Frequency of Opium Addiction in Patients with Ischemic Stroke and Comparing their Cerebrovascular Doppler Ultrasound Changes to Non-Addicts

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Original Article

Abstract

Background: Ischemic stroke is a major cause of mortality and morbidity worldwide. Various studies on the etiology of this disease are in progress. Some studies have suggested that opium abuse may is associated with increased risk of ischemic stroke. The present study aimed to analyze the frequency of opium addiction and to compare cerebrovascular ultrasound patients' changes to non-addicts.

Methods: This cross-sectional study was performed on 97 patients with ischemic stroke. The diagnosis was confirmed by imaging and paraclinical studies. All the patients underwent cerebrovascular ultrasound in the first 4 days of symptoms onset. A questionnaire containing demographic data, opium use information [based on the 4th Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria], and vascular ultrasound findings were completed for each patient and the results were analyzed using descriptive statistics and chi-square test.

Findings: In this study, 38 patients (39.18%) were addicted to opium and the remaining were non-addicts. Among the addicted patients, 31 patients were male and 7 patients were female, while 26 and 33 patients of non-addicts were male and female, respectively ($P < 0.01$). Among the risk factors for stroke, smoking was higher in the addicts than in non-addicts ($P = 0.04$). Frequency of vascular stenosis and stenosis location did not show a statistical significant difference between the addicted and non-addicted patients.

Conclusion: More than one-third of the patients with stroke were addicted to opium which was higher than general population; although the pattern of stenosis in these patients was similar to the non-addicts.

Keywords: Opium, Transcranial Doppler Ultrasound, Stroke

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Introduction

Stroke is one of the leading causes of mortality and morbidity worldwide and it consumes annually a great cost, directly and indirectly.[1] In the most prevalent type of stroke, i.e. thrombotic stroke, atherosclerosis is considered as the main pathogen.[2] Therefore, prevention of stroke through recognition of atherosclerosis risk factors, and then their treatment or modification will help to control this complication.[3] Recent studies showed that in addition to known risk factors such as hypertension, diabetes, smoking, and hyperlipidemia,[4] other factors such as substance abuse are also involved in the development or exacerbation of the atherosclerotic process. One of these substances is opium with morphine as its main ingredient.[5] Some studies showed that morphine increases plasma fibrinogen and coagulability and is ultimately associated with increased risk of atherosclerosis.[3,6] Clinical studies on patients with cardiovascular disorders showed a higher prevalence of these disorders in opium addicts.[7-9] Since atherosclerosis process is similar in heart and brain arteries,[4] opium use perhaps is associated with increased cerebrovascular stenosis. Studies are limited in this field.

A case-control study showed that opium is an independent risk factor for stroke.[3] Findings of imaging had also showed microvascular lesions in morphine dependents.[10] Due to the limitation of studies in this field and lack of a study to clarify the impact of opium abuse on brain vessels through paraclinical methods, in this study, we decided to determine the frequency of opium addiction using Doppler ultrasound, a sensitive and accurate method for the evaluation of cerebral artery stenosis,[11] and to compare vessels stenosis pattern in addicts and non-addicts with ischemic stroke, hoping to help patients with its results.

Methods

This cross-sectional study was performed through non-probability convenience sampling in Shafa Hospital (Kerman, Iran) in 2012 on ischemic stroke patients with large vessel involvement. All the admitted patients, who clinically suspected to stroke, underwent brain CT-Scan (X-ray computed tomography) and MRI (Magnetic Resonance Imaging) (1.5 Tesla), and the bleeding subjects were excluded. If necessary, contrast material was used to confirm the diagnosis. Cardioembolic and lacunar stroke patients were also excluded. In this study, cardioembolic stroke was devoted to those cases in whom the clinical symptoms were suddenly onset and the patient had simultaneously a heart condition justifying atrial fibrillation or in echocardiography, according to cardiologist, had disorders justifying embolism with or without thrombus, such as atrial myxoma. Lacunar stroke included those subjects in whom the lesion size was less than 20 mm and there were no symptoms of large vessels stenosis on ultrasound. Cases with an uncertain diagnosis[12] and patients with a history of stroke or other disease were also excluded. Then, the vasculature of those patients with stable vital signs and well cooperation was evaluated using Doppler ultrasound apparatus (DWL, Sipplingen, Germany) in the first 4 days of stroke symptoms onset.

The TCD/ECD (TransCranial Doppler/ExtraCranial Doppler) process was performed at an appropriate temperature using pulsed Doppler system and two separate probes (4-MHz probe for measuring internal and common carotid arteries, and 2-MHz probe for middle cerebral, anterior cerebral, posterior cerebral, vertebral, and basilar arteries). To record the middle cerebral artery (MCA), anterior cerebral artery (ACA), and posterior cerebral artery (PCA), the temporal bone window and to record vertebral artery (VA) and basilar artery (BA) the sub-occipital window were used, respectively. The common carotid artery (CCA) and internal carotid artery (ICA) flows were recorded over the course of the mentioned arteries in the neck. Recording of the flow was performed at the standard depth[11] to which the mentioned device was planned accordingly. Peak systolic velocity (PSV), pulsatility index (PI), and resistance index (RI) were recorded automatically by the device in each of these vessels, and to remove artifacts and improve the accuracy, the obtained data were also calculated manually. If there was a difference between automatically and manually calculated values, the manual values were considered as the final data. If a window was poor for recording the arterial flow, the subject was excluded. PSV > 120 cm/sec for MCA and ACA arteries and PSV > 100 cm/sec for BA,

VA, and PCA arteries were considered abnormal and suggestive of stenosis.[13] PSV > 125 cm/sec or ICA/CCA PSV Ratio above 2 was considered abnormal for ICA arteries.[11]

In addition, demographic data and cerebrovascular risk factors (including age, sex, hyperlipidemia, diabetes mellitus, and smoking) were collected using a questionnaire and based on the history obtained from the patient or his/her family.

Opium addiction was determined more than one year abuses based on history and 4th Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria.[14] Sample size was calculated 97 patients using β = 10%, a = 0.05, and 80% power. This study was approved by the Ethics Committee of Kerman University of Medical Sciences.

Data were analyzed using SPSS for Windows 20.0 (SPSS, Inc., Chicago, IL, USA) through descriptive statistics, and chi-square test. P < 0.05 was set as a statistical significant level.

Results

A total of 97 patients were enrolled in the study, of which 38 patients (39.18%) were addicted to opium and 59 patients (60.82%) were non-addicts. According to a recent study conducted in the general population of Kerman city, the prevalence of opiate abuse in the general population was 11.5% which was significantly lower than figure obtained in stroke patients (P < 0.01).[15] Mean age of addicts and non-addicts were 64.4 ± 10.7 and 67.39 ± 11.4 years, respectively. Among the addicted patients, 31 patients (81.58%) were male and 7 patients (18.42%) were female and among the non-addicts, 26 patients (44.1%) were male and 33 patients (55.9%) were female. Among the risk factors of stroke, the frequency of smoking and male sex was significantly higher in addicted than non-addicted patients (Table 1).

There was no statistical significant difference in frequency of vascular stenosis in left and right sides between the addicted and non-addicted patients, separately and in total (Table 2). In addition, there was no statistical significant difference between the left and right arteries in terms of stenosis, although a non-significant difference was observed in left MCA and left PCA which was considerable (Table 3).

Discussion

In our study, more than one-third of the stroke patients were opium dependents. This number is

Table 1. Comparative risk factors frequencies in addicts and non-addicts

	Gender		Mean age	Hypertension	Diabetes mellitus	Hyperlipidemia	Cigarette smoking
	Female	Male					
Non-addict	33	26	67.39 ± 11.4	36	15	12	7
Addict	7	31	64.40 ± 10.7	19	10	4	14
P	< 0.01		0.09	0.28	0.92	0.20	0.04

Table 2. Stenosis frequency of the addicted and non-addicted patients

Stenosis	Left side				Right side				Total			
Addiction	Absent	Present	Total	P	Absent	Present	Total	P	Absent	Present	Total	P
Absent	43 (44.32%)	16 (16.49%)	59 (60.82%)	0.84	39 (40.20%)	20 (20.61%)	59 (60.82%)	0.97	32 (32.99%)	27 (27.83%)	59 (60.82%)	0.88
Present	27 (27.83%)	11 (11.34%)	38 (39.17%)		25 (25.77%)	13 (13.40%)	38 (39.17%)		20 (20.61%)	18 (18.55%)	38 (39.17%)	
Total	70 (72.16%)	27 (27.83%)	97 (100%)		64 (65.97%)	33 (34.03%)	97 (100%)		52 (53.60%)	45 (46.40%)	97 (100%)	

Table 3. Stenosis frequency of cerebral arteries in the addicts and non-addicts

Stenosis	CCA		ICA		MCA		ACA		PCA		VA		BA
Addiction	Lt	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt	Rt	Lt	Rt	
Absent	0	0	0	1	6	7	6	8	4	6	2	3	2
Present	0	0	1	2	6	4	5	7	0	5	1	1	1
P	-	-	0.39	0.56	0.24	1.00	0.75	0.52	0.15	0.75	1.00	1.00	0.56

CCA: Common carotid artery; ICA: Internal carotid artery; MCA: Middle cerebral artery; ACA: Anterior cerebral artery; PCA: Posterior cerebral artery; VA: Vertebral artery; BA: Basilar artery; Lt: left; Rt: right

higher than the national provided statistics which is about 3%, according to the formal reports.[16] Although studies in this field is limited, a case-control study conducted showed that 29.5% of the patients with stroke were addicted to opium which was 20% more than the control group;[3] a finding similar to our results. The higher frequency of opium addicted patients in our study than the national statistics is undoubtedly related to patients age because the peak age of stroke incidence is over the sixth decade of life[1] and in these ages, patients have been addicted to opium many years ago, while new generations are less inclined to opium and they tend to abuse other substances,[17,18] and this difference is arisen since young people are included in the national statistics. Unfortunately, further research was not performed on high frequency of drug abuse seen in our study and the above mentioned study in Iran and other countries, but the results of some researches in this field is interesting. In a systematic review and meta-analysis study, conducted by Degenhardt et al., for evaluating the causes of mortality in users of opioid (heroin, opium, morphine, etc.)[19], the risk of mortality and crude mortality rate (CMR) of opioid consumers was higher than normal population and CMR of deaths related to cerebrovascular system was about 0.001 per 100 people annually. Case report studies also indicated the stroke in opium poisoning and infarction in newborns of mothers addicted to opium derived compounds.[20,21] Analysis of brain CT scan in cases of acute poisoning with opium, indicates stroke in less than ten percent of cases.[22]

These results show this fact that opium intoxication is associated with increased risk of stroke but further studies are necessary for chronic abuse. More studies have been performed on opium role in vascular stenosis in patients with cardiovascular disorders and their results[23] show that opium abuse is associated with increased chance of cardiovascular stenosis and regarding the similarity of many causing factors of atherosclerosis in heart and brain, the negative impact of opium on the brain vessels is expected. The reason of negative effects of opium on vascular stenosis in these studies is related to plasma fibrinogen and coagulability increment.[3,6] This issue should be further investigated clinically. There is no consensus on the opium mode of action on nervous system yet, however some of these effects are through opiate receptors naturally occurring in the brain.[24] In addition, the immunomodulatory role of opium should not be forgotten.[25] What is obtained from human and animal studies[5,7,26] about the role of opium in the development or progression of atherosclerosis, suggests that opium lonely and in the absence of major risk factors, particularly hypercholesterolemia, is unable to produce atherosclerotic lesions [probably due to LDL-c (low-density lipoprotein cholesterol) increase following opioid system activation with opium].[7,27]

According to our results, there was no statistical significant difference in the frequency of atherosclerosis and type of involved vessels among opium addicts and non-addict patients. This finding means that opium consumption does not alter vascular stenosis pattern. In our study extracranial vascular stenosis was low so that among a total of 194 studied arteries (in 97 patients), 79 arteries were stenotic in both addicts and non-addicts, of them 4 carotid arteries (5%) were involved and the remaining were intracranial of which ACA artery (particularly in right side) had the highest frequency in both addicts and non-addicts (39.91%). It seems that intracranial arteries stenosis tend to occur more in Asian population,[9] so that in a study in Pakistan on 672 patients, the findings of Doppler ultrasound showed stenosis of carotid arteries in 12% of stroke patients,[28] while this value is 16-25% in Caucasians.[29] Although with increasing age, the flow velocity decreases in basal cerebral arteries and PI increases,[11,30] and this flow velocity decreases is more prevalent in people over 40 years and in males (probably due to the lower hematocrit of women),[31] up to 30% difference can occur in flow velocity and PI of namesake arteries (right and left)[11] and our findings regarding the mean age of addicts (64.6 ± 10.7) and non-addicts (67.39 ± 11.4) which indicated high age of patients in stroke occurrence, showed a difference no more than these values in namesake arteries between the addicts and non-addicts.

The present study was the first research based on vessels ultrasound findings and thus we could not compare our results with other studies. But there is no doubt that further studies should be performed in this field. In addition, it should be mentioned that although TCD has augmented the sensitivity of diagnosis of stroke subclasses according to TOAST classification from 27% to

64%, it has a sensitivity of 60% and specificity of 81.25% in comparison to MRA.[32] Research plan with similar approach and larger sample size and comparison of findings of TCD with other common methods of cerebrovascular imaging such as MRA may provide different results from our findings. Limitation of our study was lack of performing serial ultrasound which could have more valuable outcomes. In addition, lack of using B-mode technique was another limitation of the present study and should be mentioned in future studies. In general, the findings of this research showed that a large part of people with stroke are addicted to opium although their vascular stenosis pattern has no difference with non-addict individuals and its role in stenosis incidence should be evaluated through more studies.

Conclusion

More than one-third of patients with stroke were addicted to opium which was higher than the general population; although the pattern of stenosis in these patients was similar to non-addicts.

Conflict of Interests

The Authors have no conflict of interest.

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فراوانی اعتیاد به تریاک در بیماران مبتلا به سکته مغزی ایسکمیک و مقایسه تغییرات داپلر سونوگرافی عروق مغزی آن‌ها با افراد غیر معتاد

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مقاله پژوهشی

چکیده

مقدمه: سکته مغزی ایسکمیک یکی از علل مهم مرگ و میر و ناخوشی در سراسر دنیا می‌باشد. مطالعات گوناگونی در سبب‌شناسی این بیماری در حال انجام است. برخی از بررسی‌ها نشان می‌دهند که مصرف تریاک ممکن است با افزایش شانس بروز سکته مغزی ایسکمیک همراه باشد. هدف از این مطالعه، بررسی فراوانی موارد اعتیاد به تریاک و مقایسه تغییرات سونوگرافی عروق مغزی این افراد با افراد غیر معتاد بود.

روش‌ها: مطالعه حاضر به شکل مقطعی روی ۹۷ بیمار مبتلا به سکته مغزی ایسکمیک انجام گرفت. تأیید تشخیص با بررسی‌های عکس‌برداری و پاراکلینیکی بود. کلیه بیماران در ۴ روز اول شروع علایم، تحت سونوگرافی عروق مغزی قرار گرفتند. برای هر فرد پرسش‌نامه‌ای شامل اطلاعات دموگرافیک، اطلاعات مربوط به مصرف تریاک [بر اساس معیار DSM-IV (Diagnostic and statistical manual of mental disorders-IV)] و یافته‌های سونوگرافی عروق تکمیل گردید. نتایج با استفاده از آمار توصیفی و آزمون χ^2 مورد تجزیه و تحلیل قرار گرفت.

یافته‌ها: در این مطالعه ۳۸ نفر (۳۹/۱۸ درصد) معتاد به تریاک و باقی‌مانده غیر معتاد بودند. از بین معتادان ۳۱ نفر مرد و ۷ نفر زن بودند؛ در حالی که در افراد غیر معتاد ۲۶ نفر مرد و ۳۳ نفر زن بودند ($P < ۰/۰۱$). از میان عوامل خطر سکته مغزی، مصرف سیگار در بیماران معتاد بیشتر از غیر معتاد بود ($P = ۰/۰۴$). فراوانی موارد تنگی عروق و محل تنگی عروق در گروه معتاد در مقایسه با گروه غیر معتاد تفاوت معنی‌داری را نشان نداد.

نتیجه‌گیری: بیش از ۱/۳ بیماران مبتلا به سکته مغزی معتاد به مواد مخدر بودند که نسبت به جمعیت عمومی بالاتر بود، هرچند که الگوی تنگی عروق در این افراد مشابه افراد غیر معتاد بود.

واژگان کلیدی: تریاک، داپلر سونوگرافی ترانس کرانیال، سکته مغزی

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