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ASSESSMENT OF OXIDATIVE STRESS IN PATIENTS WITH ACUTE ISCHEMIC STROKE

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Abstract: *A lot of studies showed the role of oxidative stress in more than 100 diseases, many neurodegenerative diseases and also in ischemic stroke.* ***Objective****: to assess the variation of oxidative stress in the acute phase of ischemic stroke and to find if there is any correlation with the clinical status or with any other biochemical parameter.* ***Methods****: We prospectively studied markers of oxidative stress – Total Antioxidant Status (TAS), uric acid, albumin, and copper - in 27 patients with acute ischemic stroke comparing with 19 controls.* ***Results and conclusions****: We found mean levels for TAS and copper lower in patients with acute ischemic stroke than in controls. Levels of TAS correlated almost linearly with uric acid but not with albumin or copper. TAS correlated with NIHSS score in patients who presented higher or lower levels of one of the individual oxidative stress marker – uric acid, albumin or copper.*

Key words: *oxidative stress, stroke, total antioxidant status.*

1. Introduction

Free radical formation is the pivotal mechanism of neuronal injury in ischemic and reperfused brain tissue. Enhanced antioxidant capacity (individually and total) after acute stroke, therefore, may protect against the adverse effects of free radical production during ischemia and reperfusion. Antioxidant activity is known to reflect the altered redox balance of affected fluids, tissues or organs in acute ischemic stroke patients. Therefore antioxidant concentrations or measures of their activity have been used to estimate the amount of oxidative stress. No single component of serum antioxidant complex could fully reflect the protective efficiency of blood, probably because of interactions that occur *in vivo* among different antioxidant compounds. A number of individual components present in serum have been shown to possess antioxidant capacity, including albumin, uric acid, bilirubin and protein thiols, vitamin C and E, minerals known to be involved in antioxidant enzyme activation (selenium, iron, copper and zinc). Total antioxidant status (TAS) considers the cumulative effect of all antioxidants present in blood and body fluids and is believed to be a useful measure of how much the antioxidants present can protect against oxidative damage [7, 4].

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2. Objectives

The aim of the study was to measure changes in markers of antioxidant capacity, measured individually (uric acid, albumin, copper) and total (Total Antioxidant Status - TAS), following acute ischemic stroke and to find if there is any correlation between them and with the clinical status evaluated by NIHSS (National Institutes of Health Stroke Scale).

3. Patients and methods

In a prospective study, we included 27 patients with acute ischemic stroke comparing with 19 controls, subjects defined as being free of major medical or surgical illness within 5 years and leading an active and independent life. All of controls were aged, between 41-69 years. From the stroke group we excluded patients who presented diseases that could modify the oxidative status: as sepsis, other inflammatory disease, cancer or acute renal failure, hepatitis, history of gout, other neurodegenerative disease or those taking supplemental vitamins or micronutrient supplementations. All stroke patients were clinical assessed by NIH Stroke Scale. Cerebral CT scan was done in the first 24 hours after the admission in the hospital to exclude hemorrhagic stroke.

3.1. Laboratory

Blood tests were done in the first 72 hours after the onset of stroke.

Total Antioxidant Status (TAS) was measured spectrofotometrically, Randox Laboratories Ltd. U.K. reagents were used. Uric acid, copper, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, bilirubin, albumin, C-reactive protein (CRP), were analyzed with Hitachi 717 Boehringer Mannheim automatic analyzer, using Futura System reagents.

Statistical analyses were performed by using the program STATISTICA Six Sigma version 8.0.

4. Results

Table 1 shows baseline laboratory tests of controls and stroke patients.

Laboratory tests of controls and stroke patients Table.1

	Controls			Stroke		
	Range	**Median**	**Mean±SD**	**Range**	**Median**	**Mean±SD**
Age (years)	41-69	53,00	53,42±8,51	50-85	73	69,70±11,13
Albumin (g/dL)	3,40-4,60	4,19	4,02±0.31	2,13-5.16	3.35	3,55±0,69
HDL-Cholesterol (mmol/L)	0,99-2,01	1,60	1,59±0.35	0,67-1,59	1,41	1,34±0,20
LDL- Cholesterol (mmol/L)	2,64-3,76	2,9	3,05±0,37	0,44-5,49	2,54	2,67±1,16
CRP (mg/L)	5,45-9,50	6,50	6,89±1,35	8,2-17,1	10.4	11,33±2.49
Copper (µg/dL)	80,60-145,5	128,78	125,41±18,15	79,54-137,07	110,50	111,30±14.28
TAS(mmol/L)	1,40-1,80	1,60	1,61±0,14	0,89-2,09	1.14	1,29±0.38
Uric Acid (µmol/L)	294,3-398,0	315,20	319,83±31,10	168,7-589,41	310	322,67±78.48

Mean values, for TAS and copper were lower in stroke patients than in controls.

We also found lower values for albumin, without statistical significance in patients

with acute ischemic stroke. Uric acid presented almost similar values in both lots with no significant higher levels in patients with stroke than in controls.

Values of TAS correlated almost linearly with those of uric acid (Figure1). There were no correlation between albumin, copper (Figure 2) and TAS in patients with acute ischemic stroke, nor between CRP, LDL and TAS. Regarding the relationship between oxidative stress and neurologic status for the whole lot, we found no correlation between values of TAS and NIHSS score in patients with acute ischemic stroke (Figure 3).

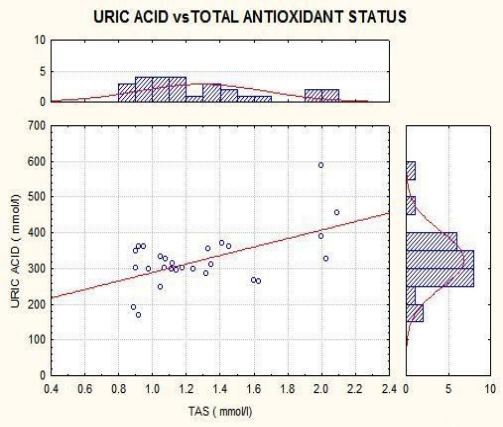

Fig. 1. *Levels of uric acid versus TAS*

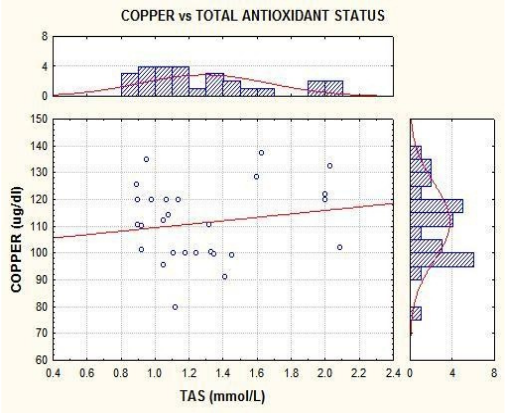

Fig. 2. *Levels of copper versus TAS*

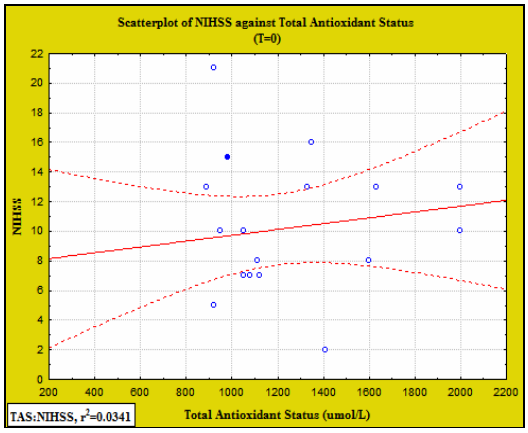

Fig. 3. *Value of NIHSS score versus TAS*

We tried to represent in tridimensional graphics how level of each individual oxidative stress marker, correlates with level of total antioxidant status (TAS) and NIHSS score. We observe some correlation between levels of uric acid, albumin, copper and TAS depending of the grade of the neurologic deficit (Figure 4).

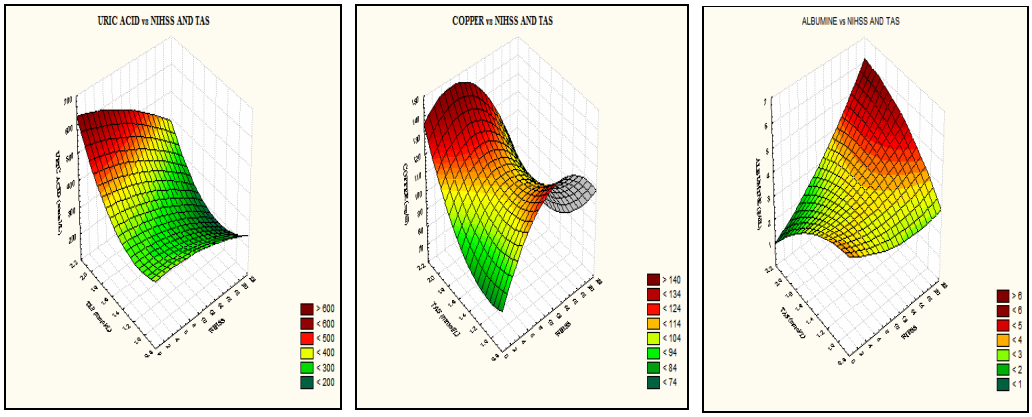

Fig. 4. *Correlation between uric acid, copper and albumin versus TAS and NIHSS*

Inflammatory status, evaluated by C-reactive protein (CRP), varied with levels of TAS depending on values of NIHSS (fig.5).

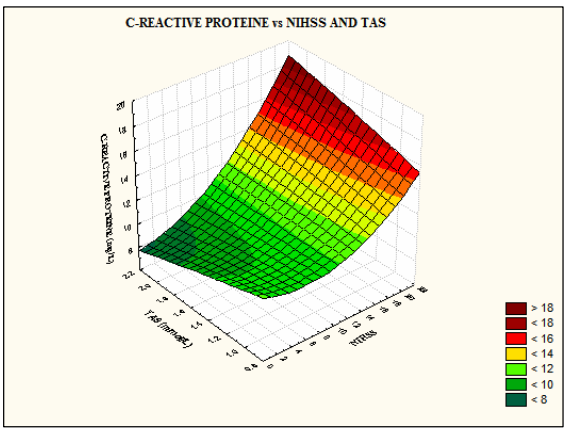

Fig. 5. *Correlation between CRP, TAS and NIHSS*

CRP was lower in patients with minor neurologic deficit and independent of the levels of TAS and presented highest levels in those with higher values of NIHSS and higher levels of TAS.

Discussion

We found lower levels of TAS in patients with acute ischemic stroke, similar to other studies [4,8].This appears, probably, by consuming of antioxidant at the place of ischemic lesion and usually correlates with the growth of infarct and with the clinical status assessed by NIHSS. Gariballa and Shikrishna found lower levels of TAS despite increased concentrations of uric acid in stroke patients compared with both control groups [7,4], while Cherubini et al. found lower levels of uric acid on admission, which showed a gradual increase over

time, in patients with acute ischemic stroke [3,6].

Despite similar values of uric acid, TAS was reduced in stroke patients compared to controls. This difference appeared, may be, because of the consumption of antioxidant concomitant with increasing in production of uric acid under ischemic conditions, immediately after onset, fact proved by recently studies [8].

There is well known that uric acid may have a direct role in the atherosclerotic process, because human atherosclerotic plaques contain more uric acid than do control arteries [4].

Contrary, more recently studies demonstrated that uric acid, the most abundant endogenous aqueous antioxidant in humans, may protect against oxidative modification of endothelial enzymes and preserve the ability of endothelium to mediate vascular dilatation during oxidative stress. Several studies have shown, also, that increased oxidative stress is associated with high circulating uric acid levels due to elevation of xanthine oxidase in stroke induced brain damage [7]. Recent studies showed neuroprotective effect of administration of uric acid, immediately after manifestation of brain ischemia [2].

We found in our study values of TAS correlated almost linearly with those of uric acid, similarly to other studies [7, 4, 9, 10]. This correlation appeared, probably, because TAS is represented in majority by the uric acid.

There was no correlation between albumin and TAS for the majority of patients. However, albumin presented highest levels in patients who associated higher levels of TAS with important neurological deficit.

Significant lower values for copper – essential coenzyme in CuZnSOD (CuZn superoxidismutase) – were obtained in patients with acute ischemic stroke than in controls. Levels of copper were highest in patients with highest values of TAS, independent of the intensity of neurologic deficit. Zimmermann and col. found no significant differences in levels of iron, copper or zinc – minerals known to be involved in antioxidant enzyme activation like SOD – in patients with acute ischemic stroke [11].

We didn`t obtain a correlation between TAS and neurological deficit (NIHSS) for the whole lot of the patients, but TAS correlated with the neurological deficit (NIHSS), in those who presented higher or lower levels of one of the individual oxidative stress marker – uric acid, albumin or copper. Many previous studies found an association between total antioxidant capacity and growth of the infarction and severity of neurological impairment assessed by NIHSS [1, 5].

Patients with lower values of NIHSS and CRP and those with important neurologic deficit with high values for CRP associated higher levels of TAS. There is also some recent evidence of an association between oxidative damage and tissue inflammation as measured by C-reactive proteins (CRPs) in subjects with stroke disease [4].

Larger clinical studies in this area are needed to clarify the temporal relationship between antioxidant capacity and oxidative damage following ischemia and reperfusion in man, and to form the basis of appropriate antioxidant intervention strategies to minimize long-term brain injury following cerebral ischemia and also its role in preventing cerebrovascular disease.

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