Association between opium use and metabolic syndrome among an urban population in Southern Iran: Results of the Kerman Coronary Artery Disease Risk Factor Study (KERCADRS)

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Original Article

Abstract

BACKGROUND: Along with the established effects of opium on metabolic parameters, stimulatory or inhibitory effects of opium on metabolic syndrome are also predictable. This study aimed to examine the association of opium use with metabolic syndrome and its components.

METHODS: This study was conducted on 5332 out of 5900 original sample participants enrolled in a population-based cohort entitled the Kerman Coronary Artery Disease Risk Study in Iran from 2009 to 2011. The subjects were divided into three groups of "non-opium users" (NOUs = 4340 subjects), "former opium users" (FOUs = 176 subjects), and dependent and occasional people named "current opium users" (COUs = 811 subjects). Metabolic syndrome was defined according to two International Diabetes Federation (IDF) and National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) definition criteria.

RESULTS: The overall prevalence of IDF defined-metabolic syndrome among NOUs, FOUs, and COUs was 36.4%, 27.3%, and 39.0%, respectively; which was significantly higher in the COUs group (P = 0.012). However, no significant difference was revealed across the three groups in prevalence of NCEP defined-metabolic syndrome (NOUs = 37.2%, FOUs = 30.1%, and COUs = 39.6%, P = 0.058). The odds for IDF defined-metabolic syndrome was higher in both COUs [odd ratio (OR) = 1.28, P = 0.028)] and FOUs (OR = 1.57, P = 0.045) compared with NOUs as the reference adjusting gender, age, body mass index, and cigarette smoking. However, the appearance of NCEP defined-metabolic syndrome could not be predicted by opium use.

CONCLUSION: Opium use can be associated with an increased risk for metabolic syndrome based on IDF criteria and thus preventing the appearance of metabolic syndrome by avoiding opium use can be a certain approach to preventing cardiovascular disease.

Keywords: Metabolic Syndrome, Opium, Substance Abuse, Addictive Behavior

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Introduction

Very long years, it was believed to the effects of opium use on preventing traditional risk factors for cardiovascular diseases, as well as equilibrating metabolic systems. Particularly, a preventive role of this substance use on diabetes mellitus, insulin resistance, and lipid profile disturbances was common among physicians and healthcare incumbents.[1] This disbelief led to spreading the opium addition in some traditional societies such as Iran so that the common use of this substance has estimated 11-69 per 1000 general population.[2,3] The use of this agent has been even accounted notable among those with high educational level that a representative sample of college students in Iran found 4.4% reporting ever use of opium and out of this 0.8% reported currently using opium.[4]

The stimulating or inhibiting role of opium on metabolic regulatory systems is now challenging. Some recent studies on animal models have shown that opium addiction had profound effects on some biochemical parameters, including fasting blood sugar, low-density lipoprotein (LDL), serum triglyceride (TG), liver enzyme[5] and it had also a

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significant influence on the thyroid function so that increased serum level of total T3 and decreased serum level of T3 resin uptake (T3RU) and serum level of free T4.[6] However, some clinical studies have also revealed that the total cholesterol level in the opium addicts is less than that in the non-addict group; there was, however, no difference in terms of LDL, high-density lipoprotein, and TG between the opium addicts and non-addicts.[7] It seems that the different effects of opium on metabolic parameters may be related to the variety of 70 known components of this substance. Moreover, duration of use, route of consumption, and even being pure or impure can be responsible for contradictory effects of opium on metabolic indices.[8]

Metabolic syndrome is a cluster of clinical conditions including increased blood pressure, increased level of blood sugar, excess body fat around the waist and abnormal cholesterol levels increasing the risk of developing cardiovascular disease.[9,10] According to the established role of opium use on some metabolic parameters individually, stimulatory or inhibitory effects of opium on metabolic syndrome are also predictable. Hence, this study was designed to examine the association of opium use with metabolic syndrome.

Materials and Methods

This cross-sectional study was conducted on 5332 out of 5900 original sample participants aged more than 15-75 years that were enrolled in a population-based cohort entitled the Kerman Coronary Artery Disease Risk Study in Iran between 2009 and 2011 to determine the state of cardiovascular and metabolic risk factors among general population.[11,12]

All participants underwent a standardized interview to completely validated questionnaires containing questions on demography, socioeconomic status, smoking behavior, opium use, physical activity, and nutritional habits. A complete clinical examination for cardiovascular evaluation and its risk factors including systolic blood pressure (SBP), diastolic blood pressures (DBP), weight, height, body mass index (BMI), and waist circumference (WC) was done. All subjects gave informed consent, and procedures followed were in accordance with the Ethical Committee of the Kerman University of Medical Sciences and complied with the recently revised Declaration of Helsinki.

Height, weight, and WC were measured on the day of the visit to the outpatient clinic. BMI was calculated as weight divided by height squared (kg/m^2). Blood pressure was measured twice in the left arm by an examining physician using a mercury column sphygmomanometer (Korotkoff Phases I and V) after the subject had been at rest in the seated position for 5 min. Hypertension was defined as an SBP of ≥ 140 mmHg or a DBP of ≥ 90 mmHg or those who were receiving antihypertensive therapy at the time of the examination. Smoking status was also considered as smoking ≥ 1 cigarette/day in the year preceding the examination. Blood was drawn after an 8-12 h overnight fasting period in the morning after completion of the 24 h urine collection. Plasma biochemical indices were measured by standard laboratory procedures.

In this study, opium use was defined as self-reported use of opium. In this regard, the subjects were divided into three groups of non-opium users (NOUs = 4340 subjects), former opium users (FOUs = 176 subjects), and current opium users (COUs) (occasionally and dependency people based on DSM-IV) (COUs = 811).

Metabolic syndrome was defined according to two definition criteria including International Diabetes Federation (IDF) Worldwide Definition[9] and The US National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) definition.[10] According to IDF definition, a participant has the metabolic syndrome if she/he had central obesity (defined as a WC ≥ 102 cm (40 inches) in men and 88 cm (35 inches) in women) and any two of the following: high-density lipoprotein (HDL) < 40 mg/dl in men and < 50 mg/dl in women or specific treatment for this lipid abnormality; TGs ≥ 150 mg/dl in men and women or specific treatment for this lipid abnormality; SBP ≥ 130 mm Hg or DBP ≥ 85 mm Hg in men and women or treatment of previously diagnosed hypertension; and fasting glucose ≥ 100 mg/dl in men and women. Furthermore, definition of metabolic syndrome according to NCEP definition requires at least three of the following: central obesity: WC ≥ 102 cm for men and ≥ 88 cm for women, serum TG ≥ 150 mg/dl, serum HDL level < 40 mg/dl for men and < 50 mg/dl for women, SBP ≥ 130 mm Hg or DBP ≥ 85 mm Hg in men and women or treatment of previously diagnosed hypertension, and fasting plasma glucose ≥ 110 mg/dl for both genders. The study endpoint was to examine differences in metabolic syndrome (according to two definitive criteria) and also its components across the three groups of NOUs, FOUs, and COUs.

Results were presented as mean ± standard deviation for quantitative variables and were summarized by absolute frequencies and

percentages for categorical variables. Continuous variables were compared using one-way analysis of variance and/or non-parametric or Kruskal–Wallis test whenever the data did not appear to have normal distribution or when the assumption of equal variances was violated across the three groups. Categorical variables were, on the other hand, compared using the chi-square test. The univariate and multiple logistic regression modeling were employed to assess the association of using self-reportedly opium and the metabolic syndrome after adjusting for gender, age, BMI, and cigarette smoking. Adjusted odds ratios (AOR) were reported. For the statistical analysis, the statistical software SPSS for Windows (version 19.0, SPSS Inc., Chicago, IL, USA) and the statistical package SAS for Windows (version 9.1, SAS Institute Inc., Cary, NC, USA) were used. P values of 0.050 or less were considered as statistically significant.

Results

Comparing the NOUs, FOUs, and COUs groups in terms of baseline characteristics (Table 1) showed significant differences. Male to female ratio was significantly higher in FOUs or COUs than in non-users as well as the COUs were significantly older than other groups. Furthermore, regarding central obesity state, the BMI value was significantly higher in NOUs compared with other two groups. The duration of opium use among FOUs was [mean ± standard error (SE): 11.0 ± 0.66 years; median (range): 8 (0.8-40) years], and among COUs was [mean ± SE: 11.8 ± 0.34 years; median (range): 10 (0.8-50) years].

According to IDF criteria, the overall prevalence of metabolic syndrome was 36.4% in NOUs, 27.3% in FOUs, and 39.0% in COUs that was significantly higher in the COUs group (P = 0.012) (Table 2). However, based on NCEP ATP III definitive criteria, no significant difference was revealed across the three groups in prevalence of metabolic syndrome (37.2% in NOUs, 30.1% in FOUs, and 39.6% in COUs, P = 0.058). Among various components of metabolic syndrome, abnormal serum fasting blood sugar and TG as well as high blood pressure were more prevalent in COUs than in NOUs. Regarding the prevalence of central obesity, abnormal WC was totally higher in NOUs than in other groups. In this context, currently addicted women had higher WC than non-addicted women (Table 2).

Based on the univariate logistic regression, the odds of developing metabolic syndrome among FOUs and COUs was 0.65 [95% confidence interval (CI): 0.46, 0.91] and 0.86 (95% CI: 0.73, 1.01) in comparison to NOUs in IDF definition. These results based on the NCEP definition was respectively 0.72 (0.52, 1.01) and 1.10 (0.94, 1.28). According to the multiple logistic regression model, the odds for metabolic syndrome (defined on IDF criteria) was higher in both COUs (AOR = 1.28, P = 0.028) and FOUs (AOR = 1.57, P = 0.045) compared with NOUs as the reference (Table 3) adjusting gender, age, BMI, and cigarette smoking. However, the appearance of metabolic syndrome defined based on NCEP ATP III criteria could not be predicted by opium use.

Table 1. Baseline characteristics of study population

Variables	NOUs (n = 4345)	FOUs (n = 176)	COUs (n = 811)	P
Sex				
Male	1568 (36.1)	156 (88.6)	642 (79.2)	< 0.001
Female	2777 (63.9)	20 (11.4)	169 (20.8)	
Age categories (year)				
≤ 30	1013 (23.3)	26 (14.8)	44 (5.4)	
31-40	809 (18.6)	57 (32.4)	112 (13.8)	< 0.001
41-50	853 (19.6)	37 (21.0)	185 (22.8)	
51-60	863 (19.9)	38 (21.6)	230 (28.4)	
> 60	807 (18.6)	18 (10.2)	240 (29.6)	
Mean age	45.08 ± 15.6	43.8 ± 12.6	52.5 ± 13.1	< 0.001
BMI				
< 25	1776 (41.2)	106 (60.2)	434 (53.8)	
25-29.99	1660 (38.5)	50 (28.4)	273 (33.8)	< 0.001
30-34.99	683 (15.8)	16 (9.1)	79 (9.8)	
≥ 35	195 (4.5)	4 (2.3)	21 (2.6)	
Mean BMI	26.25 ± 5.06	24.03 ± 4.7	24.8 ± 5.04	< 0.001

NOUs: Non-opium users; FOUs: Former opium users; COUs: Current opium users; BMI: Body mass index

Table 2. Prevalence of metabolic syndrome and its components

Variables	NOUs (n = 4345) (%)	FOUs (n = 176) (%)	COUs (n = 811) (%)	P
Abnormal WC (according to IDF)				
Only men	523 (33.5)	48 (31.0)	205 (32.0)	0.670
Only women	1702 (61.7)	12 (60.0)	126 (75.0)	0.002
Total sample	2225 (51.5)	60 (34.3)	331 (40.9)	< 0.001
Abnormal WC (according to NCEP ATP III)				
Only men	193 (12.4)	17 (11.0)	66 (10.3)	0.370
Only women	1024 (37.1)	6 (30.0)	85 (50.6)	0.002
Total sample	1217 (28.2)	23 (13.1)	151 (18.7)	< 0.001
Abnormal HDL cholesterol				
Only men	1116 (71.6)	104 (67.1)	457 (71.7)	0.480
Only women	2304 (83.4)	16 (84.2)	148 (88.6)	0.200
Total sample	3420 (79.1)	120 (69.0)	605 (75.2)	0.001
Abnormal FPG	1516 (35.0)	56 (32.2)	363 (45.1)	< 0.001
Abnormal TG	1637 (37.8)	79 (45.4)	343 (42.7)	0.007
Abnormal SBP	1217 (28.1)	40 (22.7)	290 (35.8)	< 0.001
Abnormal DBP	887 (20.5)	22 (12.5)	189 (23.3)	0.005
Abnormal blood pressure	1411 (32.6)	46 (26.1)	316 (39.0)	< 0.001
Metabolic syndrome (IDF)	1581 (36.4)	48 (27.3)	268 (33.0)	0.012
Metabolic syndrome (NCEP ATP III)	1618 (37.2)	53 (30.1)	321 (39.6)	0.058

NOUs: Non-opium users; FOUs: Former opium users; COUs: Current opium users; WC: Waist circumference; IDF: International Diabetes Federation; NCEP ATP III: National Cholesterol Education Program Adult Treatment Panel III; HDL: High-density lipoprotein; FPG: Fasting plasma glucose; TG: Triglyceride; SBP: Systolic blood pressure; DBP: Diastolic blood pressure

Table 3. Odds for metabolic syndrome adjusted for gender, age, body mass index (BMI), and cigarette smoking

Indicator variables	AOR (95% CI)	P
According to IDF definition		
NOUs	Ref	-
Opium ex-users	1.57 (1.01, 2.4)	0.045
COUs	1.28 (1.03, 1.6)	0.028
Cigarette	0.81 (0.62, 1.05)	0.120
Age (year)		
≤ 30	Ref	-
31-40	2.09 (1.6, 2.7)	< 0.001
41-50	3.52 (2.7, 4.6)	< 0.001
51-60	6.01 (4.6, 7.8)	< 0.001
> 60	8.70 (6.6, 11.3)	< 0.001
Sex (female)	1.83 (1.5, 2.15)	< 0.001
BMI		
< 25	Ref	-
25-29.99	10.90 (9.1, 13.1)	< 0.001
30-34.99	24.80 (19.7, 31.1)	< 0.001
≥ 35	33.80 (23.3, 48.9)	< 0.001
According to NCEP definition		
NOUs	Ref	-
Opium ex-users	1.02 (0.70, 1.5)	0.890
COUs	1.03 (0.84, 1.25)	0.760
Cigarette	0.99 (0.79, 1.24)	0.950
Age (year)		
≤ 30	Ref	-
31-40	2.10 (1.6, 2.7)	< 0.001
41-50	3.70 (2.9, 4.8)	< 0.001
51-60	7.30 (5.7, 9.3)	< 0.001
> 60	10.20 (8.0, 13.1)	< 0.001
Sex (female)	0.96 (0.83, 1.1)	0.640
BMI		
< 25	Ref	-
25-29.99	3.80 (3.2, 4.4)	< 0.001
30-34.99	8.90 (7.3, 10.9)	< 0.001
≥ 35	15.10 (10.6, 21.4)	< 0.001

AOR: Adjusted odds ratio; CI: Confidence interval; IDF: International Diabetes Federation; NOUs: Non-opium users; COUs: Current opium users; NCEP: National Cholesterol Education Program; BMI: Body mass index

Discussion

To the best of knowledge, the present study was the first to assess the effect of opium use on metabolic syndrome. The findings of our study can be very helpful particularly in the countries with commonly use of this substance such as Iran to prevent progression of cardiovascular disorders because of triggering effects of both opium addiction and metabolic syndrome in developing cardiac ischemic events. According to our first result, those who commonly used opium suffered more from metabolic syndrome because of higher prevalence of some metabolic components including increased serum blood sugar, serum TG, and also blood pressure. On the other hand, it can be an important hypothesized that opium consumption can mediate appearance of metabolic syndrome through its effect on blood glucose, lipid profile, and also blood pressure regulatory systems. In fact, our study could refuse preventive role of opium use on metabolic disorders such as diabetes or hyperlipidemia. Similar to our finding, some evidences have emphasized elevation of blood sugar following opium consumption. In some reports blood glucose had been increased, although this effect has been shown to be directly dose dependant.[8,13,14] It seems that the effects of opium on glucose metabolism can be mediated by the effects of opiate receptors so that these receptors may influence distribution volume and gluconeogenesis but do not play a major role in either insulin or glucagon secretion or in glucose disposal.[15,16] In addition, insulin resistance with opiate use may be coupled with β-cell dysfunction. After an intravenous glucose load, opium addicts were found to have a 42% lower acute insulin response than control subjects, accompanied by an 80% lower glucose disappearance rate.[17,18] Although, taken together, these findings suggest an association between opiate use and abnormal glucose metabolism, their clinical significance remains uncertain. Moreover, evidence from both preclinical and clinical studies demonstrates that chronic opioid exposure is associated with increased sugar intake. In this regard, elevating the role of opium on serum lipids has been also revealed in other studies that can be due to lipolytic effect of opium.[19,20] The effects of opium on blood glucose and lipids have been especially shown in diabetic patients so that opium addiction in non-insulin dependent diabetic subjects suffered increasing level of serum glucose and decreasing level of HDL-C leading metabolic disorders in these patients.[3] In total, a combination of stimulatory effects of opium on serum glucose, TG, and blood pressure can make the persons susceptible to metabolic syndrome.

Another important finding was that opium use results in different scenarios regarding its effects on weight changes so that the use of this substance led to weight gain only in women, but adversely associated with weight loss in total population. On the other hand, the pattern of weight changes after opium use may be different in men and women probably due to hormonal differences between the genders. The effects of opium addiction on weight change as well as on food intake have been widely studied. Reviews of the preclinical and clinical literature demonstrate a trend of increased eating following opiate agonist intake, with decreased eating after opiate antagonist intake in animals under acute food deprivation or stress, but not those that are chronically food deprived.[21,22] However, gender-dependent pattern of weight change following opium consumption should be more studied. In total, in light of the growing body of evidence linking the opioid system to food intake and risk of obesity, clinicians should reinforce proper exercise and dietary habits with opium users.

Another important point in our survey was obtaining different findings by employing two definitive criteria fir metabolic syndrome including IDF and NCEP criteria. In fact, by using IDF criteria, metabolic syndrome was strongly associated with opium use, while this association was not found by using NCEP criteria for defining metabolic syndrome. It seems that the rate of metabolic syndrome might be overestimated based on NCEP criteria leading incorrect estimation of the prevalence of metabolic syndrome especially in opium users. Hence, using the modified pattern of these criteria is preferred in this population.

Multiple studies have shown that metabolic syndrome has a strong association with socio-economic status of the people. In the current study, we could not to control the effect of such variables on the line of association of opium and metabolic syndrome, because the SES variables were not completely gathered, especially for economic section like income. Another limitation of the current study is that, about less than 600 cases due to having a lack in dependent or independent variables were removed from the study. Another limitation is that we could not define the time for cleaning from the addiction for those people who were classified as former users; however, we think this point cannot have a misleading effect on the results. With consideration of having such

information, we could not control the effect of these durations because this type of variable did not exist among other groups.

In conclusion, opium use can be associated with higher prevalence of metabolic syndrome. This association is explained by triggering effects of opium on serum levels of blood sugar and TG as well as on blood pressure. According to the observed relationship between metabolic syndrome and opium use and due to this fact the two pointed arms have been identified as potential risk factors for coronary artery disease, preventing appearance of metabolic syndrome by avoiding opium use can be a certain approach to prevent these diseases.

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Conflict of Interests

Authors have no conflict of interests.

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