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Can opium abuse be a risk factor for carotid stenosis in patients who are candidates for coronary artery bypass grafting?

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Abstract

Background: *Over the centuries, opium has been the most frequent substance abused in the Middle East. There are many controversial aspects about the effects of opioids on the atherosclerosis process, which is still unclear.*

Methods: *All patients who were candidates for coronary artery bypass graft in Tehran Heart Center were registered and evaluated for risk factors such as diabetes mellitus, hypertension, smoking status and duration, opium abuse, involved coronary arteries and left main branch lesion > 50%, carotid stenosis ≥ 70%.*

Results: *A total of 1,339 patients were enrolled in the study, of whom 400 (29.9%) were female and the other 939 (70.1%) male. Female patients were omitted from analysis due to the low numbers of female opium addicts. Our study revealed that in the addicted population, the risk of diabetes and hypertension was lower than in the non-addicted group ($p < 0.05$ for each variable) and fasting blood sugar tended to be less in addicted ones, but the number of involved coronary arteries, left main stenosis > 50% and extent of carotid stenosis was not significantly different between the two groups.*

Conclusions: *Our investigations demonstrate that opium is not cardioprotective, as has been claimed by some previous studies, and does not even decelerate atherosclerosis of carotid arteries in opium-addicted patients, but more evidence is still needed to completely prove the case.* (Cardiol J 2010; 17, 3: 254–258)

Key words: opium abuse, carotid stenosis, atherosclerosis

Introduction

Opium dependence is one of the major health problems in the developing countries of the Middle East, and particularly our country Iran. Over many decades, opium has been the substance most frequently abused in Iran. Opium, in contrast to pure opioid drugs, is a complex and variable mixture of substances. It is reported that between 1 and 30 g of opium may be used by an addict, either orally or inhaled.

More than 180 million people around the world have tried illegal drugs at least once, of whom 13.5 million are opium-dependent [1]. The effects of opium are essentially those of morphine. The major effects of opium are on the central and autonomic nervous system and the bowels, while it also influences other organ systems including the respira-

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tory and cardiovascular systems [1]. Orthostatic hypotension has been reported after opium consumption. Several investigations about the effects of opioid peptides on the cardiovascular system have also been performed. They show that hypotension, bradycardia, peripheral vasodilatation (or sometimes hypotension and tachycardia) are among the cardiovascular effects of opioids [2, 3] which proceed mainly through their effects on K and Ca channels as well as adenylate cyclase [4, 5]. It is estimated that the prevalence of opium addiction has grown three fold in the past 20 years in Iran; now it is thought to be 2–2.8%, according to official figures [6–8]. Numerous studies have shown the effects of opium on the cardiovascular system, but few studies have focused on its distinct effect on carotid artery stenosis or the number of carotid plaques. A study of Iranian drivers showed significantly lower cholesterol levels, as well as lower diastolic blood pressure, which in combination with other effects of opium can influence the outcome of cardiovascular disease [9–12].

Considering this data, we decided to perform this study to evaluate the probable effects of opium on the vascular system. The aim of the present study was to determine opium consumption as a risk factor for carotid artery stenosis and its influence on the number of atheromatous plaques, and to compare the characteristics of opium addicts to non-addicts.

Methods

From January 2006 to January 2007, all patients who were candidates for coronary artery bypass graft (CABG) in Tehran Heart Center were registered. Patients were examined by hospital cardiologists and heart surgeons, and a complete history was taken to reveal cardiovascular risk factors such as diabetes mellitus, hypertension, smoking status and duration. Patients who fulfilled the DSM-IV-TR criteria for substance (opium) dependence (by smoking or oral intake) were enrolled as opium dependent patients. Meanwhile, the data from patients' coronary angiography report (the number of involved coronary arteries and left main branch lesion > 50%) were also added to our data. All CABG candidates underwent a Doppler sonography of both carotid arteries to detect any atheromatous plaque and stenosis prior to surgery. This completed the set of our data. The definitions of cardiovascular risk factors were those set out by the Society of Thoracic Surgeons of America. Degrees to define carotid stenosis were based on the NASCET criteria. Due to the very low percentage of opium dependence in our female patients, they were excluded from the study except in primary analysis about demographic report and frequency of risk factors.

Our study was approved by the medical ethics committee of the Hospital and University of Tehran, and the Faculty of Medicine.

Statistical analysis

For continuous variables including age and consumption of opium per day, the values are expressed as mean ± standard deviation. For discrete variables, values are expressed as percentages. For continuous variables t-test was used to access the difference between the two groups. For qualitative variables, chi- square test was used. For small sizes we used Fisher's exact test. All statistical analyses were performed using SPSS for Windows ver. 13.

Results

A total of 1,339 patients were enrolled in this study of whom 400 (29.9%) were female and 939 (70.1%) male. The characteristics of risk factors in our patients are shown in Table 1.

The next step was to analyze the probable differences between addicts and non-addicts. Demographic data revealed that there was a significant difference ($p < 0.05$) between the mean age of opium dependent and non-dependent patients (55.8 ± 9.2 *vs* 59.2 ± 9.5). As we mentioned earlier in Table 1, there was a marked difference between addicted male and female patients. Male patients tended to use opioids more than female ones ($p < 0.05$). Comparing body mass index between the two groups, we realized that opium addicts were significantly slimmer than non-addicts (26.4 ± 3.45 *vs* 59.2 ± 9.5).

In the addict group, the incidence of diabetes and hypertension was markedly less than in the non- addicted group. Involved coronary arteries and left main branch stenosis > 50% was not significant between two groups. Post-operative mortality did not show significant differences between the two groups. The number of involved coronary arteries, left main stenosis > 50% and carotid stenosis at each side were not significantly different between the two groups. The addicted group had both more pack years and duration of smoking than the non-addicted group ($p = 0.01$). Surprisingly, we did not find any notable difference between the serum level of lipid profile (triglycerides, cholesterol, HDL and LDL) of opium-addicted and non-opium addicted patients. Further analysis showed that opium consumption cannot be assumed to be a risk factor for significant carotid stenosis (≥ 70%). Fasting

Table 1. Patient characteristics between female and male group.

	Female	Male	P
Age	60.8 ± 8.5	58.7 ± 9.7	0.001
Opium addiction	No addiction: 98.5%	No addiction: 84.3%	0.001
	< 10 years: 0.5%	< 10 years: 7.8%	0.001
	≥ 10 years: 0.1%	≥ 10 years: 7.9%	0.001
Hypertension	68.6%	46.5%	0.00
Diabetes	61.7%	27.8%	0.00
Smoking	10.5%	48.1%	0.00
Right carotid stenosis ≥ 70%	1.1%	1.5%	NS*
Left carotid stenosis ≥ 70%	1%	0.8%	NS
Carotid stenosis ≥ 70% any side	1.8	2.2%	NS
Involved coronary arteries			
1 vessel disease	9%	4.4%	NS
2 vessel disease	20.2%	20.1%	NS
3 vessel disease	70.8%	75.5%	NS
Left main lesion > 50%	12.2%	13.8%	NS

*NS — not significant

blood sugar was significantly less in the addicted population (p = 0.02). Moreover, we detected that HbA_{1c} was markedly less in the addict group (p = = 0.03). Serum level of CRP was also higher in addicted patients (p = 0.04; Table 2).

Discussion

The word opium is derived from the Greek name for juice, the drug being obtained from the juice of the poppy, papaver somniferum [13]. According to official reports, the prevalence of opium addicts is 2–2.8% in Iran [6–8]. But our study indicated that 12.6% of all (and 15.7% of our male) patients use opium, which tends to be much more than official reports. There are beliefs about the protective effect of opium.

In Middle Eastern countries, opium consumption has traditionally been regarded as a way to lower blood lipids and thus prevent cardiovascular diseases, which could ultimately lead to addiction. Even some scientific studies have proved that opium use may have a cardioprotective effect [14–16].

Schulz and Gross [14] found numerous receptors for opium in the hearts of large animal models. They believed that opioids decrease the pain after myocardial infarction as well as infarct size, and so could be cardioprotective. Our study showed no evidence for an association between atherosclerosis in carotid and coronary arteries and opium usage, which does not support the notion of cardioprotectiveness of opioids. However, other researchers assume opioids to be an aggravating factor, or even a probable risk factor, for cardiovascular diseases [17]. The theory of atherogenic effects of opioids offered by Mohammadi et al. [17] claimed that opium use can increase serum levels of lipids that ends up as atheroma formation in the aorta of addicted rats.

They also found out an association between the duration of addiction and increase in serum level of lipids. Asgary et al. [18] showed that there was a direct correlation between opioids blood levels and duration of addiction. In their study, they also noted that the levels of HbA_{1c}, C-reactive protein, factor VII, Fibrinogen, apo B, Lpa, SGOT, and SGPT were significantly higher in the case subjects as compared with controls, and that HDL-cholesterol and apo-a were significantly lower in the case subjects, That would mean that opium acts as a cardiovascular disease risk factor. In contrast, our findings support the fact that the lipid profile of addicted and non-addicted people does not differ. This has been claimed previously by other researches [19, 20]. In short, there is no definite answer regarding the cardiovascular effects of opium consumption.

Opium dependents were at the same time cigarette smokers (65.5%), as we had predicted. This is no surprise because most opium dependent patients are smokers as well. However, in the smoker category, a significant difference was observed between opium users and non-users in the pattern of three vessel disease distribution, but not enough to prove that opioids have protecting vascular effects. As we mentioned earlier, the mean age of opium addicts was markedly

Table 2. Patient characteristics according to opium addicted and non-addicted.

	Normal range	Addict	Non addict	P
Biochemical factors				
FBS [mg/dL]	70–115	98.6 ± 30	106.2 ± 33	0.02
HbA_{1c} (%)	5–7.5	8.1 ± 1.01	6.83 ± 1.03	0.04
Cholesterol [mg/dL]	200–239	170 ± 8.5	168 ± 12	0.2
Triglicerydes [mg/dL]	≤ 220	142 ± 53	122 ± 25	0.4
HDL cholesterol [mg/dL]	29–80	42 ± 3	43 ± 6.8	0.5
LDL cholesterol [mg/dL]	≤ 130	95 ± 17	108 ± 12.1	0.6
CRP [mg/dL]	< 10	5.12 ± 1.06	2.89 ± 0.66	0.03
Cardiovascular risk factors				
Age		55.8 ± 9.2	59.2 ± 9.5	0.000
Gender		9%	19.7%	0.000
Body mass index		26.4 ± 3.45	27.55 ± 4.3	0.00
Diabetes		11.4%	17%	0.008
Hypertension		11.4%	88.6%	0.000
Smoking		65.5%	27.1%	0.000
Smoking duration (year)		16.5	15	0.01
Pack/year		12	10.1	0.01
Left main lesion > 50%		14.7%	15.2%	0.8
Involved coronary arteries				
1 vessel disease		5%	5.3%	0.6
2 vessel disease		21.6%	21.3%	0.6
3 vessel disease		73.4%	73.2%	0.6
Left carotid stenosis ≥ 70%		0.62	0.33%	0.4
Right carotid stenosis ≥ 70%		1.1%	0.5%	0.3
Mortality		9.1%	15.2%	0.4

FBS — fasting blood sugar; CRP — C-reactive protein; HDL — high density lipoprotein; LDL — low density lipoprotein

lower than non-dependents. This may be an explanation for the matter above. Some studies [9––12, 19, 20] suggest that opium addicts have a lower cholesterol level diastolic blood pressure than the normal population. In our study, we did not detect significant changes between serum levels of lipids between two groups. Hence, the effect of opioids on the cardiovascular system is still unclear and controversial. Further larger scale studies are needed to throw light on this subject.

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