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Evaluation of MMP-9, TIMP-1 and S-100B concentrations in asymptomatic and symptomatic carotid artery stenosis as a potential marker of cerebral ischemic events.

ABSTRACT

Background and purpose:

Stroke is the third most common cause of death and a major cause of permanent disability and loss of independence in adult patients. Every year, 3 million women and 2.5 million men die from this disease worldwide. For the causes of ischemic stroke, among others, include carotid artery stenosis. The aim of this dissertation was to assess the concentrations of MMP-9, TIMP-1 and S-100B in patients with ischemic stroke (with and without internal carotid stenosis), and in patients after endarterectomy of the internal carotid artery as possible prognostic factors of stroke. In addition, the effect of S-100B protein concentration in relation to the risk of malignant edema in patients after ischemic stroke.

Material and methods:

113 patients were examined - 80 with symptoms of ischemic stroke admitted to the Neurology Clinic of the Central Clinical Hospital of the Ministry of Interior and Administration in Warsaw and 33 patients undergoing carotid endarterectomy in the Department of General and Vascular Surgery of the Central Clinical Hospital of the Ministry of Interior and Administration in Warsaw. In each patient on admission, the clinical status, biochemical and haematological parameters, and concentrations of MMP-9, TIMP-1 and S-100B protein were evaluated. In the next days of hospitalization, the clinical status was reassessed and biochemical and haematological control tests were performed, and in the case of patients with ischemic stroke, differential diagnosis was performed. Neuroimaging (TK/MR) was performed twice (on admission and on the 7th day), while in those subjected to thrombolysis an additional 24 hours after the procedure.

Results:

63 women and 50 men were subjected into the analysis. The median age was 74 years (range 34-98). In patients with an ischemic stroke with accompanying neurological deterioration a higher mean value of the MMP-9 (89.81 ng / ml vs. 74.35 ng / ml) and TIMP-1 (192.61 ng / ml vs. 160.63 ng / ml) was found when compared to other patients with previous ischemic stroke, while a lower mean concentration of S-100B (28.97 pg / ml vs. 45.38 pg / ml). However, no statistical significance was found in any of abovementioned markers.

We found higher concentration of S-100B protein in patients with ischemic stroke with concomitant malignant cerebral swelling than in all patients with previous ischemic stroke (79.71 pg / ml vs. 45.38 pg / ml).

We found lower concentration of MMP-9 in patients with ischemic stroke without haemodynamically significant stenosis of internal carotid artery (ICA) when comparing to the whole group (59.897 ng / ml vs. 71.051). In the same time we observed a lower mean concentration of MMP-9 in those individuals without ICA stenosis than in patients with stroke with concomitant stenosis more than 50% (59.897 ng / ml vs. 93.902) and slightly higher than patients after carotid artery surgery (56.625 ng / ml vs. 59.897 ng / ml).

We also found lower concentration of TIMP in patients with ischemic stroke without haemodynamically significant stenosis of internal carotid artery (ICA) when comparing to the whole group (150.284 ng / ml vs. 128.96 ng / ml). We observed a lower mean concentration of TIMP in patients without ICA stenosis than in patients with stroke with concomitant stenosis more than 50% (129.860 ng / ml vs. 195.248 ng / ml) and slightly higher than in patients after carotid artery surgery (122.457 ng / ml vs. 128.960 ng / ml).

The mean concentration of S-100B in patients with ischemic stroke without haemodynamically significant stenosis was higher when comparing to the whole group (47.66 pg / ml vs. 41.34 pg / ml), whereas only slightly higher then in patients with stroke and stenosis > 50% (47.660 pg / ml vs. 41.920 pg / ml) and significantly higher than in patients after carotid artery surgery (47.660 pg / ml vs. 13.580 pg / ml).

Conclusions:

Elevated levels of MMP-9 and TIMP-1 in patients with carotid stenosis $\geq 50\%$ may be important factor of increased risk of stroke at the side of stenosis or even death. Elevated concentration of MMP-9 may be also a marker of neurological deterioration in patients in the

early period after endarterectomy as well as in those in the acute phase of ischemic stroke. The post-stroke higher release of protein S-100B may have positive predictive value for occurrence of life-threatening malignant cerebral swelling.