Original Article

Comparing cardiovascular factors in opium abusers and non-users candidate for coronary artery bypass graft surgery

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Abstract

Background: In some opinions, opium consumption has traditionally been considered to be a means to lower blood lipids and to put off heart diseases. In this study, the relationship between opium consumption and risk factors of coronary artery diseases, hemodynamic factors and cardiac related functions before and after surgery was evaluated.

Materials and Methods: In a cross-sectional study 325 patient's candidate for elective coronary artery bypass grafting were enrolled in a period of 6 months. Opium addicted patients were recognized based on taking history from the patients by an anaesthesiologist. Serum lipid profile was determined at the beginning of the study. Frequency and distribution of coronary artery diseases were assessed according to the pre-operative coronary angiography.

Results: From 325 patients, 117 patients were opium abusers and 208 patients were not. Mean duration of opium abuse was 12.6 ± 7.7 years. Mean total serum cholesterol levels were not significantly different in abusers and non-users patients (185 ± 47 vs. 190 ± 49, $P > 0.05$). Mean level of low-density lipoprotein cholesterol was significantly higher in addicted group (121 ± 27 vs. 81 ± 22, $P < 0.05$). Mean triglyceride level was also higher in addicted patients (203 ± 114 vs. 162 ± 98, $P < 0.05$). The prevalence of diabetes and glucose levels was considerably lower in opium addicted cases. Mean body mass index was also lower in addicted patients significantly (25.3 ± 3.7 vs. 27.5 ± 4.1, $P < 0.05$).

Conclusion: There may be a relationship between opium abuse and aggravating lipid profile and hypercholesterolemia and coronary artery disease.

Key Words: Coronary disease, opium/adverse effects, risk factors

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INTRODUCTION

Opium as one of the oldest drugs in the community has been used to create euphoria, reduce pain and treat diseases. Opium is the crude substance derived from the opium poppy; it has been used by people since as early as 4000 Before Christ. Opium consumption is very effective for the treatment of acute and chronic

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pain, but also has the potential to be abused. Opium abuse is the most type of substance abuse in Iran.[1] The major effects of opium are on the central and autonomic nervous system and the bowels, whereas it also influences other organ systems, including the respiratory and cardiovascular systems.[2]

In many Asian and Middle East societies like Iran, the popular use of opium as a treatment for cardiovascular problems is discussed. However, few studies exist to prove or disprove this belief.[3]

Studies on cardiovascular effects in addicts in the community have expressed different opinions.

An extensive survey by Schultz and Gross in the animal models found many different opioid receptors in the heart. They showed opioid drugs such as morphine had cardioprotective effects. These drugs not only decrease the pain due to myocardial infarction (MI) but also minimize the infarct size.[4]

On the other hand, some of the studies suggested that the drug use could be considered as a risk factor for cardiovascular disease such as coronary artery disease, acute MI, sudden death, aortic aneurysm and peripheral vascular diseases.[5,6]

Misra *et al*. in their study have reported chronic consumption of opium as a strong risk factor in cardiovascular disease in the first 6 months after coronary artery bypass surgery.[7]

Due to the increasing growth of opiate abuse and addiction to these substances at the community, understanding the effects of opium in various diseases, including heart disease is important. Meanwhile, there was no comprehensive study about the impact of opium consumption on hemodynamic factors after coronary bypass surgery. Therefore, a study on opium effects on factors influencing cardiovascular problems in patients referred for coronary artery bypass surgery was performed.

MATERIALS AND METHODS

This cross-sectional study was performed on 325 patients having elective coronary artery bypass surgery in surgical ward of Chamran Hospital and Heart Center in Isfahan. Inclusion criteria included: Age of 20-80 years, no history of mental illness, serum creatinine lower than 1.5 mg/dL, forced expiratory volume in 1 s above 80% of predicted in recent spirometry. Exclusion criteria included: No consent to participate in the study and grossly psychological disorders. Data collection device was researcher made a check list.

All patients were enrolled after obtaining institutional approval and informed consent. In the day before surgery, patients visited by the anesthesiologist and the opium consumers were identified among the patients based on patient's history of opium use.

Patients with a history of opium abuse were added to study after matching with Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV-TR criteria for opium addiction.[8] Systolic, diastolic and mean arterial blood pressure and heart rate were measured by the physician and were recorded in the check-list. Patient's electrocardiogram (ECG) changes were surveyed before and after surgery. Information, including demographic factors, duration of opium use, history of heart disease (previous acute MI, unstable angina and stable angina), cardiac disease (valvular insufficiency and unstable angina), other risk factors affecting heart disease (lipid profile, diabetes, body mass index, smoking and hypertension, systolic blood pressure (SBP) above 140 mmHg or history of antihypertensive drugs) was assessed.

Patients were operated according to the protocol of cardiac surgery and anesthesia professionals for coronary artery bypass graft surgery. All patients were studied with similar conditions under the pre-operative premedication with 10 mg morphine, 25 mg promethazine intramuscular and anesthetized with sodium thiopental induction with a dose of 5 mg/kg, pancronium with a dose of 1/0 mg/kg, fentanyl with an intravenous dose of 4 μg/kg and lidocain with 1.5 mg/kg intravenously. The administration of anesthesia was done by 0.5-1.5 minimum alveolar concentration isoflurane and oxygen with 100% concentration.

Patients underwent on pump coronary artery bypass graft surgery with sternotomy and mild hypothermia during cardiopulmonary bypass time. At least one major artery (internal mammary artery or radial artery) and also greater saphenous vein grafts were used for bypass grafts. During the surgery (on oxygenator pump) and immediately after surgery in the recovery room and also in the first and 2nd days after surgery, hemodynamic factors, including systolic, diastolic, mean arterial blood pressure and heart rate of patients were measured. We also recorded duration of anesthesia and surgery. The blood pressures were measured every 6 h after surgery and mean values were recorded in the checklist. Furthermore on the 5th day after surgery ECG and evaluation of ejection fraction (EF) with echocardiography after surgery were taken. We also recorded duration of mechanical ventilation (time between intensive care unit [ICU] arrival until discontinuation of ventilator) and ICU stay.

The data collected and analyzed using statistical software Predictive Analytics SoftWare (PASW Statistics) version 18.0. *t*-test was used for means comparison and logistic regression was used for determine risk factors in the cardiac problems. To determine the relationship between cardiovascular and time spent on opium consumption in terms of tests, Chi-Square, ANOVA and Pearson and Spearman correlation co-efficient was used.

RESULTS

In this study, 325 patients having elective coronary artery bypass surgery and with inclusion criteria, were evaluated. The mean age of patients were 58.76 years (standard deviation 9.02 years, age range 29-77 years) included 256 men (78.8%) and 69 women (21.2%). From total patients 117 cases (36%) had a history of opium or juice of opium consumption and were placed in group of opium abusers. While 208 patients had not history of opium use, were placed in group of non-users. Men comprised 96.58% of the addicts in the age range 39-75 years. Non-addicted individuals were in the age range 29-77 years.

The average age of non-addict patients was higher than addicts significantly (56.5 ± 9.6 years in the addict group vs. 58.8 ± 9.0 years in the non-addict group) ($P = 0.001$). The average years of drug use in opium abuser patients were 12.6 ± 7.7 years.

To determine the correlation between quantitative variables with duration of opium consumption of Pearson were used Spearman correlation and for qualitative variables used ANOVA.

Other results are presented in Tables 1-5 and Figures 1 and 2 below.

DISCUSSION

The prevalence of opium addiction in coronary artery bypass grafting (CABG) patients is relatively high but studies about cardiovascular effects of opium in patients undergoing coronary artery bypass surgery are not noticeable. Most of these studies have been done in Iran and it shows the importance of drug abuse problem, especially about opium, in Iran.

In a study by Kouros *et al.* in the city of Kerman from Iran, it was shown that fasting blood sugar (FBS) levels were significantly lower in opium addicts compared with the control group.[9]

In our study, there was a significant difference in the history of diabetes and blood sugar levels before and after the operation between opium users and non-users and number of diabetic patients were lower in opium abusers group. Also in opium abusers, blood sugar levels before and after the surgery, were clearly lower than non-users. These results may reflect the fact that opium has a positive effect in lowering blood sugar.

Shirani *et al.* concluded that the prevalence of diabetes mellitus and hypertension in opium users was clearly lower than those non users. As well fasting blood glucose and Hemoglobin A1c (HbA1c) levels in opium users were significantly lower. However, there was no significant difference in lipid profile in both groups.[10] Karam *et al.* have reported that HbA1c in addicted men was higher than the control group, but FBS levels were not significantly different between two groups. High-density lipoprotein cholesterol (HDL-C) levels also decreased significantly in addict men.[11] The reasons for the differences between our study and the Asadi Karam's and Katebi's studies results can be low sample sizes in these two studies. But in Shirani's study with high sample size, the results are consistent with our study results.

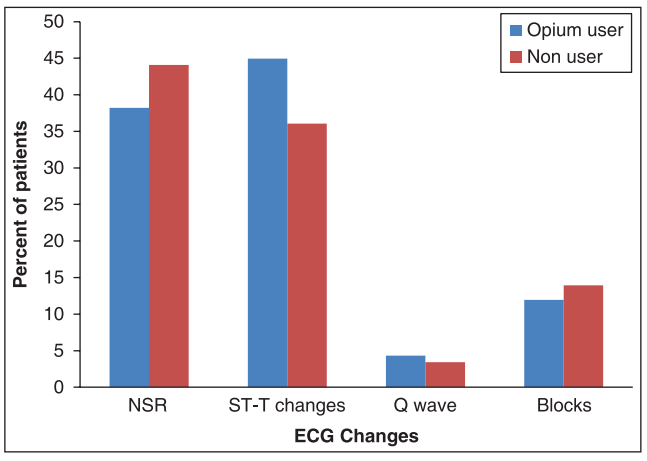

Figure 1: Electrocardiogram changes before surgery in opium abusers and non-users ($P < 0.01$)

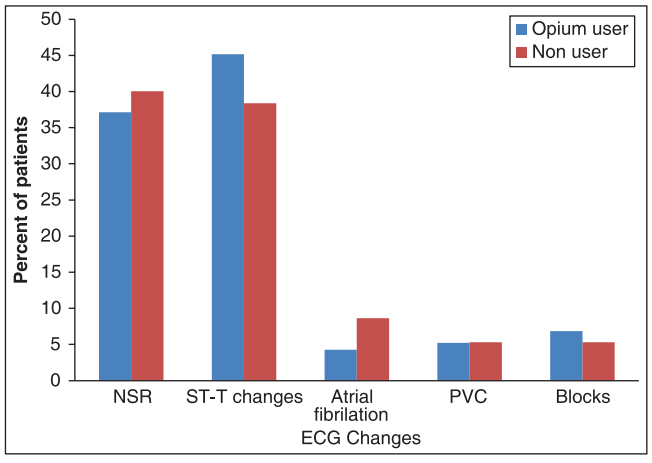

Figure 2: Electrocardiogram changes after surgery in opium abusers and non-users ($P < 0.01$)

Table 1: Risk factors affecting the cardiovascular system in opium abusers and non-users

Variable	Group		*P* value
	Non user *N* = 208	Opium abuser *N* = 117	
Heart diseases			
Hx of CAD	195 (97.0)	114 (97.4)	1.000
Hx of stable angina	34 (16.9)	16 (13.7)	0.444
Hxof unstable angina	146 (72.6)	92 (78.6)	0.235
Hx of MI	92 (45.8)	54 (46.2)	0.947
Hx of valvular heart disease	24 (11.9)	2 (1.7)	0.001
DM			
Hx of DM	74 (36.5)	23 (20.2)	0.003
Pre-operative FBS (mg/dL)	140.5±67.0	111.6±35.4	<0.001
Post-operative FBS	189.1±58.3	167.0±49.7	<0.001
HTN			
Hx of HTN	69 (34.3)	24 (21.1)	0.013
Pre-operative mean SBP (mmHg)	119.5±27.6	121.5±23.4	0.521
Pre-operative mean DBP	79.9±8.5	77.8±11.0	0.089
Duration of HTN (years) in hypertensive patients	3.5±6.1	1.8±3.9	0.005
Hyperlipidemia			
Hx of hyperlipidemia	84 (41.4)	62 (55.9)	0.014
Pre-operative mean total cholesterol (mg/dL)	190±49	185±47	0.344
Pre-operative mean LDL	81±22	121±27	<0.001
Pre-operative mean triglyceride	162±98	203±114	0.003
Duration of hyperlipidemia (years)	3.1±4.1	3.0±3.4	0.702
Respiratory disease			
Hx of COPD	11 (9.6)	26 (12.9)	0.036
Duration of respiratory disease (years)	4±1.2	8±2.7	0.021
Smoking			
Hx of smoking	70 (33.7)	80 (69.6)	<0.001
Duration of smoking (years)	9.7±15.1	17.4±14.5	<0.001
Pack. year	9.1±14.5	17.1±15.8	<0.001
Obesity			
BMI (kg/m^2)	27.5±4.1	25.3±3.7	<0.001

Data are presented as number (%) or mean ± SD, Hx: History, CAD: Coronary artery disease, MI: Myocardial infarction, HTN: Hypertension, LDL: Low density lipoprotein, COPD: Chronic obstructive pulmonary disease, BMI: Body mass index, SD: Standard deviation, FBS: Fasting blood sugar, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, DM: Diabetes mellitus

Table 2: Peri-operative hemodynamic parameters in two groups of patients

Time of measurement	Variable	Group		*P* value
		Non user *N* = 208	Opium abuser *N* = 117	
Before operation	SBP (mmHg)	126.9±16.2	127.3±20.2	0.847
	DBP	80.7±10.9	79.3±10.4	0.277
	MBP	96.1±12.66	95.5±13.6	0.250
	HR (beat/min)	81.2±8	80.2±6.8	0.312
On pump	MBP	74.3±11.8	76.7±11.9	0.104
After operation in recovery	SBP	121.3±18.3	118.4±20.4	0.210
	DBP	67±11.2	67.8±12.1	0.579
	MBP	82.6±13.3	82.9±10.8	0.869
	HR	97.6±14.3	95.2±14.7	0.167
First day after operation	SBP	123.2±73.2	119.2±17.9	0.587
	DBP	66.0±12.1	70.7±11.3	0.001
	MBP	79.6±13.1	81.4±12.2	0.262
	HR	99.9±15.1	104.8±13.2	0.008
Second day after operation	SBP	125.0±18.5	128.7±15.4	0.073
	DBP	68.5±11.9	75.4±8.5	<0.001
	MBP	86.6±13.3	92.6±10.3	0.035
	HR	91.5±14.5	89.8±13.9	0.320
Surgery duration (min)		262.3±51.2	250.2±44.6	0.036
Cardiopulmonary bypass duration (min)		96.3±31.7	93.3±25.8	0.407
Mechanical ventilation duration after surgery (min)		361.2±112.6	331.6±105.2	0.023
Length of ICU stay (h)		52.2±15.3	53.1±14.3	0.865

Data are presented as mean ± SD, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MBP: Mean blood pressure, HR: Heart rate, SD: Standard deviation, ICU: Intensive care unit

Table 3: Number and type of vessels involved in the pre-operative angiography in two groups

Variable	Group		*P* value
	Non user	Opium abuser	
Number of vessels involved in the pre-operative angiography	3.2±0.8	3.0±0.7	0.049
LAD	161 (88.0)	96 (88.9)	0.815
D1	82 (44.8)	31 (28.7)	0.006
D2	12 (6.6)	4 (3.7)	0.302
Cx	96 (52.5)	58 (53.7)	0.837
RCA	109 (59.6)	61 (56.5)	0.606
OM1	86 (47.0)	44 (40.7)	0.300
OM2	15 (7.9)	17 (14.9)	0.056
OM3	0 (0.0)	9 (7.9)	<0.001
PDA	25 (13.7)	7 (6.5)	0.059

Data are presented as number (%), LAD: Left anterior descending, D: Diagonal, Cx: Circumflex, RCA: Right coronary artery, OM: Obtuse marginal, PDA: Posterior descending artery

In some previous, studies also surveyed the effects of opiates (opium) on atherosclerosis making factors such as a lipid profile. Mohammadi *et al*. in a study on animal models reported that levels of total cholesterol, triglycerides, low-density lipoprotein (LDL) and HDL were significantly different between non-addict rabbits and addict rabbits. Furthermore, production of ateromatous plaques was higher in addict rabbits significantly. They reported that the opium consumption can have aggravating effects in atherosclerosis formation related with hypercholesterolemia, mainly affecting lipid profile.[12] The studies of Davoodi *et al*. in 2005,[13] Sadeghian *et al*. in 2007,[14] Azimzadeh-Sarwar *et al*. in 2005,[15] and Spinella in 2001[16] also expressed that opium consumption is effective on making atheromatous plaques.

In the present study, the mean total serum cholesterol levels was not significantly different in abusers and non-users but the mean level of LDL cholesterol and mean triglyceride levels were significantly higher

Table 4: Number and type of vessel grafts in two groups

Variable	Group		*P* value
	Non user	Opium abuser	
Number of grafts	3.9±3.9	3.3±0.7	0.147
LAD	192 (97.0)	113 (100)	0.090
D1	139 (70.2)	69 (61.1)	0.100
D2	5 (2.5)	4 (3.5)	0.728
Cx	3 (1.5)	0 (0.0)	0.556
RCA	72 (36.4)	23 (20.4)	0.003
OM1	160 (80.8)	84 (74.3)	0.182
OM2	24 (12.1)	11 (9.7)	0.522
OM3	2 (1.0)	11 (9.7)	<0.001
PDA	81 (40.9)	60 (53.1)	0.038

Data are presented as number (%), LAD: Left anterior descending, D: Diagonal, Cx: Circumflex, RCA: Right coronary artery, OM: Obtuse marginal, PDA: Posterior descending artery

Table 5: Correlation between quantitative variables with duration of opium consumption

Variable	Number	The correlation co-efficient	*P* value
Post-operative SBP	113	0.217	0.021
Post-operative DBP	113	−0.053	0.577
Post-operative MBP	113	0.045	0.652
Post-operative HR	113	−0.01	0.913
MBP on pump	101	0.215	0.031
Pre-operative ejection fraction	113	−0.132	0.162
Post-operative ejection fraction	105	−0.136	0.166
Ejection fraction changes	105	−0.051	0.606
Number of stenotic vessels in angiography before surgery	108	−0.169	0.081
Number of grafts	113	0.154	0.103

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MBP: Mean blood pressure, HR: Heart rate

in addicted group. Also 55.9% of opium abusers and 41.4% of non-users were hyperlipidemic in our study. It could show the adverse effect of opium abuse on blood lipid profile in patients.

In Asgary study, it was found that a significant difference in HbA1c, C-reactive protein, Factor VII, fibrinogen, lipoprotein A and apo lipoprotein B (apoB) existed between two groups. In their study, HDL-C and apoA levels were significantly lower but other factors were higher in addict group.[17] The results of these studies about the adverse effects of opium consumption on blood lipid profile and atherosclerosis is consistent with our study.

However, studies of Molina *et al.*,[18] Ipp *et al.*,[19] Kamei *et al.*,[20] Hashiguchiy *et al.*[21] and Barham and Trinder[22] reported that the derivatives of opium, significantly reduced levels of blood sugar and Lipid profile test in animal models.

Effect of morphine and its derivatives on the cardiovascular system is controversial.[15] The study of Azimzadeh-Sarwar *et al.*, showed no significant relationship between opium consumption and increase the risk of MI. Furthermore, Sadeghian *et al.* found no significant relationship between opium dependence and other cardiac and non-cardiac in hospital complications following CABG in patients with opium dependence.[23] Chen *et al.* in their study have reported that level of beta-endorphin (endogenous opioid peptide) after MI was elevated. They explained that this peptide had an important role in ischemic heart disease pathophysiology.[24]

In the present study, ischemic changes such as ST-T changes and present of Q-wave were higher in opium abusers. High prevalence of ischemic changes in the ECG of opium abuser could be attributed to the effects of opium in removing of chest pain and high prevalence of silent MI in these patients.

In Afraz study, the prevalence of non-silent MI in opium abusers was 17.5% compared with 6.5% in non-users. This study reported that opium addiction could not have an association with silent MI.[25] In the study of Sadr Bafghi *et al.*, the prevalence of opium addiction in patients with MI was 19% compared with 2-2.8% in the general population. Mortality rates in addicts were 18.6% compared to 6.2% in the other patients. This study discussed that opium addiction as a risk factor for coronary artery disease.[26] In some studies, the cardiovascular effects of opioids has been attributed to its effects on pituitary hormones. It has been shown that increase testosterone levels in plasma can be associated with increased risk of coronary disease in opium addicts.[26-29]

In our study, 36% of patients had a history of opium consumption; the prevalence rate is higher than the previous studies. It can be due to ignoring DSM-IV-TR criteria for diagnosis of opium addiction in those studies.

In the present study, post-operative hemodynamic factors in opium abusers and non-users were different. There were significant difference in diastolic blood pressure (DBP) and heart rate after the surgery between two groups. It shows that the consumption of opium could have a greater effect on DBP and heart rate and has less on SBP after CABG. The study also induces the hypothesis that opiate drugs (opium and juice) with their effect on the sympathetic system can block hemodynamic response. But more studies are needed to prove this hypothesis.

A study of Davoodi *et al.* on 160 males hospitalized in coronary care unit with a diagnosis of MI showed that 45 (28.1%) of patients were addicted to opium and they

considerably had lower EF, wider area of MI, more need for invasive procedures such as angiography, higher cardiac enzyme levels and lower activity during the 6 months follow-up after surgery.[13]

In our study, cardiac EF in 5th day after surgery was significantly different between opium users and non-users. Also changes in ECG after surgery were more prevalent in addicts. However, the incidence of postoperative atrial fibrillation (AF) in opium abusers was less. In the study of Maisel *et al*.,[30] and Villareal *et al*.,[31] the prevalence of AF was between 15 and 40% and it was the most common arrhythmia after CABG. Old age and problems in structure of atria are two important risk factors of this type of arrhythmia.[32,33]

In our study, the number of vessels involved in pre surgical angiography was different between two groups, but there was no significant difference in type of coronary arteries.

As it was mentioned previously, it is still not clearly understood the protective effect of opium consumption on the heart. These differences may be due to the differences in the compounds found in opium. As we know, opium on the market is not a pure substance and especially in Iran, has a variety of impurities such as lead.[34] This could reflect the differences in the results of performed studies on opium in different parts of the world. Therefore, we recommended further studies to be performed on the pattern of drug abuse in patients with heart disease, compounds and impurities in drugs, especially opium in Iran. Given the high prevalence of opium use in patients undergoing coronary artery bypass in the country, we also recommend further studies performed on the impact of opium consumption and complications after coronary artery bypass surgery in patients with the history of opium abuse.

Limitations of our study were lack of co-operation of some patients for giving history of opium abuse and having missing data because of the large number of items from the check-list.

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