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Serum uric acid level in acute stroke patients

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Abstract

Background: The role of uric acid as a risk factor for vascular disease and acute stroke is controversial and there is little information about it. In this study, we determined serum uric acid levels in patients with acute stroke and assessed its relationship with cerebrovascular risk factors.

Methods: In this cross sectional study, we assessed patients with acute stroke who were admitted in Firoozgar Hospital from September 2010 to March 2011. Clinical records of patients and their serum uric acid level was investigated. Finally, collected data were analyzed using SPSS software Ver.16.

Results: Fifty five patients with acute stroke were evaluated who 25 of these patients (45.5%) were female and 30 of them (54.5%) were male. The mean age of patients was 67±14 years. Mean serum uric acid levels in the patients studied 5.94±1.70 mg/dl, and about half of the patients (47.3%) were hyperuricemic. There was a significant negative correlation between age of patients and their serum uric acid level (p=0.04, R =-0.27). Uric acid level was significantly higher in men than women (p=0.03). Hyperuricemia was associated with increased amounts of triglycerides and Low-density lipoprotein (LDL) cholesterol (p=0.03, p=0.02). In patients with acute stroke, there was no significant association between serum uric acid level and diabetes mellitus, hypertension, history of ischemic heart disease, smoking, prescription rTPA, and type of stroke.

Conclusion: Due to the high prevalence of hyperuricemia in patients with acute stroke, and its accompanying increase in triglyceride and LDL cholesterol levels, it can be considered as a risk factor for acute stroke.

Keywords: Uric acid, Acute stroke, Triglyceride.

Introduction

Stroke is a growing disease; according to a recent report. About 780000 Americans experience a new or recurrent stroke each year, on average, one stroke every 40 seconds (1). Stroke is the third common cause of death in the world after coronary heart disease and cancer especially in the elderly (2,3). The mortality rate of stroke in the acute phase is as high as 20% and it remains higher for several years after the acute event in stroke patients than in the general population (2). Stroke is the second cause of disability and dementia in adults aged ≥ 65 years worldwide: close to 25% of stroke survivors develop dementia (4). Stroke is also an important cause of morbidity and long term

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disability: up to 40% of survivors are not expected to recover their independence with self-care and 25% become unable to walk independently (2).

Uric acid is the ultimate catabolite of purine metabolism in human and higher primates (5). It exists in the extracellular compartment as sodium urate, and it is cleared from the plasma through the kidney (6). Uric acid levels are influenced by age and sex. Prior to puberty, the average serum uric acid is 3.6 mg/dl for males and females. Following puberty, value rises to adult levels with women typically 1 mg/dl less than men. This lower level in women apparently reflects estrogen related enhancement of renal urate clearance (5).

It has been reported that increased levels of uric acid are associated with established cardiovascular risk factor such as elevated serum triglyceride and cholesterol concentration, hypertension, obesity, insulin resistance and metabolic syndrome (2, 6).On the other hand uric acid has been known to exert neuroprotective effects by acting as a free radical scavenger (6, 7).In humans, approximately one half the antioxidant capacity of plasma comes from uric acid (7, 8).

The role of urate in ischemic stroke is poorly understood. A retrospective analysis of hospitalization data of 2495 patients in Glasgow suggested that higher serum urate on admission predicted poor outcome (dead or in care) and higher vascular event rate following ischemic stroke (9). By contrast a prospective hospital-based study involving 881 patients found that higher level of serum urate predicted better outcomes following stroke, suggesting that serum urate may be beneficial and protect against poor outcomes (10). In addition an experimental study showed that uric acid administered early after thromboembolic stroke is neuroprotective in the rat brain and it extends the benefits of recombinant tissue plasminogen activator (rTPA) (11).

Therefore the role of uric acid as a risk factor for vascular disease and acute stroke is controversial and there is little information about it, so in this study we decided to determine serum uric acid levels in patients with acute stroke and assess its relationship with cardiovascular risk factors.

Methods

Patients

A total of 55 patients aged from 30 to 90 years old, who were admitted in Firoozgar hospital (Tehran, Iran) were evaluated in a cross-sectional study. The patients were recruited from September 2010 to March 2011 with acute stroke. All patients were informed and the consent was obtained from all patients. Demographic data, including age, sex, and history of diseases like diabetes mellitus, hypertension, and Ischemic Heart Disease was recorded based on medical records of the patients. Smoking history and its duration was asked from the patients. As acute stroke patients were included in the study, if rTPA was administered for them, it was recorded. Baseline blood pressure of the patients was recorded (in supine position). Blood sample was taken from all patients with acute stroke during 24 hour of admission to check uric acid level, Fasting blood sugar and lipid profile.

Statistical analysis

Statistical analysis was done using SPSS software for windows ver.16. Mean and standard deviation (SD) of all continuous data are reported. To compare means in 2 independent groups (like diabetics and non-diabetics), independent samples T-test in normally distributed variables and Mann-Whitney U test if the distribution was not normal were used. Chi-square test was used for nominal data comparison and Spearman correlation test was used to determine relation of two continuous variables. R was reported for correlation tests. Level of significance was considered 0.05 (two-sided).

Results

Fifty five acute stroke patients were studied of whom 25 (45.5%) were female and 30 (54.5%) were male. Mean age of the patients was 67(SD=13.6) years. 46 (83.6%) had ischemic stroke and 9 (16.4%) had hemor-

rhagic stroke. 9 (16.4%) patients received rTPA.

Eleven patients had a known history of diabetes mellitus with mean fasting blood sugar (FBS) of 126.33 (SD=61.02) *mg/dl*. HbA1c was higher than normal in 16 (29.1%) patients. Regarding the data obtained, 18(32.7%) patients had diabetes (7 diagnosed by admission blood tests). Serum triglyceride level was 133.56 mg/dl (SD=58.90), a total of 9(16.4%) patients had higher than normal level of triglyceride (>150mg/dl). Serum total cholesterol level was 180.09 mg/dl (SD=47.70), Low-density lipoprotein (LDL) was 115.85(SD=36.90) and high-density lipoprotein (HDL) level was 40.29 (SD=12.20). Based on the data, 9 (16.4%) had low levels of HDL (<40 *mg/dl*).

Baseline mean blood pressure of the patients was 135/80 mmHg after stroke. 33 (60%) had a known history of hypertension.

15 (27.3%) patients smoked, 24 (43.6%) patients had a history of ischemic heart disease.

Mean serum uric acid level was 5.94 (SD=1.70) *mg/dl*. Regarding the definition of high uric acid level (more than 7 mg/dl in men and more than 6 in women), 26 (47.3%) patients had hyperuricemia.

There was a negative relationship between age of the patients and serum uric acid level (r= -0.27, p=0.04; Fig. 1). There was a statistically significant difference in uric acid level between men and women (p=0.03, Fig. 2). There was no statistically significant difference between uric acid levels in diabetics and non-diabetics, hypertensive and non-hypertensive patients.

There was a statistically significant difference in uric acid level between patients with dyslipidemia (triglyceride >150 mg/dl and LDL > 130 *mg/dl*) and normal lipid levels (p=0.03 and p=0.02, respectively).

The data for risk factors related to acute stroke are summarized in Table 1. There was no statistically significant difference between uric acid levels in patients receiving rTPA and non-receivers (p>0.05).

Table 1. Mean and Standard deviation of stroke risk factors in relation with uric acid (All evaluated associations have non-significant p-value of >0.05)

Risk Factors	Mean (SD)	Spearman's r
Age (years)	67 (13.6)	-0.27
FBS on admission (mg/dl)	126.33 (61.0)	0.06
HbA1c(mg/dl)	6.30 (2.1)	0.18
SBP (mmHg)	135.51 (23.8)	0.08
DBP (mmHg)	80.73 (11.9)	0.10
Triglyceride (mg/dl)	133.56 (58.9)	0.15
Total Cholestrol (mg/dl)	180.09 (47.7)	0.02
HDL (mg/dl)	40.29 (12.2)	-0.01
LDL (mg/dl)	115.85 (36.9)	-0.03

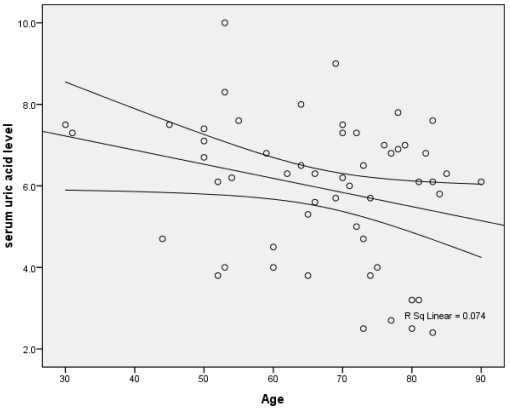

Fig. 1. Negative relationship between age of the patients and serum uric acid level (r= -0.27, p=0.04)

Discussion

In this study we determined the serum uric acid levels in patients with acute stroke. Mean serum uric acid level was 5.94 (±1.70) mg/dl and about half of the patients were hyperuricemic. According to a large 10 years follow up study the prevalence of hyperuricemia in United state is 20.1% (12). Another large study in Bangkok population showed that prevalence of hyperuricemia is 24.4%(13) and a study in a developing country reported the prevalence of hyperuricemia is 35.2% in men and 8.7% in women (14). According to these studies prevalence of

hyperuricemia is significantly higher in patients with acute stroke than normal population.

Stroke is the one of the main clinical manifestation of CVD and studies investigating the relation between the uric acid and stroke have been inconsistent. Some studies reported a positive independent relationship between uric acid and stroke whereas others demonstrated that uric acid did not relate significantly to stroke occurrence (2).

Bansal et al studied 50 patients with ischemic thrombotic cerebrovascular disease: thirty percent of the cases showed hyperuricemia and they concluded that elevated serum uric acid level may be a playing a role in the causation of ischemic thrombotic cerebrovascular disease in general and especially in patients below 40 years of age (15). Kim et al conducted a systematic review and meta-analysis of 16 prospective cohort studies including 238449 adults to assess the association between hyperuricemia and risk of stroke incidence and mortality. They found that hyperuricemia may modestly but statically significant increase the risk of both stroke incidence and mortality (1). According to results of Milionis et al study, elevated serum uric acid levels associated with increased risk of acute ischemic stroke in the elderly (16). On the other hand in the Syst-Eur trial that included patients with isolated systolic hypertension, no significant relationship was detected between serum uric acid levels and fatal and non fatal strokes (17). Moreover ,in a Japanese middle-aged population, hyperuricemia was not associated with stroke mortality in 108284 person-years of follow up(18).Goldberg et al studied middle aged men and followed them for 20 years and they did not show a significant correlation between serum uric acid and thromboembolic stroke (19). Cazzato et al. reported no difference in uric acid level between patients with stroke and control group and their results demonstrated that hyperuricemia was not a high risk factor in cerebrovascular disease (20). Recently Chen et al studied 226 hemodialysis patients and

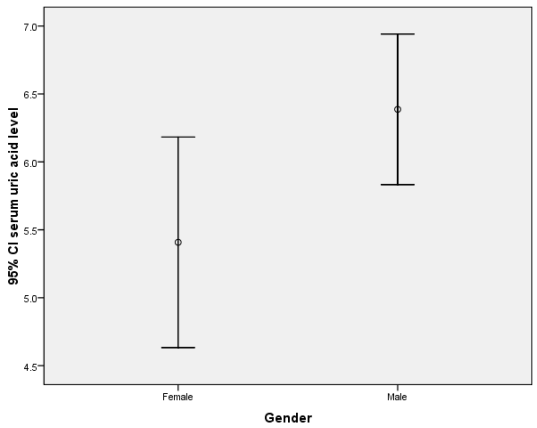

Fig. 2. significant difference in uric acid level between men and women (p=0.03)

followed them for 18 months, 43 patients experienced acute ischemic stroke; serum uric acid is inversely related to acute ischemic stroke morbidity in hemodialysis patients (21). There is some explanations for discrepancies; there are several limitations including the study design, the population studied (different ethnicities with different CVD risk) and the confounders measured (2).

In our study, there was a significant negative correlation between age of patients and their serum uric acid levels. This result in contrast to study there was a weak but significant positive association between age of patients and their serum uric acid levels (14).

Similarly to the previous studies, our study showed that the significant differences in uric acid level between men and women. In the other word, uric acid level was significantly higher in men than women (22, 23, 24) but there was no difference in prevalence of hyperuricemia between men and women. In contrast, another study by Conen et al demonstrated that prevalence of hyperuricemia is higher in men than women and higher alcohol consumption in men may be the cause of this difference (14).

In this study, there was no significant association between serum uric acid level and diabetes mellitus, hypertension and smoking. In contrast some previous studies reported significant association between insulin resistant, systolic and diastolic blood pressure

and serum uric acid levels (10,25).

Chammaro et al. assessed prognostic significance of serum uric acid concentration in patients with acute ischemic stroke and they reported that diabetic had lower uric acid concentration than other patients and uric acid concentration inversely associated with fasting blood glucose (10).A study by Bonora et al showed that there is no significant association between smoking and uric acid level (25).

In this study there was no significant association between serum uric acid level and serum triglyceride, total cholesterol, HDL cholesterol and LDL cholesterol but hyperuricemia was associated with serum triglyceride and LDL cholesterol. Some previous studies including different groups of patients, for example patients with gout, reported the association between uric acid levels and triglyceride levels (24, 26). Bonora et al studied 957 young men and demonstrated that there was a significant positive correlation between serum uric acid levels and levels of serum triglyceride, total cholesterol and LDL cholesterol (25). Another study including healthy people in developing countries showed a closely association between serum uric acid level and amount of serum triglyceride (14). Moreover, Chammaro et al reported the association between serum uric acid level and amount of serum triglyceride (10).

The mechanism of this strong association between serum uric acid levels and triglyceride levels is still poorly understood. Although some studies reported the role of genetic factors in the occurrence of gout and hypertriglyceridemia (27, 28), most of researchers believed that hyperuricemia and hypertriglyceridemia may reflect the patient's life style as a part of metabolic syndrome (14).

According to our study there was no association between serum uric acid levels and history of ischemic heart disease. In contrast a study by Freedman et al reported that hyperuricemia often exists in patients with ischemic heart disease and it can be a risk factor for these diseases (22).

In this study there was no association between type of stroke (hemorrhagic or ischemic) and serum uric acid levels. Different studies assessed the uric acid levels exclusively in patients with ischemic stroke where there was significant association between uric acid level and incidence of acute ischemic stroke (16, 29). According to results of Bos et al. ,hazard ratio of elevated serum uric acid levels in ischemic stroke was 1.77 and in hemorrhagic stroke was 1.68 (30).

Recombinant tissue plasminogen activator (rTPA) is the only approved treatment in patients with acute ischemic stroke, but because of bleeding complication of this treatment rTPA use for a little part of patients (31).In the present study, rTPA administered for 16.4 percent of patients and there was no significant difference in uric acid levels between these patients and the other patients.

Our study has some limitations. First, this study was cross-sectional descriptive, we can assess the association between uric acid level and incidence of stroke if we used cohort study. In addition, we didn't consider a control group; if we used the control group we can assess the risk factor of stroke incidence and their association with serum uric acid levels. Therefore further studies will be a cohort prospective and use the control group beside case group.

Conclusion

Our study showed that prevalence of hyperuricemia in patients with acute stroke was significantly higher than normal population. There was a significant negative correlation between age of patients and their serum uric acid levels. Uric acid level was significantly higher in men than women. Hyperuricemia was associated with increased amounts of triglycerides and LDL cholesterol. In patients with acute stroke, there was no significant association between serum uric acid level and diabetes mellitus, hypertension, history of ischemic heart disease, smoking, prescription rTPA, and type of stroke. Due to the high prevalence of hyperuricemia in patients with acute stroke, and its accompanying increase in triglycer-

ide and LDL cholesterol levels, it can be considered as a risk factor for acute stroke.

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