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Association between Serum Uric Acid Level and Stenosis in Atherothrombotic Infarction

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Abstract

Background: Previous studies show that serum level of uric acid is significantly correlated with mortality and functional outcome in patients with ischemic stroke and according to some other studies, ischemic stroke is associated with stenosis of some stenoisis of some specific brain vessels. The aim of this study was to investigate the frequency of hyperuricemia and its association with intra and extra cerebral vessels stenosis in patients with acute ischemic stroke.

Method: In this cross-sectional study, 169 patients with acute atherothrombotic stroke were evaluated. Blood samples were collected in the first 24 hours after stroke for the assessment of uric acid. Doppler ultrasound was done in the first 5 days of stroke. To analyze data, t-test and logistic regression were used.

Results: In this study, 22.4 % of patients had hyperuricemia. There was no significant statistical relationship between uric acid level and stenosis. Also, there was no significant statistical relationship between uric acid level and cerebrovascular risk factors. Mean serum uric acid level was 5.09±1/63 in patients with intracerebral vessels stenosis, 5.42±1.11in patients with extracerebral vessels stenosis and 6.18± 1.75 in patients with both intracerebral and extracerebral vessels stenosis. There was no significant statistical relationship between uric acid level and site of stenosis.

Conclusion: Hyperuricemia is frequent in patients with acute ischemic stroke. The site of cerebral vessels stenosis is not associated with hyperuricemia.

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Introduction

Stroke is considered as the most common and at the same time the most fatal neurological disease. The frequency of ischemic strokes is about 75% (1, 2). Its incidence is related to different cerebrovascular risk factors, including hypertension, smoking, Hyperlipidemia and diabetes (3). Recent studies show that other factors may be effective in the course of stroke that one of them is serum level of uric acid. According to some studies, level of serum uric acid in patients with ischemic stroke is higher than that in normal population (4). Recent studies also show that the mortality rate in patients with stroke is significantly associated with the level of uric acid; some of the related studies have been reported from Iran, Norway, Germany and China (5-9). This finding is true about stroke complications, too (10, 11). At present, there are some evidences about the role of uric acid in coronary atherosclerosis; for this, it has been referred as a potential marker for prognosis in myocardial infarction and stroke in some articles, though the nature of this relation is not clear (12,13). Although studies show that increase in uric acid level is associated with arterial stenosis (13, 14), there are few published articles about this relationship. Some evidences of ultrasound show that in patients with abnormal serum uric acid level, the incidence rate of carotid stenosis is high (15, 16). This finding has been reported also in relation to asymptomatic carotid stenosis (8); but such relationship between uric acid and intracranial artery stenosis is not clear. Due to the limitations of the studies in this field and the absence of a study on both intracranial and extracranial cerebral arteries, the present study was done to measure serum uric acid level in patients with atherothrombotic infarction and to find its relationship with intracranial and extracranial vessels stenosis severity and location.

Methods

This cross-sectional study was conducted on 169 patients with atherothrombotic infarction admitted in Shafa Hospital of Kerman/ Iran in 2015. All patients had experienced stroke for the first time and had been hospitalized in the first 24 hours of the onset of symptoms. Diagnosis was confirmed based on paraclinic methods of CT scan and MRI (T1, T2, DWI) and, if necessary, the contrast material was used and the suspect cases were excluded. Then, all patients were visited by a cardiologist and ECG as well as transthoracic (and if required transesophageal) echocardiography was done for all of them and patients with emboli, Lacunar strokes and history of other diseases (such

as gout or kidney disease) or consumption of drugs (except for ischemic heart disease, diabetes, hypertension and hyperlipidemia) were excluded.

Blood sample of patients was collected in the first 24 hours of disease onset for measurement of uric acid. Serum level of uric acid was measured by photometry method and values higher than 7mg/dl in men and 5.7mg/dl in women were considered as abnormal (9). For all patients, transcranial and extracranial Doppler sonography was done by CW/PW Doppler, connected to the DWL software box (Sipplingen, Germany) in Shafa Hospital of Kerman in the first 5 days of hospitalization. This device uses 2 separate 4 MHz probes for investigating common carotid arteries (CCA) and internal carotid artery (ICA) and 2 MHz probe for evaluation of anterior cerebral artery (ACA), Middle cerebral artery (MCA), posterior cerebral artery (PCA), ophthalmic artery (OA), vertebral artery (VA) and basilar artery (BA). The blood flow in arteries was investigated in standard depth and for each mentioned artery. Peak systolic velocity (PSV), end diastolic velocity (EDV), mean flow velocity (MFV), pulsatility index (PI) and resistance index (RI) were calculated automatically by the device. The criterion for the narrowing of MCA and ACA arteries was MFV > 120 cm/sec and for BA, VA and PCA was MFV>100 cm/sec. If the difference is more than 30 percent in MCA and ACA blood vessels and 50% in VA, and PCA BA ones, both sides of this case was deemed narrowing, too. Also, for ICA in the carotid siphon area, MFV > 100 cm/sec and in neck area, PSV>125 cm/sec or ICA/CCA PSV Ratio > 2 were considered as stenosis (17,18). A questionnaire was completed for each patient containing demographic information and other variables. The record of risk factors included the following: arterial hypertension (treated or systolic blood pressure > 160 mmHg or diastolic > 90 mmHg after the seventh post-stroke day), diabetes (treated or fasting glucose ≥ 126 mg/dL), dyslipidemia (treated), coronary heart disease (history of angina, myocardial infarction, or congestive heart failure) and smoking (> 10 cigarettes per day for 6 months or during the recent year regardless of the number of cigarettes) (9, 10,19). Demographic data and other findings were analyzed through SPSS20 software. Descriptive statistics, t-test and logistic regression test were used for analysis and the significance level was considered 0.05.

Results

In this study 169 patients with the age range of 34 to 91 years were evaluated. Mean serum level of uric acid of patients was 465.25± 15.25 mg/dl. Table 1 shows the frequency of demographic

factors and other variables. Level of uric acid was abnormal in 22.4% of patients. There was not any significant relationship between the serum uric acid level and arterial stenosis. Also there was not any significant relationship between the serum uric acid level and stroke risk factors (Table 2). After using logistic regression, this relationship did not show any changes too (Table 3). Mean serum level of uric acid was 5.09±1.63, 5 mg/dl in patients with intracranial vessels stenosis, 5.42±1.11mg/dl in patients with extracranial vessels stenosis and 6.18±1.75mg/dl in patients with both intracranial and extracranial vessels stenosis. There was no significant correlation between serum uric acid level and the location of the stenosis (Table 2).

Table 1. Demographic characteristics of patients

	Number	%
Under 60 years	610	36.1
61-80 years	91	53.8
above 80 years	17	10.1
Female	64	37.9
Male	105	62.1
Hypertension	106	62.7
Diabetes	64	37.9
Smoking	35	20.7
Ischemic heart disease	42	24.8
Hyperlipidemia	51	30.2
Hyperuricemia	38	22.4
intracranial vessels stenosis	26	15.4
Extracranial vessels stenosis	15	8.9
intracranial and extracranial vessels stenosis	6	3.5

Table 2. The relationship between serum uric acid level and stroke risk factors

Variable	Uric acid	P
sex		
Female	1.52±4.98	0.065
Male	1.40± 5.41	
Age Group		
Under 60 year	1.68±5.23	
61-80 year	1.32±5.21	0.824
above 80 year	1.38±5.45	
Hypertension		
Positive	1.50±5.37	0.180
Negative	1.37±5.06	
Ischemic heart disease		
Positive	1.13±5.12	0.124
Negative	1.25±5.09	
Diabetes		
Positive	1.48±5.05	0.169
Negative	1.44±5.37	
Smoking		
Positive	1.47±5.20	0.829
Negative	1.46±5.26	
Hyperlipidemia		
Positive	1.45±5.34	0.618
Negative	1.46±5.22	
Vessel stenosis		
positive	1.45±5.21	
negative	1.50±5.34	
Cranial vessel stenosis		
Extracranial vessel stenosis	1.11±5.42	0.619
Intracranial vessel stenosis	1.63±5.09	
Extracranial and intracranial vessel stenosis	1.75±6.18	

Table 3. *Results of logistic regression*

Variable	crud		Adjusted	
	P	OR	P	OR
Gender	0.032	0.247	0.470	0.730
Hypertension	0.669	0.765	0.003	0.875
Diabetes	0.614	0.759	0.263	0.810
Smoking	0.104	4.42	0.562	1.63
Narcotic drugs consumption	0.398	0.54	0.779	1.08
Ischemic heart disease	0.421	0.590	0.211	0.865
Hyperlipidemia history	0.278	1.04	0.169	1.45
Uric acid	0.336	0.81	0.703	1.07
Age	0.293	0.97	0.204	1.37

Discussion

In the present study, 22.4 % of the patients with ischemic stroke had abnormal uric acid level. This finding is similar to some of the studies done in other countries; for example, in a study in Bangladesh conducted on 60 patients with ischemic stroke, 23.3% of patients suffered from hyperuricemia (20). In a cohort study in Norway, 33% of the patients and in another study in Banglades, 22% of patients suffered from hyperuricemia (6,21). However, in some places like Rafsanjan/ Iran a low rate (10.7%) has been reported (4), while the rates reported for some places such as Ghana (46.3%) , Tehran (47.3%), India (54.9%) and Finland (50%) are very high (10, 22-24). It is clear that factors such as population, age and time of doing test affect the results. Our findings also did not show any significant difference between serum uric acid level in patients with and without stenosis. In other words, there is no relationship between the intensity of stenosis and the level of uric acid. Although we did not find a similar study to compare the results, this finding is consistent with the results of some limitted studies. For example, in a research done in Bangladesh, no relationship between serum uric acid level and the stroke has been observed (15). In a case-control study, Cazzato et al did not find any difference between the serum uric acid level of stroke and control groups (25). This finding has been confirmed in Singapore (26) and Rafsanjan studies (4). The results of the present study and aforementioned studies are consistent with the results of recent studies that disputed the negative role of uric acid in the incidence of stroke and even showed

therapeutic effect for uric acid; it seems that uric acid level may have an important role in the treatment of patients with stroke. For example, one meta-analysis that has evaluated all the studies up to 2014, shows that the increase in level of uric acid is associated with good prognosis (5).This increase also has been associated with a decrease in hemorrhagic transformation after thrombotic treatment (7) and also taking exogenous uric acid may be associated with more recovery (27). However, negative effect of uric acid on stroke cannot be disregarded (6, 8, 10, 11). The presence of these studies shows that we cannot come to a certain conclusion about the relationship between uric acid and stroke. A recent study suggests that these different results may be related to fluctuation of serum level of uric acid in the course of stroke (13). Our study also showed that the pattern of arterial stenosis is not associated with uric acid level and both intracranial and extracranial vessels are involved. We did not find a similar study in which all cerebral vessels are evaluated according to serum level of uric acid and studies in this field are limited and mainly are limited to the carotid artery. Based on the ultrasound study of cerebral vessels, in a prospective study, increase in level of uric acid is strongly associated with the intima media thickness and finally carotid artery stenosis (15). This relationship is stronger in old patients (16). Another cross-sectional study shows that carotid plaques are strongly correlated with high level of uric acid in men and it seems that sex is an important factor in stroke assessment (28). The other cross-sectional studies show that increase in uric acid is associated with increase in rigidity and resistance of all body blood vessels including carotid (14, 20). It has been reported that in people with high uric acid level the frequency of carotid stenosis is significantly high (29,30). Also, the results of another study, published in 2015 and based on the findings of the cerebral artery ultrasound, indicates that in individuals with asymptomatic carotid stenosis increase of uric acid is associated with high mortality (8). It has been observed that the incidence rate of inflammatory reactions is high in stroke patients (19,31). It seems that these negative effects of uric acid are caused through mechanisms such as increase in proliferation of smooth muscle cells of blood vessels, Endothelial dysfunction, increase in platelet aggregation and leukocytes activation (10,33), but anti oxidant and neuroprotective effects of uric acid should not be disregarded (10). In this research, we did not find any relationship between uric acid and common stroke risk factors. This finding is similar to a research conducted in Ghana (10). A study conducted in Tehran is also almost similar to ours (22); sample size of our study and the above mentioned studies might affect this conclusion. However, some articles have mentioned the relationship of uric acid with diabetes, hypertension and hyperlipidemia (15,29).

Our study also had some limitations that must be considered. First, the amount of uric acid was

measured only one time; serial measurements may increase work accuracy. Secondly, our study was based on Doppler and it is evident that Dopplex increases the value of findings. Also due to being unable to perform ultrasound for some ill patients, they were excluded from our study and this might affect the results. Generally, our study showed that a considerable portion of patients with stroke suffered from hyperuricemia. The pattern of cerebral vascular involvement in ischemic stroke patients with and without hyperuricemia was the same.

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