

Is opium addiction a risk factor for ischemic heart disease and ischemic stroke?

Mohammad Reza Rezvani, Kavian Ghandehari¹

Department of Internal Medicine, Birjand University of Medical Sciences, ¹Department of Neurology, Ghaem Hospital, Ahmabad Street, Mashhad, Iran

Background: The main source of studies about effects of opium consumption on heart and brain attacks originates from Iran Therefore the aim of the present study was to assess opium addiction as a probable influencing factor for ischemic heart disease and ischemic stroke. **Materials and Methods:** A cross-sectional study was carried out in two Cardiology and Neurology clinics in Eastern Iran in 2011. Diagnosis of Ischemic Heart Disease (IHD) and Ischemic Stroke (IS) was made by Cardiologist and Stroke Neurologist respectively. The influence of gender, hypertension, diabetes, hyperlipidemia, cigarette smoking, oral and inhaled opium consumption on distribution of IHD and IS were evaluated. **Results:** Five hundred fifty eight patients (307 females, 251 males) with mean age 56.2 years enrolled the study. On adjusted odds ratios of our whole 558 patients, only hypertension and diabetes had a significant influence on occurrence of IHD; ($P = 0.000$ and $P = 0.000$) respectively. Oral and inhaled routes of opium addiction did not have a significant effect on occurrence of IHD; [OR = 1.172, 95% CI = 0.624-2.203, $P = 0.621$] and [OR = 1.820, 95% CI = 0.811-4.085, $P = 0.147$] respectively. Hypertension and diabetes were significant risk factors of IS in our 558 patients at multivariate analysis; ($P = 0.000$, $P = 0.020$). Oral opium addiction was as significant protective factor of IS in our study group; OR = 0.211, 95% CI = 0.079-0.564, $P = 0.002$, while inhaled opium addiction did not have a significant effect on occurrence of IS in our patients at; OR = 1.760, 95% CI = 0.760-4.076, $P = 0.187$. **Conclusion:** Oral opium consumption is a protective factor of IS but not IHD. Inhaled opium addiction does not have a significant influence on occurrence of IS and IHD.

Key words: Addiction, heart, ischemic, opium, stroke

INTRODUCTION

The word opium is driven from Greek name for juice, the drug being obtained from the juice of the poppy, *Papaver somniferum*. Opium is not a pure substance. The alkaloids constitute about 25% by weight of opium. Opium abuse is a major social problem in Middle East countries. Opium is found to be the most prevalent form of opioid used in Iran.^[1] In a medicosocial survey in a rural population in the northern part of Iran, an addiction rate to opium was reported to be 69/1000.^[2] In a survey done in Iranian cardiovascular patients with the mean age of 52.6 years, 5.2% were opium dependent.^[3] In Iran, eating opium pipe scrapings (opium dross) and inhaling the pyrolysates are the most common forms of opium usage.^[4] One of the reasons for this high prevalence is the misconception among some people

that opioids can prevent or have ameliorating effects in the process of hypertension, diabetes and occurrence of cardiovascular disease. There is controversy among physicians about the effects of opium on cardiovascular and cerebrovascular systems. Due to decreasing production of opium in Afghanistan since 2005 and increasing price of opium in Iran, prevalence of opium consumption has been decreased since 2005. The main source of studies about effects of opium consumption on heart and brain attacks originates from Iran Therefore the aim of the present study was to assess opium addiction as a probable influencing factor for ischemic heart disease and ischemic stroke.

MATERIALS AND METHODS

Consecutive patients referring to Cardiology and Neurology clinics of Birjand, Province of Southern Khorasan. Eastern Iran enrolled a cross-sectional study in 2011. Ischemic Stroke (IS) was defined as a sudden focal neurologic deficit of presumed arterial origin lasting ≥ 24 hrs with or without corresponding ischemic lesion on brain imaging.^[5] Ischemic Heart Disease (IHD) defined as evidence in the baseline ECG or documented prior history of angina pectoris or myocardial infarction.^[6] Diabetes was defined

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Address for correspondence: Dr. Kavian Ghandehari, Department of Neurology, Ghaem Hospital, Ahmabad Street, Mashhad, Iran.
E-mail: ghandeharik@mums.ac.ir

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as a physician diagnosis, a fasting blood glucose level ≥ 126 mg/dL or use of diabetes medication.^[7] Hyperlipidemia defined as physicians diagnosis, use of medication, serum cholesterol concentration >220 mg/dL, LDL cholesterol >130 mg/dL, or serum triglyceride concentration >150 mg/dL.^[7] Hypertension was defined as the current use of antihypertensive medication or an average blood pressure $>140/90$ mmHg on two separate recordings.^[7] Current smoking habits in recent year were recorded.^[7] Criteria for being opium addicted were set based on the DSM-IV-TR classification.^[8] Opium addiction is diagnosed when three of seven physiological (e.g., tolerance and withdrawal); behavioral (e.g., taking drug in larger amounts than intended); and cognitive (e.g., persistent desire to cut down) symptoms are met within the previous 12 months. Opium addiction leads to clinically significant impairment or distress occurring in any of the following areas, within a 12-month period: 1-failure to fulfill major job obligations at work, school or home; 2-recurrent opioid use in hazardous situations, such as driving; 3-opioid-related legal problems; 4-social or interpersonal problems caused by or exacerbated by opioid use.^[8] Opium users categorized as those who inhaled the smoke of ignited opium or ate it in a crude form. Evaluation of opium dosage and purity of opium were not among assessment aims of this study. Based on DSM-IV criteria all of addicted patients had ≥ 12 months usage of opium. Patients who were dependent to heroin derivatives, amphetamine derivatives and cocaine were excluded.

Data on demographics and above variables were recorded in a standardized questionnaire and entered in SPSS 16 software package, Chicago, IL, USA. Differences of all variables in the univariate analysis was evaluated by Chi² and Fisher exact tests. Multivariable or adjusted odds ratios (OR) with 95% CI were calculated in the secondary analysis using a multiple logistic regression model. Using multivariate analysis the effects of overlaps in risk factors is omitted. If range of 95% CI is above 1 the factor is categorized as risk factor and if its range is below 1 the factor is considered as a protective factor.

The research was approved by local ethics committee (Code Number1412) and ethical committee agreement of the hospital was achieved. An inform consent was taken by the patients.

RESULTS

Five hundred fifty eight patients (307 females, 251 males) with mean age 56.2 years enrolled the study. Eighty one patients (42 females, 39 males; 14.5%) had IHD and 78 patients (24 females, 54 males; 13.9%) had IS. The frequency rate of hypertension, diabetes, hyperlipidemia, cigarette smoking, oral opium addiction and inhaled opium

addiction in our 558 patients was 29.4, 15.9, 20.9, 3.9, 20.2 and 8.6% respectively. Table 1 represents influence of evaluated factors on distribution of IHD in our study group at univariate analysis. Hypertension and diabetes had significant effects on IHD in our study group at univariate analysis. Oral and inhaled routes of opium addiction did not have a statistically significant influence on occurrence of IHD in our patients at univariate analysis. Table 2 represents univariate analysis of influence of evaluated factors on distribution of IS in our study group. Hypertension, diabetes, hyperlipidemia, and cigarette smoking were significant risk factors of IS at univariate analysis in our study group. Oral opium addiction had a significant effect on occurrence of IS at univariate analysis in our 558 patients, while the influence of inhaled opium addiction on IS was not statistically significant. On adjusted odds ratios our whole 558 patients, only hypertension and diabetes had a significant influence on occurrence of IHD. Oral and inhaled routes of opium addiction did not have a significant effect on occurrence of IHD in multivariate analysis. Table 3 represents effects of evaluated factors on occurrence of IHD at adjusted odds ratios of 558 patients. Hypertension and

Table 1: Influence of factors on distribution of ischemic heart disease in our study group at univariate analysis

Influencing factor	X ²	df	P	Odds ratio	95% CI
gender	2.384	1	0.548	1.161	0.724-1.860
Hypertension	23.035	1	0.000	3.134	1.935-5.074
Diabetes	15.72	1	0.000	2.880	1.679-4.943
Hyperlipidemia	0.090	1	0.764	1.091	0.618-1.926
Cigarette smoking	0.543	1	0.756	0.578	0.133-2.524
Oral opium addiction	0.084	1	0.883	0.916	0.508-1.651
Inhaled opium addiction	0.759	1	0.391	1.404	0.652-3.021

Table 2: Influence of factors on distribution of ischemic stroke in our study group at univariate analysis

Influencing factor	X ²	df	P	Odds ratio	95% CI
gender	21.544	1	0.000	3.232	1.933-5.405
Hypertension	31.899	1	0.000	3.882	2.371-6.356
Diabetes	14.854	1	0.000	2.838	1.647-4.905
Hyperlipidemia	5.257	1	0.025	1.849	1.087-3.147
Cigarette smoking	13.814	1	0.001	4.680	1.951-11.372
Oral opium addiction	11.396	1	0.000	0.225	0.089-0.571
Inhaled opium addiction	0.994	1	0.381	1.475	0.684-3.179

Table 3: Effect of factors on occurrence of ischemic heart disease at multivariate analysis of 558 patients

Effecting factor	Odds Ratio	95% CI	df	P
Gender	1,231	0.841-1.740	1	0.581
Hypertension	2.853	1.712-4.756	1	0.000
Diabetes	2.176	1.215-3.896	1	0.009
Hyperlipidemia	0.820	0.448-1.500	1	0.520
Cigarette smoking	0.458	0.154-1.361	1	0.160
Oral opium addiction	1.172	0.624-2.203	1	0.621
Inhaled opium addiction	1.820	0.811-4.085	1	0.147

Table 4: Effect of factors on occurrence of ischemic stroke at multivariate analysis of 558 patients

Effecting factor	Odds ratio	95% CI	df	P
Gender	1.891	1.845-3.402	1	0.011
Hypertension	2.980	1.761-5.061	1	0.000
Diabetes	4.891	2.680-4.941	1	0.020
Hyperlipidemia	0.758	0.424-1.357	1	0.351
Oral opium addiction	0.211	0.079-0.564	1	0.002
Inhaled opium addiction	1.760	0.760-4.076	1	0.187

diabetes were significant risk factors of IS in our 558 patients at multivariate analysis. Oral opium addiction was a significant protective factor of IS in our study group, while inhaled opium addiction did not have a significant effect on occurrence of IS in our patients at adjusted odds ratios. Table 4 represents effect of evaluated factors on occurrence of IS at multivariate analysis of 558 patients.

DISCUSSION

There are beliefs about protective effects of opium on cardiovascular system in some societies or even among a few physicians. It is assumed that opium can be used as an alternative treatment for some of cardiovascular risk factors especially diabetes.^[9] A cross-sectional study was conducted on 2405 patients admitted with coronary artery disease for angiography at Tehran heart center in 2005.^[11] After adjusting for other risk factors, opium consumption was a significant risk factor for coronary artery disease, OR = 1.8, $P = 0.01$. Moreover, the amount of opium consumption was associated significantly with severity of coronary atherosclerosis, $P = 0.002$.^[11] A case-control study was carried out on 600 Iranian patients undergoing Coronary Artery Bypass Graft (CABG).^[10] Prevalence of opium usage was 12% in these patients.^[10] Another study on 275 patients' candidate for CABG in Tehran revealed that mean quality of life domains were statistically similar between opium addicted and non-opium addicted patients.^[11] A study of 782 males undergoing CABG in Tehran revealed that 7.1% were current opium users and 2.3% were past users.^[12] The prevalence of opium addiction on 4398 patients with IHD was 15.6% in another study in Tehran.^[13] Oral and inhaled routes of opium addiction did not have a significant effect on occurrence of IHD in multivariate analysis of our study group. The effect of opium addiction on cardiovascular risk factors was evaluated on 360 patients in Isfahan.^[14] In the opium addicted subjects, HbA1C, CRP, factor VII, and Fibrinogen were significantly higher than control subject.^[14] Fasting blood sugar reduced non-significantly in opium addicted subjects and the amount of reduction of fasting blood sugar was related to the duration of opium addiction.^[14] Since HbA1C level was increased in these patients and it provides an integrated measurement of blood glucose during last 3 months, opium might decrease

blood glucose temporarily.^[14] Similar effects of opium on blood sugar markers were also reported by Karam *et al.*, in Rafsanjan.^[15] Smoking opium increased serum glucose and decreases HDL, and thus adds to metabolic disorders in diabetic patients.^[15] Cholesterol tends to be lower in diabetic addicted males, and HbA1c is higher in addicted females compared to non-addicted diabetics.^[15] Another case-control study was performed on 23 diabetic males with opium addiction and control group in Yazd.^[16] Mean fasting blood sugar and 2 hr post-prandial sugar were significantly lower in opium addicted patients, $P = 0.04$.^[16] While HbA1C, total cholesterol, triglyceride, LDL, and HDL were not significantly different between two groups of diabetic patients.^[16] Their results revealed that opium consumption may decrease blood glucose temporarily.^[16] A case control study was conducted on 60 opium addicted subjects in Kerman.^[17] Serum Fibrinogen level in opium addicted subjects was significantly higher than control group, $P = 0.018$.^[17] Elevated plasma Fibrinogen is an independent risk factor of stroke.^[18] However the mechanism of elevation of serum Fibrinogen in opium user subjects is unknown.^[17] A study about influence of route of opium consumption in acute Myocardial Infarction (MI) patients was done in Rasht.^[19] The prevalence of opium inhalation in non-silent MI was higher than silent MI patients.^[19] While the effect of oral opium consumption on MI patients was not significant.^[19] Opium withdrawal symptoms was not a trigger of acute MI in opium addicted patients admitted in coronary care units in Kerman.^[20] A hospital based case control study on candidates of coronary angiography in Isfahan revealed that on univariate analysis, current opium users had higher odds of sever coronary artery disease compared with nonusers. But it was roughly confounded by other cofactors.^[21] A survey was carried out for evaluation of risk factors in patients with intracranial atherosclerotic stenosis in Isfahan.^[22] Opium addiction was found in 14% of patients with intracranial arterial stenosis.^[22] There is few published study on effect of opium addiction on development of ischemic stroke. A case-control study was carried out on IS patients in Kerman. 29.5% of IS patients and 10.5% of controls had opium addiction in Kerman, $P < 0.0001$.^[23] Cigarette smoking was a significant risk factor of stroke OR = 2.2, $P < 0.012$.^[22] Opium addiction was also a significant risk factor of IS in Kerman, OR = 2.36, $P = 0.04$.^[23] Oral opium addiction was as significant protective factor of IS in our study group, while inhaled opium addiction did not have a significant risk or protective effect on occurrence of IS in our patients at multivariate analysis. Assessment of opium dosage, mean duration of opium consumption and purity of opium has not performed in our research; therefore conclusions derived from our study are limited. We recommend other researchers to evaluate these opium consumption parameters in their future studies.

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