Cerebrovascular Reactivity and Carotid Intima-Media Thickness in Opium Dependents: A Case-Control Study

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Abstract

Background: There is still no consensus among researchers on the impact of opium dependency on cerebrovascular stenosis. Some studies suggest that opium may be a risk factor for ischemic stroke. This study compared carotid intima-media thickness (CIMT) and cerebrovascular reactivity between opium-dependent and healthy people.

Methods: This case-control study was done among opium addicts at Shafa hospital in Kerman, Iran, in year 2018. People with systemic disease or who took any medicine were excluded from our study. The control group were selected from healthy non-addicted volunteers. The control group was matched in age and sex with the case group. Cerebrovascular reactivity of middle cranial artery and intima-media thickness of carotid artery were measured for all in both groups. The results were analyzed using chi-square, independent samples t, and logistic regression tests.

Findings: 47 opium addicts and 47 healthy people entered this study. 88% of them were men and 12% were women. 68.1% of the case group and 31.9% of the control group were cigarette smokers; this difference was statistically significant. Comparison of cerebrovascular reactivity and CIMT between the two groups was statistically significant (P < 0.001). This relationship remained significant for the CIMT after removing confounding factors (P = 0.018).

Conclusion: Overall, our findings show that opium dependency affects the carotid intima-media thickness as an indicator of cerebral atherosclerosis.

Keywords: Opium; Intima-media thickness; Cerebrovascular diseases; Stroke; Transcranial Doppler sonography

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Introduction

Ischemic stroke is one of the most common neurological disorders due to a high prevalence of vascular atherosclerosis risk factors among people. The most common causes of ischemic stroke include large vessels atherosclerosis, cardiac embolism, and small vessels disease. Up to now, hypertension, hyperlipidemia, diabetes mellitus, and cigarette smoking have been known as risk factors for atherosclerosis.

In recent years, opium addiction has been studied as one of the possible causes of atherosclerosis, and its impact on myocardial infarction (MI) has been illustrated in some studies. Previous studies showed a high prevalence of opium dependency in patients with ischemic stroke but the pattern of vascular stenosis of them did not differ from the control group. In another study, oral usage of opium known to be a protective factor for ischemic stroke.

B-Mode Doppler sonography can be used to study the process of atherosclerosis in cerebrovascular arteries. Abnormal results of carotid intima-media thickness (CIMT) are one of the most important predictors of vascular events. Cerebrovascular reactivity is another indicator of asymptomatic carotid artery stenosis that is measured by examination of intracranial blood flow changes by a vasodilatory stimulus such as CO₂. It can also predict ischemic events in carotid stenosis.

Due to high prevalence of opium addiction in some countries, and lack of consensus on the role of opium in ischemic diseases, our study tried to compare CIMT and cerebrovascular reactivity between opium addicts and the control group.

Methods

This case-control study was done among opium addicts at Shafa hospital in Kerman, Iran, in year 2018. The inclusion criteria for the case group was all people over 30 years old who were opium dependents according to the 10th version of the International Statistical Classification of Diseases and Related Health Problems (ICD10). Individuals with any systemic disease such as diabetes mellitus, respiratory disorder, rheumatoid or any other inflammatory disease, pregnancy, and taking any medicine or oral contraceptive pill (OCP) were excluded from our study. These people were selected from Addiction Treatment Centers in Kerman City (before treatment started). They were addicted to "opium only" or "opium and cigarette". Since cigarette smoking is often an accompaniment to opium addiction in society, we measured and recorded the amount of smoking as a confounding factor in both case and control groups.

For all cases, ultrasonography was performed with a Multi-Dop X Digital-DWL ultrasound instrument, and cerebrovascular reactivity and CIMT were calculated. IMF at the far wall of common carotid artery was measured and recorded, Cerebrovascular reactivity was determined by apnea test. In this test, a 2.5-Hz probe was fixed on temporal window, and focused on middle cerebral artery at a depth of 5 cm until the maximum flow was detected; and then, the middle cerebral arterial (MCA) flow was recorded continuously. After recording of mean flow velocity (MFV) in a 4-second period, the patient was asked to have a normal breath, and then hold it for 30 seconds (without Valsalva maneuver). At the end of this period, MFV was recorded again. After a rest for 3 minutes, the patient was asked to breathe fast for one minute, and MFV was recorded. Finally, reactivity was calculated by the following formula:

\[ \text{MCA Reactivity} = \frac{\text{MFV}_{\text{Apnea}} - \text{MFV}_{\text{Hyperventilation}}}{\text{MFV}_{\text{Rest}}} \times 100 \]

The control group were selected from healthy non-addicted volunteers, and matched in age and sex with the case group. The sample size of 47 people was estimated within each group (P < 0.050, and statistical power of 80%).

This study was approved by the Ethics Committee of Kerman University of Medical Sciences, Kerman, Iran. All results were analyzed using chi-square, independent samples t, and logistic regression tests via SPSS software (version 22, IBM Corporation, Armonk, NY, USA). P < 0.050 was the statistical significance level.

Results

The opium-dependent group included 43 men (91.5%) and 4 women (8.5%). 40 men (85.1%) and 7 women (14.9%) were admitted to the healthy control group. These two groups did not differ significantly in gender (P = 0.336). The mean age was not significantly different between the two groups (P = 0.520) (Table 1).
Table 1. The comparison of dependent variables between the groups

| Variable                  | Opium addict (mean ± SD) | Control (mean ± SD) | P*   |
|---------------------------|--------------------------|---------------------|------|
| Age (year)                | 47.87 ± 1.18             | 49.04 ± 1.37        | 0.520|
| Cigarette usage (pack-year)| 8.06 ± 1.25              | 2.74 ± 0.95         | 0.010|
| CIMT (mm)                 | 0.84 ± 0.03              | 0.62 ± 0.02         | < 0.001|
| MCA reactivity (%)        | 64.82 ± 1.44             | 74.04 ± 1.42        | < 0.001|

SD: Standard deviation; CIMT: Carotid intima-media thickness; MCA: Middle cerebral arterial

*Independent samples t test

32 cases in opium-dependent group (68.21%) and 15 (31.9%) in the control group were cigarette smokers, and this difference was significant between two groups (P < 0.001). Besides, the cigarette pack-year index was significantly higher in opium users compared to control group (P = 0.010) (Table 1).

In preliminary analysis by independent samples t test, the mean CIMT in opium-dependent group was significantly higher than control group, too (P < 0.001) (Table 1).

The mean percentage of MCA reactivity was also significantly less in opium-dependent group (P < 0.001) (Table 2).

After using logistic regression to eliminate the effect of cigarette as a confounding factor, the difference between CIMT in studied groups remained significant (P = 0.018). However, this did not happen for the reactivity (P = 0.507) (Table 2).

Discussion

This study was conducted to evaluate the effect of opium addiction on cerebrovascular ultrasonography tests. Our study illustrates that opium addiction is associated with an increase in IMT of carotid arteries. This finding remained significant even after the removal of confounding factors such as cigarette smoking. Our findings indicate an increased risk of atherosclerosis in opium addicts.

In previous studies, the high value of this test was confirmed for detection of atherosclerosis and prediction of ischemic events. It also associated with presence of brain white matter lesions, left ventricular hypertrophy, and kidney diseases. Lorenz et al. reported that for an absolute CIMT difference of 0.1 mm, the future risk of MI increases by 10-15 percent, and the stroke risk increases by 13-18 percent. Another study by O'Leary and Bots showed that IMT of internal carotid artery was more associated with MI and common carotid artery ischemic stroke.

Moreover, Saadatnia et al. compared CIMT in a group of 20 opium users and control group. In their study, CIMT was higher in opium-addicted group, but there was no significant relationship after removal of confounding factors such as cigarette smoking. As a result, further investigations with larger sample sizes were proposed.

Although no more similar studies were found to allow us to compare our results with them, the following studies are noteworthy. In a study by Hamzei-Moghadam et al., 105 patients with ischemic stroke and healthy control group were compared. The opium dependency was significantly higher in patients with stroke. They also found in another study that, despite the higher prevalence of opium addiction in patients with ischemic stroke, the pattern of their stenosis did not differ with other non-addict patients. From 2005 to 2013, five studies have been conducted on the association of opioid addiction and ischemic heart disease in Iran. All of them showed that opium addiction had a significant relationship with the incidence of ischemic heart disease.

The second vascular examination technique we used was the determination of cerebrovascular reactivity by transcranial Doppler ultrasonography.

Table 2. The results of logistic regression test for variables

| Variable                  | Crude OR  | Crude P | Adjusted OR | Adjusted P | CI       | Adjusted OR | Adjusted P | CI       |
|---------------------------|-----------|---------|-------------|------------|----------|-------------|------------|----------|
| CIMT                      | 0.004     | < 0.001 | 0.004       | 0.018      | 0.0-0.39 | 0.004       | 0.018      | 0.0-0.39 |
| MCA reactivity            | 0.10      | < 0.001 | 1.04-1.15   | 1.03       | 0.94-1.13| 0.507       | 0.94-1.13 | 0.94-1.13|

OR: Odds ratio; CI: Confidence interval; CIMT: Carotid intima-media thickness; MCA: Middle cerebral arterial
Although we did not see any significant differences between two groups after eliminating the confounding factors, but the impact of atherosclerosis risk factors such as hypertension, cigarette smoking, and diabetes mellitus on cerebrovascular reactivity has been confirmed in previous studies. It can also be used as a predictor of ischemic events in carotid stenosis.

Acquiring history of underlying illnesses from individuals, and the absence of internal and cardiac examinations were the main limitations in our study, which we propose to consider in subsequent studies.

**Conclusion**

In conclusion, our findings show that opium dependency affects the CIMT as an indicator of atherosclerosis. The high prevalence of opium addiction in the Middle East, and its impact on increasing mortality indicates the importance of this issue. So, the role of opium in the atherosclerosis process as a risk factor of vascular events should be taken into account.

**Conflict of Interests**

The Authors have no conflict of interest.

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**References**

1. Ropper AH, Samuels MA, Klein J. Adams and Victor's principles of neurology. New York, NY: McGraw-Hill Education; 2014.
2. Grau AJ, Weimar C, Buggle F, Heinrich A, Goertler M, Neumaier S, et al. Risk factors, outcome, and treatment in subtypes of ischemic stroke: The German stroke data bank. Stroke 2001; 32(11): 2559-66.
3. Ohira T, Shahar E, Chambless LE, Rosamond WD, Mosley TH Jr, Folsom AR. Risk factors for ischemic stroke subtypes: The Atherosclerosis Risk in Communities study. Stroke 2006; 37(10): 2493-8.
4. Ebrahimzadeh HA, Saba M, Sedighi B, Kamali H. Study of the involved vascular territories in patients with ischemic stroke in Kerman, Iran. ARYA Atheroscler 2016; 12(5): 250-3.
5. Khosooosi Niaki MR, Hamid M, Farshidi F, Mohammadpour M, Salehi Omran MT. Evaluation of the role of opium addiction in acute myocardial infarction as a risk factor. Caspian J Intern Med 2013; 4(1): 585-9.
6. Hamzhei Moghadam A, Ahmadi Mosavi S, Khademi Zadeh K. The relationship between Opium Dependency and Stroke. J Kerman Univ Med Sci 2006; 13(4): 203-8. [In Persian].
7. Hamzhei-Moghadam A, Shafa MA, Khanjani N, Farahat R. Frequency of opium addiction in patients with ischemic stroke and comparing their cerebrovascular doppler ultrasound changes to non-addicts. Addict Health 2013; 5(3-4): 95-101.
8. Rezvani MR, Ghandehari K. Is opium addiction a risk factor for ischemic heart disease and ischemic stroke? J Res Med Sci 2012; 17(10): 958-61.
9. Baldassarre D, Amato M, Bondioli A, Sirtori CR, Tremoli E. Carotid artery intima-media thickness measured by ultrasonography in normal clinical practice correlates well with atherosclerosis risk factors. Stroke 2000; 31(10): 2426-30.
10. Bots ML, Evans GW, Tegeler CH, Meijer R. Carotid intima-media thickness measurements: Relations with atherosclerosis, risk of cardiovascular disease and application in randomized controlled trials. Chin Med J (Engl) 2016; 129(2): 215-26.
11. Reinhard M, Schwarzer G, Briel M, Altamura C, Palazzo P, King A, et al. Cerebrovascular reactivity predicts stroke in high-grade carotid artery disease. Neurology 2014; 83(16): 1424-31.
12. Silvestrini M, Vernieri F, Pasqualetti P, Matteis M, Passarelli F, Troisi E, et al. Impaired cerebral vasoreactivity and risk of stroke in patients with asymptomatic carotid artery stenosis. JAMA 2000; 283(16): 2122-7.
13. Markus H, Cullinane M. Severely impaired cerebrovascular reactivity predicts stroke and TIA risk in patients with carotid artery stenosis and occlusion. Brain 2001; 124(Pt 3): 457-67.
14. Vernieri F, Pasqualetti P, Passarelli F, Rossini PM, Silvestrini M. Outcome of carotid artery occlusion is predicted by cerebrovascular reactivity. Stroke 1999; 30(3): 593-8.
15. Silvestrini M, Troisi E, Matteis M, Cupini LM, Caltagirone C. Transcranial Doppler assessment of cerebrovascular reactivity in symptomatic and asymptomatic severe carotid stenosis. Stroke 1996; 27(11): 1970-3.
16. O’Leary DH, Bots ML. Imaging of atherosclerosis: Carotid intima-media thickness. Eur Heart J 2010; 31(14): 1682-9.
17. Markus HS, Harrison MJ. Estimation of cerebrovascular reactivity using transcranial Doppler ultrasound. Stroke 1995; 26(9): 1580-4.
18. Markus HS, Harrison MJ. Estimation of cerebrovascular reactivity using transcranial Doppler ultrasound. Stroke 1995; 26(9): 1580-4.
Doppler, including the use of breath-holding as the vasodilatory stimulus. Stroke 1992; 23(5): 668-73.

18. Bagheri Lankarani K, Ghaffarpasand F, Mahmoodi M, Delghandehlili M, Honarvar B, Lotfi M, et al. Predictors of common carotid intima-media thickness and atherosclerosis in a sample of Iranian general population. Shiraz E-Med J 2015; 16(5): e27906.

19. Lorenz MW, Markus HS, Bots ML, Rosvall M, Sitzer M. Prediction of clinical cardiovascular events with carotid intima-media thickness: A systematic review and meta-analysis. Circulation 2007; 115(4): 459-67.

20. Saadatnia M, Ebrahimi H, Tajmirriahi M. The effect of opium/INS; addiction on carotid intima media thickness. J Neurol Sci 2013; 333: e217.

21. Hamzei-Moghadam A, Ahmadi Musavi SM, Khademizadeh K. Relationship of opium dependency and stroke. Addict Health 2009; 1(1): 6-10.

22. Sadeghian S, Darvish S, Davoodi G, Salarifar M, Mahmoodian M, Fallah N, et al. The association of opium with coronary artery disease. Eur J Cardiovasc Prev Rehabil 2007; 14(5): 715-7.

23. Masoumi M, Shahesmaeili A, Mirzazadeh A, Tavakoli M, Ali AZ. Opium addiction and severity of coronary artery disease: A case-control study. J Res Med Sci 2010; 15(1): 27-32.

24. Masoumi M, Ramezani MA, Karimzadeh H. The relationship of opium addiction with coronary artery disease. Int J Prev Med 2010; 1(3): 182-6.

25. Sadr Bafghi SM, Rafiee M, Bahadorzadeh L, Namayeh SM, Soltani MH, Motafaker M. Is opium addiction a risk factor for acute myocardial infarction? Acta Med Iran 2005; 43(3): 218-22.

26. Settakis G, Pall D, Molnar C, Berezcki D, Csiba L, Fulesdi B. Cerebrovascular reactivity in hypertensive and healthy adolescents: TCD with vasodilatory challenge. J Neuroimaging 2003; 13(2): 106-12.

27. De Chiara S, Mancini M, Vaccaro O, Riccardi G, Ferrara L, Gallotta G, et al. Cerebrovascular reactivity by transcranial doppler ultrasonography in insulin-dependent diabetic patients. Cerebrovasc Dis 1993; 3(2): 111-5.

28. Silvestrini M, Troisi E, Matteis M, Cupini LM, Bernardi G. Effect of smoking on cerebrovascular reactivity. J Cereb Blood Flow Metab 1996; 16(4): 746-9.

29. Moghaddasi M, Mamarrabadi M, Habibi AH. A comparison of cerebral vasomotor reactivity in diabetic and nondiabetic Iranian patients. J Res Med Sci 2010; 15(1): 50-3.

30. Goode SD, Altaf N, Munshi S, MacSweeney ST, Auer DP. Impaired cerebrovascular reactivity predicts recurrent symptoms in patients with carotid artery occlusion: A hypercapnia BOLD fMRI Study. AJNR Am J Neuroradiol 2016; 37(5): 904-9.

31. Meysamie A, Sedaghat M, Mahmoodi M, Ghodsi SM, Eftekhar B. Opium use in a rural area of the Islamic Republic of Iran. East Mediterr Health J 2009; 15(2): 425-31.

32. Khadem H, Malekzadeh R, Poursams A, Jafari E, Salahi R, Sennani S, et al. Opium use and mortality in Golestan Cohort Study: Prospective cohort study of 50,000 adults in Iran. BMJ 2012; 344: e2502.
واکنش پذیری عروق مغزی و ضخامت اینتیما مدیای شریان کاروتید در افراد معتاد به تریاک: یک مطالعه مورد-شاهدی

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چکیده

مقدمه: هنوز در مورد تأثیر مصرف تریاک بر تنگی عروق مغزی، در میان محققان اتفاق نظر وجود ندارد. برخی از مطالعات نشان داده که تریاک ممکن است عامل خطری برای برخی بیماران مغزی باشد. هدف از انجام پژوهش حاضر، مقایسه ضخامت اینتیما مدیای شریان کاروتید و واکنشپذیری عروق مغزی در معتادان به تریاک و افراد سالم بود.

روش‌ها: این مطالعه بر روی 94 فرد معتاد به تریاک در بیمارستان شفای کرمان در سال 1397 انجام گردید. افرادی که بیماری‌های سیستمیک و یا سابقه مصرف سیگار دارو داشتند، از مطالعه حذف شدند. نمونه‌های گروه نماد از افراد داوطلب سالم غیر معتاد به تریاک انتخاب شدند. واکنشپذیری شریان مغزی میانی و ضخامت اینتیما مدیای شریان کاروتید مشترک در بیماران هر دو گروه محاسبه گردید. داده‌ها با استفاده از آزمون‌های χ² و Independent t و Logistic regression مورد تحلیل قرار گرفت.

یافته‌ها: 47 فرد معتاد به تریاک و 47 فرد سالم در تحقیق شرکت نمودند. 88 درصد از نمونه‌ها مرد و 12 درصد زن بودند. 80/00 درصد از افراد کاروتیدی، 64 درصد از افراد معتاد به تریاک سیگار مصرف می‌کردند. اختلاف معنی‌داری در ضخامت اینتیما مدیای شریان کاروتید و واکنشپذیری در شریان مغزی میانی بین دو گروه وجود نداشت (P > 0/10). اختلاف معنی‌داری در ضخامت اینتیما مدیای شریان کاروتید معنی‌دار بود (P = 0/18).

نتیجه‌گیری: بر اساس نتایج بدست آمده از مطالعه حاضر، احتمال بر تریاک بر ضخامت اینتیما مدیای شریان کاروتید مشترک، به عنوان شاخصی از روند آترواسکلروزیس، تأثیرگذار می‌باشد.

واژگان کلیدی: تریاک، ضخامت اینتیما مدیای شریان کاروتید، شریان مغزی

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