

Methods

In a cross sectional study, 304 patients (include 152 consecutive opium dependents and equal number of independents) with acute MI admitted from May 2010 to October 2011 to coronary care units (CCU) of Bou-Ali Sina Hospital of Qazvin University of Medical Science were enrolled. All the patients were chosen on a strict "first-come, first-chosen" basis and all eligible patients were included. Diagnosis of acute MI was established based on clinical presentation, serial electrocardiography (ECG) changes and cardiac enzyme analysis. For patients who fulfilled the criteria, essential data including demographics, clinical and paraclinical characteristics (i.e. information on cardiovascular risk factors such as hypertension, hyperlipidemia, diabetes mellitus, family history of CAD and smoking) were gathered. Hypertension was defined as the recent use of antihypertensive medication or a blood pressure more than 140/90 mmHg on two different occasions. Hyperlipidemia was defined by serum cholesterol level more than 200 mg/dl, serum triglyceride more than 200 mg/dl or use of antihyperlipidemia drugs. A diagnosis of diabetes mellitus history was made if the patient used insulin or oral hypoglycemic agents as well as evidence of previous fasting blood glucose ≥ 126 or postprandial blood sugar (BS) ≥ 200 mg/dl (14). Localization of infarction was defined according to criteria proposed by The New England Journal of Medicine (NEJM) (15). In all patients, Killip class (a system to risk stratification in patients with acute MI) was determined. All patients were examined at rest in supine and left lateral decubitus positions. Two-dimensional, M-mode and Doppler-echocardiographic examination were performed using a 2.5 MHZ phased array transducer. Echocardiographic examination was performed using standard views and techniques for detection of mitral regurgitation and regional wall motion abnormality (WMA). During CCU stay, all patients were subjected to check by 12-lead ECG (and posterior or right precordial

leads if necessary) in a daily basis to assess ST segment shifts, arrhythmia, MI site, and atrioventricular or interventricular block. Follow-up was carried out on entire duration of hospital stay.

Opium dependency was diagnosed by patients' self-report of daily consumption of at least 200 mg opium in different ways from oral to inhalation, and according to DSM-IV definition and criteria of substance dependency (16), and confirmed by interview. Type and duration of substance abuse were recorded through interview. Data was compared between the opium users and non-users by using chi-square and Fisher's exact tests for nominal and student's t-test for continuous variables. The Mann-Whitney U test was used to compare differences between two groups when the dependent variable is either ordinal or continuous, but not normally distributed. To assess effect of opium dependency on in-hospital mortality, we used a binary logistic regression model. Relationships were examined by Pearson Chi-Square test. SPSS for Windows, Version 19 (SPSS Inc., Chicago, IL) was used for statistical analyses. Values are expressed as mean ± SD, and $p < 0.05$ was considered statistically significant. The study received approval by ethical board of Qazvin University of Medical Sciences and all patients completed the informed consent form.

Results

All 304 participants were selected from patients admitted to CCU, with a mean age of 63.66±11.38 years (range: 40–89). Nearly 3/4 of the participants (74.1%, N = 301) were male (Table 1). The mean age was 63.01±12 years for opium users and 64.3± 10 years for non-users (p= 0.319). In our study, men had a higher rate of opium use [(53.81%; 95% CI: 47.26-60.23) versus (38.46%; 95% CI: 28.45-49.56), p = 0.02], while women had a higher rate of in-hospital mortality than men [(5.74%; 95% CI: 3.31-9.77) versus (9.86%; 95% CI: 4.86-18.98),], although this difference was not significant (p=0.271).

Overall length of hospital and CCU stays were 6.96±3.25 and 2.69±1.54 days. No significant difference regarding length of stay was observed between the two groups (p=NS). Educational attainment was higher in patients who used opium (p= 0.024). Table 1 shows the demographic and clinical characteristics of the two groups.

No significant differences were found between opium users and non-users considering hypertension, diabetes mellitus, and hyperlipidemia (Table 2). The mean duration of experienced chest pain in hospital stay was higher in non-opium users compared to opium users (1.78± 0.63 vs.1.52±0.54), and the difference was statistically significant (p< 0.001).

Although total number of blocks were not different in two groups, opium non-users more frequently had left bundle branch block (LBBB). Localization of acute MI and Killip class at admission were not different between the two groups. Overall in-hospital mortality was 7.8% among opium users and 6.3% among other group (p= 0.6). In our study, opium addiction did not show any impact on arrhythmias development, ejection fraction and worsening of wall motion. In binary logistic regression model (to assess effect of opium dependency on in-hospital mortality) included variables were opium dependency, age, sex, Killip class, hypertension, diabetes, MI Site, arrhythmia as covariate. After an enter method analysis, Killip class and age remained in the model (Table 3).

Discussion

In our study, we did not find any difference in the prevalence of risk factors of CAD (e.g. diabetes mellitus, hypertension, and lipid profile) between the two groups of opium users and non-users. During recent years in Iran, most studies conducted on this context did not reveal beneficial effect of opium consumption on DM, hyperlipidemia and CAD (7, 11, 17-18). A study for evaluation of opium effect on lipid profile revealed that opium did not have any impact on triglyceride, low density lipopro-

Table 1. The frequency of demographic variables of patients according to opium usage

Variable		Group		
		Opium Users (%)	Opium Non-users (%)	Chi² P Value
Sex	Male	120 (80.0)	103 (68.2)	0.020*
	Female	30 (20.0)	48 (31.8)	
Education	Not educated	14 (10.7)	33 (23.6)	0.024*
	Primary school	53 (40.5)	55 (39.3)	
	High school	46 (35.1)	41 (29.3)	
	Academic	18 (13.7)	11 (7.9)	
Smoking status	Active Smoker	14 (9.9)	23 (16.4)	0.225
	quitter	31 (21.8)	32 (22.9)	
	Non Smoker	97 (68.3)	85 (60.7)	
History of MI	No	136 (89.5)	141 (94.0)	0.154
	Yes	16 (10.5)	9 (6.0)	
History of CABG	No	140 (94.0)	138 (92.6)	0.643
	Yes	9 (6.0)	11 (7.4)	
History of IHD	No	114 (76.5)	105 (69.5)	0.174
	Yes	35 (23.5)	46 (30.5)	
Hypertension	No	78 (51.3)	80 (52.6)	0.053
	Yes	74 (48.7)	72 (47.4)	
CRF	No	149 (99.3)	147 (98.0)	0.314
	Yes	1 (0.7)	3 (2.0)	
Diabetes mellitus	No	97 (66.0)	112 (74.7)	0.101
	Yes	50 (34.0)	38 (25.3)	
FBS	Normal	107 (70.4)	114 (75.0)	0.812
	Up	45 (29.6)	38 (25.0)	
BS in admission time	Normal	108 (71.1)	107 (70.9)	0.001
	Up	44 (28.9)	44 (29.1)	
cholesterol	Normal	138 (91.4)	144 (94.7)	0.252
	Up	13 (8.6)	8 (5.3)	
triglyceride	Normal	103 (67.8)	112 (74.2)	0.219
	Up	49 (32.2)	39 (25.8)	
Mitral regurgitation	No	86 (57.7)	80 (53.0)	0.409
	Yes	63 (42.3)	71 (47.0)	
WMA	No	99 (65.6)	87 (57.2)	0.137
	Yes	52 (34.4)	65 (42.8)	
Kind of Block	No Block	148 97.3	142 93.4	0.026*
	LBBB	0 0	7 4.6	
	RBBB	4 2.63	3 1.9	
Arrhythmia	No Arrhythmia	134 88.1	136 89.4	0.757
	VF	11 7.2	8 5.2	
	VT	7 4.6	8 5.2	
Killip class	1	79 (53.4)	93 (61.2)	0.387
	2	65 (43.9)	56 (36.8)	
	3	4 (2.7)	3 (2.0)	
MI Site	Inferior Group	63 (41.4)	66 (43.4)	0.728
	Anterior Group	89 (58.6)	86 (56.6)	
Mortality	Live	141 (92.8)	143 (94.1)	0.644
	Death	11 (7.2)	9 (5.9)	

Abbreviations: MI: Myocardial Infarction, CABG: Coronary artery bypass surgery, IHD: Ischemic heart disease, CRF: Chronic Renal Failure, WMA: wall motion abnormality, LBBB: Left bundle branch block, RBBB: Right bundle branch block, VF: ventricular fibrillation, VT: ventricular tachycardia. * $p < 0.05$. Data are number (%).

tein (LDL), and high density lipoprotein (HDL), but total cholesterol levels were lower in opium ad dicted patients (introduce as a known side effect of opium). Nevertheless, researchers' findings were not sufficient to make an exact judgment about the direct effect of opium on serum lipids because of many confounding factors on lipid profile such as dietary habits (19,20). Also, these data indicated that the belief of protective effect of opiates on cardiovascular disease is used to justify substance abuse.

In our study, opioids users and smokers had higher levels of education. As a matter of fact, the unprecedented growth in use of

Table 2. Baseline characteristics of two study groups

Variable	Mean (SD)		p
	Opium users	Opium non-users	
Age (years)	63.01 (12.20)	64.31 (10.49)	0.319
FBS (mg/dl)	121.34 (55.29)	118.71 (47.85)	0.658
BS in admission time (mg/dl)	175.20 (84.06)	176.42 (83.58)	0.899
Cholesterol (mg/dl)	166.07 (48.40)	157.70 (42.63)	0.111
LDL (mg/dl)	106.93 (27.93)	105.43 (25.02)	0.621
HDL (mg/dl)	37.26 (8.19)	37.15 (7.71)	0.904
TG (mg/dl)	151.28 (73.79)	151.41 (89.61)	0.989
Duration of experienced chest pain (day)	1.52 (0.54)	1.78 (0.63)	0.000[*,1]
hospital stay(day)	7.12 (3.42)	6.80 (3.06)	0.397
CCU stay (day)	2.86 (1.64)	2.53 (1.42)	0.061

Abbreviations: FBS: Fasting blood sugar, BS: blood sugar, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, TG: Triglyceride, CCU: coronary care unit. * $p < 0.05$. Data are mean ± SD, 1::the Mann-Whitney U test was used to compare differences

Table 3. Independent variables associated with in-hospital mortality (Method = Enter)

		p	Exp(B)	95% C.I.for EXP(B)	
				Lower	Lower
Step 1[a]	age	0.034*	1.077	1.006	1.154
	sex	0.245	3.421	0.430	27.205
	hypertension	0.978	1.022	0.217	4.815
	Killip class	0.172			
	Killip class (1)	0.063	0.094	0.008	1.135
	Killip class (2)	0.106	0.149	0.015	1.494
	smoking status	0.037	0.114	0.015	0.876
	arrhythmia	0.000*			
	arrhythmia (1)	0.002*	0.053	0.008	0.334
	arrhythmia (2)	0.097	5.585	0.731	42.663
	Myocardial Infarction site	0.810	1.194	0.280	5.086
	diabetes	0.468	1.718	0.399	7.408
	Constant	0.104	0.007		

a; Variable(s) entered on step 1: age, sex, hypertension, diabetes mellitus, Killip class, smoking status, arrhythmia, MI Site. b: * $p < 0.05$

narcotics among educated people is one of the major concerns of many social pathologists in Iran (21-24). In prevention strategies, it is suggested to target messages and attitude changes on addiction and its adverse effects, especially to the older people with higher levels of education. The association of education and opium use should be studied with a representative sample. In our study, in-hospital mortality was similar among opium-users and non-users. Similarly, in a recent cohort of patients who were admitted with AMI, there was no significant difference in specifications, short term outcome and prognosis of AMI between opium-users and non-users except for duration of hospitalization (9). In our patients, the average time of experienced chest pain in hospital was higher in non-opium users while CCU stay was significantly shorter in opium users. This dif-

ference may partly be due to self-medication or more request of opium in user group. Results of our study indicate that opium addiction in hospitalized patients does not have an important impact on development of arrhythmia, ejection fraction and WMA after MI.

From the current study strengths are prospective design, availability of data to adjust for confounders, and multiple outcome measurement of acute myocardial infarction. These outcomes include clinical findings (e.g. Killip class, in-hospital mortality), ECG findings (e.g. localization of infarction, arrhythmia), echocardiographic examinations (e.g. ejection fraction, WMA) and laboratory findings (lipid profile, glycemic situation). Our study limitations included inaccurate amount of causes and route of abuse, the study observational design and therefore the potential for residual

confounding, a possibility of measurement bias in determining the actual amount and route of opium consumption because these data were collected solely based on self-reporting.

Conclusion

In our study, higher Killip class and age identified as the most important independent predictors of early in-hospital mortality and addiction do not act as a major risk or protecting factor in this context. Nevertheless, we believe that a more comprehensive study with follow-up should be carried out for evaluation of opium addicted patients, their outcome after MI, and a better decision making for their treatment.

Conflict of interest

The authors declared no competing interests.

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