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Effects of opium consumption on coronary artery disease risk factors and oral health: Results of Kerman Coronary Artery Disease Risk factors Study a population-based survey on 5900 subjects aged 15-75 years

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ABSTRACT

Background: Opium abuse as a relatively common behavior among Iranian population may have an association with the other coronary artery disease (CAD) risk factors. Here, we reported the prevalence of opium abuse and its co-exposures with oral health and other CAD risk factors.

Methods: We recruited 5900 inhabitant aged 15-75 years using a randomized cluster household survey. All were interviewed for level of physical activity (PA), depression, anxiety and opium use and assessed for hypertension, diabetes, hyperlipidemia, and oral health status. Regarding to opium abuse, participants were grouped into: "Non-," "occasional," and "dependent" users. Using logistic regression model for every CAD risk factor, we assessed whether the co-exposure of opium and CAD risk factor is significant.

Results: Overall, 10.6% reported ever opium use including 5.6% dependent and 5% occasional users. The prevalence of opium abuse was increased from 2.1% in 15-25 years to 24.5% in 55-64 years group. Opium abuse, in occasional and dependent forms, was associated with depression (adjusted odds ratio [AOR] 1.81 and 2.49) and low PS (AOR 1.43 and 1.71 respectively). Dependents were less obese than nonusers ($P < 0.01$). Opium abuse had no significant association with hypertension, diabetes, oral health status and lipid profile.

Conclusions: Opium abuse was associated with depression and low PA. No ameliorative effect was observed on hypertension, diabetes, and plasma lipid profile. Therefore, positive association of opium with depression and LPA and the incorrectness of belief on its ameliorative effect on three other important risk factors of CAD should be clearly highlighted in public health messages to the community.

Keywords: Coronary artery disease, opium addiction, prevalence, risk factors

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INTRODUCTION

Opium addiction is one of the challenging public health problems in most communities including Iran that is among the most affected countries in the world. It is estimated that between 2.8 and 9% of Iranian adult population are addicted to opium.[1-3] The prevalence was reported even higher (22%) in some rural areas.[4]

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The high prevalence of opium abuse may be partly due to some misconceptions that exist among the folks. In some societies, especially in Asia and Middle East, there is a belief that opium consumption has a preventive effect against coronary artery diseases (CADs) and related risk factors such as hyperlipidemia, hypertension, and diabetes.[5]

Despite the well-known beneficial effects of morphine in the acute phase of cardio-vascular events, it seems that chronic consumption of opium may be harmful for the cardiovascular system.[6] Several studies have been assessed the relationship between opium abuse and some CAD risk factors, but there are some controversies in this regards. Some of them reported the hazardous effect of opium abuse on CAD risk factors such as hyperlipidemia, diabetes and hypertension,[7-10] while others reported no effect[11-13] and in some others even protective effect was observed.[14,15] Some of these controversies may be due to limitations such as variation in study samples (restriction to males, animal studies), low sample size and hospital-based (not population-based) sampling. A population-based study with proper sampling and sufficient sample size is required to address all these limitations.

Kerman Coronary Artery Disease Risk factors Study (KERCADRS) is a population-based cohort study with repeated surveys that has been conducted to identify the persons in higher risk of cardiovascular diseases and behavioral and biological risk factors for CAD by a comprehensive assessment of self and familial past medical history, demographics, occupational and educational status as well as laboratory examinations. The first round of the study was done in 2009-2011 and a preliminary report of the results and methodology were published recently.[16] Here we reported the age-sex standardized prevalence of occasional and dependent abuse of opium and also the prevalence of main conventional (diabetes, hyperlipidemia, hypertension, obesity, low physical activity, depression etc.) and less conventional (oral health and psychological status) CAD risk factors in each subpopulation regarding opium abuse. Then, for every CAD disease or risk factor, we assessed whether the opium abuse could be an independent predictor when adjusted for important covariates. The results of the study may also be an index of effectiveness of Iranian health system program in prevention of noncommunicable diseases, here CAD.

METHODS

Study population and sampling method

From June 2009 to December 2011, 5900 individuals aged between 15 and 75-year-old were recruited into KERCADRS, first round. The sampling method was a one-stage cluster sampling. First, 250 postal codes (called seeds) were selected randomly from a roster of residential addresses updated by the local, provincial postoffice. Then, the social mobilizers mapped the seeds and attended to the specified addresses. After briefing the household's member and checking the eligibility criteria, all eligible individuals were asked to participate in the study. The recruitment was continued to reach 24 subjects in each cluster (include seed and neighborhood households). All recruited people were given an appointment card and asked to be fasted for 12-14 h at the time of attending the clinic for assessment.

Data collection

Written informed consent was collected from all subjects who have agreed to participate in the study at the time of interview. First, 10 ml venues blood was collected from each person for laboratory examinations (fasting plasma glucose, total cholesterol, high-density lipoprotein [HDL], low-density lipoprotein [LDL], triglyceride) and then breakfast was provided. In brief, by self-reported face-to-face interview, all demographic characteristics, and behaviors such as smoking and physical activity, depression and anxiety symptoms (using Beck related questionnaires) data were collected systematically by trained interviewers. The score range for the different levels of depression was as: 0-15, without symptom; 16-30, mild; 31-46, moderate; and 47-63, severe. The score range for anxiety was as: 0-7, normal; 8-15, mild; 16-25, moderate; and 26-63, severe.[17] Blood pressure, weight and height and past medical history including all medications were measured by trained physicians. Overweight/obesity status was defied as the body mass index (BMI) more than 25 kg/m^2.[18] Oral examination was performed by a trained dentist and Gingival Inflammation Index (GI) and Community Periodontal Index (CPI) were recorded or calculated.[19] GI was scored as: mild (score = 0.1-1.0), moderate (score = 1.1-2.0) and severe (score = 2.1-3.0) inflammation. CPI was scored as: 0 = Healthy, 1 = Bleeding on probing, 2 = Supra or subgingival calculus, 3 = Pocket with 4-5 mm depth, 4 = Pocket > 6 mm depth.[20,21] Every individual with previously diagnosed diabetes (by a physician) and/or taking insulin or noninsulin drugs and/or had fasting blood sugar ≥ 126 mg/dl was considered as diabetic cases. Uncontrolled diabetes was specified as HbA1c > 7% for all individuals.[22] Daily physical activities at home and workplace were recorded using World Health Organization Global Physical Activity Questionnaire. To evaluate the intensity of physical activity, metabolic equivalent (MET) was used. MET is the use of energy in an adult individual while he/she is sitting. Low physical activities are considered as

consuming energy <4 times, in proportion to sitting equal to MET minutes per week <600.[23] Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, that was the mean of two measurements (with 30 min interval), and/or taking any antihypertensive drug.[24] Hypertriglyceridemia and hypercholesterolemia were determined as serum triglyceride and cholesterol levels more than 200 mg/dl. High LDL was defined as serum LDL more than 130 mg/dl, and low HDL was considered when serum HDL was <50 mg/dl in women and <40 mg/dl in men.[25]

Opium addiction was defined according to DSM-IV criteria. The physician was the person who asked the participants to disclose whether they have ever used any type of drug and then narrowed down to specific questions about opium abuse. A previous study indicates that self-reported opium use is a valid and reliable method of opium abuse assessment in Iran.[26] The physician assured them that the information will be analyzed anonymous and used only for research purposes. Then, subjects were categorized into three groups: "Nonusers" who had never use opium, "occasional users" who were not dependent but irregularly used opium (mostly for entertainment) and "dependent users" who were continuously dependent on opium with regular opium consumption either by inhalation or eating.

More details of sampling method, data collection, and quality control strategies are presented elsewhere.[16] All medical examinations and laboratory blood tests were free of charge and people diagnosed with any disorders or abnormalities were referred to other specialties for further assessment and treatments. The study protocol and procedures were reviewed and approved by the ethic committee of Kerman University of Medical Sciences (Permission No. 88/110KA).

Statistical analysis

All data were analyzed under survey data analysis by STATA version 12 (StataCorp. 2011 College Station, TX, USA: StataCorp LP.) Households were considered as the primary sampling units. The prevalence of dependent and occasional opium abuse were standardized based on Kerman population distribution in 2006. Prevalence of opium consumption among genders and among different age groups, as well as frequencies of CAD risk factors among different types of opium consumers were compared using Chi-square test. For every CAD risk factor, we fitted a logistic regression model having opium use as the independent variable (with three level) and all the other risk factors, age, and sex as covariates. The adjusted odds ratio (AOR) was reported as the measure of association between opium use and every CAD risk factor controlling the potentially confounding effect of age, sex and other CAD risk factors such as hypertension, diabetes mellitus, mood disorders and hyperlipidemia. Finally, for each of the significant associations, we performed likelihood ratio test (LR test) to assess the significance of the interaction between opium addiction and cigarette smoking.

RESULTS

Data from 5895 people were used for this study. They had an average age of 33.5 (SD = 4) years. Most participants were women (54.9%), have been living in Kerman more than 10 years (90.7%), and mostly had education level as of primary to high-school (67.1%). In general, the response rate was more than 90%.

The age-sex standardized prevalence of opium abuse, dependent- and occasional-use are reported in Table 1. Overall, 10.6% (95% confidence interval [CI]: 9.7-11.5%) of participants reported opium abuse (either as dependent or occasional user), with a mean duration of 6.15 years. People started opium abuse at an average age of 27.7 (95% CI: 26.5-29) years. On average, men started opium use at age of 25.5 (95% CI: 24.8-26.3%) years, which is about 4.6 years earlier than women ($P < 0.01$). The age-sex standardized prevalence of opium-dependency was 5.6% (CI 95%: 5.0-6.2%), in addition to 5.0% (95% CI:

Table 1: The age-sex standardized prevalence of opium abuse, dependent- and occasional-use, community-based study (KERCADR-1st round-*n*=5895), Kerman, Iran, 2011

Variables	Subgroups	Standardized* prevalence (95% CI) of opium abuse			
		Dependent	Occasional	Total (dependent and occasional)	*P*
Total		5.6 (5.0-6.2)	5.0 (4.3-5.7)	10.6 (9.7-11.5)	
Gender	Male	9.2 (8.7-9.8)	8.6 (7.9-9.2)	17.8 (17.0-18.7)	<0.01
	Female	1.8 (1.6-2.0)	1.3 (1.1-1.5)	3.0 (2.7-3.3)	
Age groups	15-24	0.5 (0.4-0.8)	1.6 (1.2-2.1)	2.1 (1.7-2.6)	<0.01
	25-34	3.4 (3.0-3.7)	5.1 (4.8-5.5)	8.5 (8.0-9.0)	
	35-44	9.6 (9.2-9.9)	6.0 (5.7-6.3)	15.6 (15.1-16)	
	45-54	12.5 (12.2-12.7)	10.2 (9.9-10.4)	22.6 (22.3-23)	
	55-64	13.7 (13.6-13.9)	10.8 (10.7-10.9)	24.5 (24.4-27)	
	65-74	15.9 (15.8-16.1)	6.5 (6.4-6.6)	22.5 (22.3-22.6)	

*The direct standardization was done based on Kerman population in 2006. KERCADR=Kerman Coronary Artery Disease Risk Study; CI=Confidence interval

4.3-5.7%) who reported occasional opium abuse. Men were more likely to be opium abusers than women (17.8% vs. 3.0%) ($P < 0.01$). Opium abuse prevalence was constantly increased by age to the maximum of 24.5% in people aged 55-64 years ($P < 0.01$).

While the prevalence of diabetes was almost similar among the three groups (7.4-7.7%), 62.6% of the diabetic cases who smoked, opium had poor glycemic control in compare to the other two groups.

Prevalence of depression was 32.4% in nonusers and 60% in dependent and occasional users. 76% of nonusers and 86% of opium users had mild to severe symptoms of anxiety. Hypertriglyceridemia was detected in 14.4% of nonusers, in 12.3% of dependents and in 11.8% of occasional users.

The maximum prevalence of poor HDL/LDL ratio and hypertension was observed in occasional user group (42.7% and 13.3%, respectively). Poor GI was observed in 2.7% of nonusers, 2.6% of dependents, 1.5% of occasional users. High CPI was 5.1% in nonusers, 5.7% in occasional users and 6.5% in dependent users [Table 2].

After adjustment for covariates, such as sex, age, and other CAD risk factors, occasional users had higher odds of depression (AOR: 1.81 - $P = 0.01$) and low physical activity (AOR: 1.43 - $P = 0.01$) in compare to nonusers as the control group [Table 2].

Table 2: Prevalence and AOR for the association between the status of opium consumption and CAD risk factors

Risk factor	Addiction status	Risk factor prevalence		Adjusted analysis		
		% (*n*)	95% CI	AOR	*P*	95% CI
Diabetes (normal vs. diabetic)	Nonusers	7.7 (689)	7.0-8.5	1		
	Occasional users	7.6 (77)	5.6-10.3	1.20	0.32	0.84-1.70
	Dependent users	7.4 (83)	5.6-9.7	0.87	0.43	0.62-1.22
Abnormal HbA1c in diabetics (under 7 vs. >7)	Nonusers	45.1 (372)	35.3-55.3	1		
	Occasional users	47.7 (43)	43.5-52.0	0.85	0.66	0.42-1.73
	Dependent users	62.6 (46)	58.1-66.8	0.96	0.91	0.44-2.09
Depression (BDI <15 vs. BDI >15)	Nonusers	32.4 (1875)	30.6-34.2	1		
	Occasional users	60.6 (160)	51.7-68.9	1.81	0.01	1.32-2.46
	Dependent users	60.1 (267)	53.7-66.1	2.49	0.01	1.89-3.28
Anxiety (BAI <7 vs. BAI >7)	Nonusers	76.0 (3875)	74.3-77.7	1		
	Occasional users	86.5 (273)	81.8-90.2	1.31	0.12	0.93-1.86
	Dependent users	86.2 (381)	80.3-90.5	1.24	0.17	0.91-1.70
Hyper TG (TG <200 vs. TG >200)	Nonusers	14.4 (927)	13.3-15.7	1		
	Occasional users	11.8 (79)	7.3-18.5	0.87	0.44	0.60-1.24
	Dependent users	12.3 (113)	9.7-15.5	0.93	0.68	0.68-1.28
Poor HDL/LDL ratio (under 0.3 vs. above 0.3)	Nonusers	40.2 (2293)	38.5-42.0	1		
	Occasional users	42.7 (202)	33.8-52.0	0.88	0.37	0.66-1.16
	Dependent users	38.2 (257)	30.5-46.7	1.09	0.50	0.85-1.40
Hypertension (BP <140/90 vs. BP >140/90)	Nonusers	10.9 (1088)	10.1-11.7	1		
	Occasional users	13.3 (105)	9.1-19.0	1.05	0.75	0.76-1.47
	Dependent users	13.1 (139)	10.5-16.2	0.93	0.64	0.67-1.27
Poor GI (GI <1 vs. GI >1)	Nonusers	2.7 (120)	2.1-3.4	1		
	Occasional users	1.5 (9)	0.7-3.1	0.98	0.95	0.61-1.58
	Dependent users	2.6 (14)	1.6-4.2	1.69	0.09	0.91-3.12
High CPI (CPI <2 vs. CPI >3)	Nonusers	5.1 (236)	4.4-6.0	1		
	Occasional users	5.7 (19)	2.4-12.7	1.16	0.62	0.65-2.05
	Dependent users	6.5 (23)	4.4-9.6	1.17	0.59	0.67-2.05
Overweight/obesity (BMI <25 vs. BMI >25)	Nonusers	43.6 (2783)	41.9-45.4	1		
	Occasional users	40.6 (196)	32.7-49.0	0.79	0.12	0.59-1.06
	Dependent users	30.4 (190)	23.8-38.0	0.41	0.01	0.31-0.53
Low physical activity (weekly MET >600 vs. MET <600)	Nonusers	41.0 (2162)	39.1-42.9	1		
	Occasional users	41.2 (187)	32.5-50.5	1.43	0.01	1.11-1.84
	Dependent users	51.9 (256)	40.4-63.1	1.71	0.01	1.35-2.15

Percentage and (*n*) in risk factor prevalence column are related to values in their own subgroup. CI=Confidence interval; BMI=Body mass index; HbA1c=Glycated hemoglobin; GI=Gingival index; BP=Blood pressure; TG=Triglyceride; CAD=Coronary artery disease; HDL=High-density lipoprotein; LDL=Low-density lipoprotein; CPI=Community Periodontal Index; AOR=Adjusted odds ratio (controlling for demographic and CAD risk factors). BDI=Beck Depression Inventory; BAI=Beck Anxiety Inventory; MET=Metabolic equivalent of task

Using nonusers as the control group, dependent users had higher odds of depression (AOR: 2.49 - $P = 0.01$) and low physical activity (AOR: 1.71 - $P = 0.01$). Obesity was significantly lower in dependent users (AOR: 0.41 - $P = 0.01$) [Table 2].

Regarding cigarette smoking 10% of study participants reported themselves as smokers %8.3 as daily smokers and %1.7 as nondaily smokers. Passive smoking was %27.5 while women experienced more exposure than men (%30.1 vs. %25.0, *P* value 0.01).

Table 3 shows AORs for the status of opium consumption and CAD risk factors considering the interactions between addiction and cigarette smoking for those three risk factors that had a significant association with opium abuse. There was no significant interaction between opium addiction and smoking on developing depression (*P* value for heterogeneity LR test = 0.1) and on overweight/obesity (*P* value for the heterogeneity LR test = 0.2). However, there was an interaction between opium addiction and cigarette smoking in developing low physical activity (*P* value for heterogeneity LR test = 0.052).

DISCUSSION

According to our findings, more than 10% of Kerman adult population has ever used opium, with dependency rate of 5.6%. The opium dependency was considerably higher among men and people aged more than 35 years. Opium use was associated with depression, low physical activity (LPA) and had the reverse direction with obesity. The observed data indicated that first use usually occurs before the age of 30 years. Regarding the association with opium abuse, three risk factors of depression, LPA and obesity showed significant association [Table 2]. Depression and LPA are two important risk factors of CAD that are socially less acceptable compared with other risk factors such as hyperlipidemia, diabetes or hypertension. This may intensify the effect of these risk factors on CAD progression. The less BMI in opium dependents may be due to their poorer nutrition and financial status. As most of the opium consumers are cigarette smokers, it may be argued that the association found between these three risk factors with opium abuse may have been affected by cigarette smoking. The results of testing this interaction presented in Table 3 shows that the significant associations between opium consumption and depression/overweight/obesity were not modified by the effect of cigarette smoking. The observed effect of opium on low physical activity can be altered by smoking but in the reverse direction (antagonistic effect). Here AOR for smokers is, in fact, less than nonsmokers in both occasional and dependent users (1.11 vs. 1.58 and 1.03 vs. 1.78, respectively). Therefore, the association of opium consumption with all three risk factors may not have been affected by cigarette smoking.

Table 3: AOR* for the status of opium consumption and CAD risk factors considering the interactions between addiction and cigarette smoking

Risk factors	Addiction status	Nonsmokers		Smokers	
		AOR	*P*	AOR	*P*
Depression (BDI <15 vs. BDI >15)	Nonusers	1		1	
	Occasional users	1.85	<0.0001	1.28	0.2
	Dependent users	2.84	<0.0001	1.73	0.06
Overweight/obesity (BMI <25 vs. BMI >25)	Nonusers	1		1	
	Occasional users	0.54	<0.0001	0.40	0.30
	Dependent users	0.79	0.1	1.08	0.20
Low physical activity (weekly MET >600 vs. MET <600)	Nonusers	1		1	
	Occasional users	1.58	0.001	1.11	0.20
	Dependent users	1.78	<0.0001	1.03	0.02

*AOR=Adjusted odds ratio for age, sex, and other CAD risk factors; CAD=Coronary artery disease; BDI=Beck Depression Inventory; BMI=Body mass index; MET=Metabolic equivalent of task

Using opium did not decrease the odds of hypertension and diabetes, contradictory to the common believes about the curative or ameliorative effect of opium. Although it is well-established that opiates lower the systemic blood pressure via vasodilatation mechanism, but this is an acute effect, and there is a growing body of evidences that suggests opium addiction may be a risk factor for atherosclerosis and coronary artery stenosis.[27-29] Furthermore, the withdrawal symptoms associated with morphine addiction are usually experienced shortly before the time of the next scheduled dose, sometimes within as early as a few hours (usually between 6 and 12 h). During the acute withdrawal period systolic and diastolic blood pressure and heart rate increases,[30] which have potential to cause a heart attack, blood clot,[31] or stroke. Furthermore, the data did not show decreased risk of diabetes in opium abusers (occasionally and dependents). Diabetes control (HbA1c < 7%) was even poorer in those who regularly use opium. It has been shown that opiates can induce insulin resistance, metabolic syndrome, increased plasma glucose and diabetes, but there are some controversies in this regard. Golozar *et al*. in 2011 reported that opium consumption can increase the prevalence of diabetes.[8] Mami *et al*. in their experimental study on rabbits made the same conclusion,[9] while the other studies didn't find an association between opium consumption and blood glucose or diabetes.[11-13] A few studies have reported decreased level of blood glucose in opium addicted subjects.[14,15] Part of the observed heterogeneity could be due to duration of opium use, dose, and style of consumption, time after diabetes induction, study being performed on animal (controlled) or on human (mostly uncontrolled conditions), and random or nonrandom sampling.

Two animal studies have shown that exposure to opium in long times increased LDL cholesterol and total

cholesterol to HDL ratio.[7,32] We did not observe an association between opium use and hypertension or poor HDL/LDL ratio. However, opium abuse was associated with depression and low physical activity, which put opium users at higher risk of CAD.

Although this study was based on random sampling of a defined urban population and included psychological status and oral health risk factors, we should acknowledge the limitation of the study. Like any other cross-sectional, we can't ignore the reverse causation while we interpret the findings. Some people may start opium consumption to relief depression or individual with low physical activity may prone to become the opium dependent more. We may also misclassify the opium use, as people may have a problem in recall or report their opium use status, but this seems to be less problematic in Iran. A previous population-based study in Golestan indicated that the validity and reliability of self-reported opium abuse in Iran was relatively high. In that study, the validity and reliability of self-reported opium use were assessed by comparing questionnaire response with the results of urine test in a subgroup of studied population. The sensitivity and specificity of self-reported opium use were reported 0.93 and 0.83, respectively. The reliability of ever opium use and duration of opium use had the Kappa statistics of 0.96 and 0.74, respectively.[22] Nonetheless, some people who categorized as occasionally users may be actually dependent to opium, so, we may have underestimated dependents. Both of the above limitations can be addressed by prospectively follow people over time to measure both the exposure level and outcome accurate and timely.

CONCLUSIONS

The present study showed that opium abuse is associated with depression and low physical activity, and no association was observed with other CAD risk factors such as hypertension, diabetes, and plasma lipid profile. Therefore, the positive association with depression and LPA along with no ameliorative effect on hypertension, diabetes and plasma lipid profile verifies the incorrectness of the belief that opium may have curative or ameliorative effect on CAD risk factors. This should be clearly highlighted in public health messages to the community.

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