Original Research Article

Evaluation of Serum Uric Acid, Glucose and Nitrite-Nitrate Levels in Ischemic Stroke Patients

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ABSTRACT

Introduction: In this study, we evaluated serum levels of uric acid, nitrite-nitrate and glucose in ischemic stroke patients. **Materials and Methods:** The study was performed on 60 ischemic stroke patients admitted to the Rouhani Hospital in Babol and 60 healthy volunteers as controls. The subjects were matched in terms of age and gender. Uric acid and glucose levels were measured with standard biochemical kits. Level of nitrite-nitrate was evaluated by the Griess method. Data were analyzed with SPSS (version 19). **Results:** Serum uric acid, glucose and nitrite-nitrate levels were higher in ischemic stroke patients compared to healthy controls. However, these differences were not statistically significant ($P>0.05$). **Conclusions:** Serum uric acid, glucose and nitrite-nitrate levels are higher in ischemic stroke patients compared to healthy controls. Therefore, these factors could be used as useful markers for identification of elderly subjects at risk of ischemic stroke.

KEYWORDS: Ischemic stroke, uric acid, glucose, nitrite-nitrate

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INTRODUCTION

The incidence and mortality of stroke are increasing worldwide [1]. Ischemic strokes account for 87% of all strokes [2]. It is also the second cause of disability and dementia in adults aged ≥ 65 years, as 25% of stroke survivors develop dementia [3]. The prevalence of stroke mortality in Iran has been reported to be about 9.8% [4,5].

Uric acid (UA) is the end product of purine metabolism in humans [6]. Epidemiological studies suggest that increased serum UA level increases the risk for vascular disease [7-10]. It has been reported that medications that lower serum UA levels can reduce vascular disease morbidity and mortality [11,12]. Serum UA could be used as a marker for identification of elderly subjects at risk of ischemic stroke [13]. Moreover, hyperglycemia in acute phase of ischemic stroke, even in the absence of preexisting diabetes, has been thought to increase the stroke mortality and morbidity rates [14,15]. Post-stroke hyperglycemia is also independently associated with infarct volume in magnetic resonance spectroscopy studies and poor functional outcome [16]. Therefore, measuring serum glucose could be useful for identification of patients at risk of acute stroke. Nitric oxide has important roles in the human body, and acts as a vasodilator, neurotransmitter, immune-modulator, and antagonist of platelets and leucocytes [17]. It is also an important marker for inflammation and oxidative stress [18]. Nitric oxide synthases are a family of enzymes that produce nitric oxide from L-arginine. Endothelial nitric oxide synthase regulates vascular function, especially vasomotor tone and platelet and leucocytes activity. It has a short lifetime, and is ultimately converted to nitrite and nitrate (NOx) [19]. Therefore, measuring NOx may predict the risk of stroke. In this study, we aimed to evaluate

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serum UA, glucose and NOx levels in ischemic stroke patients.

MATERIALS AND METHODS

Subjects

The study included 60 ischemic stroke patients admitted to the Emergency Department of Rouhani Hospital in Babol and 60 healthy volunteers. The subjects were matched in terms of age and gender. Diagnosis of ischemic stroke was based on history taking, physical and neurological examination and neuroimaging studies. A neurologist confirmed diagnosis of ischemic stroke. Inclusion criteria included the following: 1. admission within 24 hours after the onset of symptoms, 2. persistence of neurological deficit on admission. Subjects with renal disease, liver disease, gout and hyperlipidemia were excluded from the study. Informed consent was taken from all subjects. Study protocol was approved by the Ethics Committee of Babol University of Medical Sciences. Clinical characteristics, age, gender, and medical history of patients were recorded. Blood samples were taken from all patients with ischemic stroke during the first 24 hour of admission, and then serum was separated and immediately stored at -80 °C.

Assays

Serum levels of glucose and UA were measured using commercial kits according to the manufacturers' instructions (UA and Glucose kits, Tehran, Iran), with some modification [20,21]. NOx levels were measured by the Griess method as described previously with some modification [22]. Briefly, 100 µl of standard or sample solution were mixed with 1 ml Griess reagent (containing 10 mg/mL sulfanilic acid (1%) in phosphoric acid (5%) and 0.1% N-(1-naphthyl) ethylene-diamine di-hydrochloride), and then incubated for 10 min at 37 ^{o}C. Absorbance was read at 450 nm, and level of NOx was calculated by using calibration curve. For this purpose, mean of the absorbance values for the blank and test samples was calculated, and then the blank value was subtracted from absorbance values of the samples.

Statistical analyses

Data are presented as mean ± standard deviation (SD). Statistical analysis was performed in SPSS (version 19). Differences between groups were assessed using two-sample independent t-test. Relationships were evaluated using the Spearman's rank correlation coefficient (rs).

RESULTS

Serum UA, glucose and NOx levels in patients were higher than in the controls, but these differences were not statistically significant (P>0.05). There was no correlation between serum UA and glucose levels of patients (rs=-0.035). However, there was a positive correlation between serum UA and NOx levels of patients (rs=0.02). P-values less than 0.05 were considered as statistically significant.

Table 1. Serum UA, glucose and NOx levels in acute stroke patients and healthy controls

Variable	Patients (n=60)	Controls (n=60)	P-value
UA (mg/dl)	4.83±3.7	4.14 ±1.8	0.08
Glucose (mg/dl)	193.06±26.00	158.06±32.9	0.145
NOx (mg/dl)	58.0±6.7	52.0 ±9.2	0.192

DISCUSSION

In this study, serum UA level was higher in ischemic stroke patients compared to healthy controls. Numerous studies have reported the relationship between serum UA and ischemic stroke. A study reported that UA is significantly increased in acute ischemic stroke patients [23]. Increased serum UA in elderly patients is associated with increased risk of cerebral infarction [13]. In contrast, some studies indicated that there is no association between serum UA level and risk of acute ischemic stroke. In addition, some studies reported no significant difference in serum UA levels between patients with

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cerebrovascular disease and controls [24]. The discrepancies in the results of these studies could be related to the difference in the study design and the characteristic of populations were studied [25]. Increased UA level could be attributed to capacity of ATP production in the brain following ischemia and antioxidant and protective role of UA [26-31]. Serum uric acid is inversely related to acute ischemic stroke morbidity in hemodialysis patients. [26].In our study, serum glucose level in patients was higher than in healthy controls. Some studies reported that hyperglycemia is present in patient without diabetes mellitus [14,15]. Several studies showed that hyperglycemia is a stress response to acute stroke [21,32,33], independent of diabetes mellitus [34]. This clinical characteristic of the disease could be due to stress response, metabolic and hormonal response and cytokines-induced insulin resistance [35]. High serum glucose concentration in the acute phase of ischemic stroke increases lesion size and worsens clinical status of patient. This can be attributed to high pH in brain caused by glucose metabolism in hypoxic conditions.
In this study, serum NOx was higher in ischemic stroke patients. A study showed that NOx increased in ischemic stroke patients before neurorehabilitation [35]. In consistent with our results, Rashid et al. showed that plasma NOx level is lower in acute stroke patients ,they reported that low levels of NOx are present in stroke and are associated with severity and outcome [19].

CONCLUSION

Serum UA, glucose and NOx levels are higher in ischemic stroke patients compared to healthy controls. Therefore, these factors could be used as useful markers for identification of elderly subjects at risk of ischemic stroke.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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