Change in Platelet Monoamine Oxidase Activity in the Acutest Period of Ischemic Stroke Is Associated with the Degree of Neurological Recovery

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We studied monoamine oxidase activity (MAO) in platelets of patients in the acute period of ischemic stroke. Neurological deficit was evaluated by the data of clinical examinations and scales. In 80% patients MAO activity was considerably increased on 3-5 day after stroke. We found a correlation between increased MAO activity on 3-5 day after ischemic stroke and regression of neurological deficit on day 21 after ischemic stroke. The increase in MAO activity during the acute period of ischemic stroke is presumably a compensatory response aimed at stabiliziation of tissue homeostasis.

Key Words: *monoamine oxidase; ischemic stroke*

Effective treatment of ischemic stroke (IS) requires studies of new pathogenetic factors possessing a prognostic value during the acute period of the disease for the prognosis of subsequent recovery of neurological functions. In local cerebral ischemia, one of the pathogenetic mechanisms affecting neuroplasticity is related to metabolic changes in biogenic monoamines such as serotonin and dopamine [2,10,12]. Monoamine oxidase (MAO) as a key enzyme inactivating serotonin and dopamine via oxidative deamination determining the functional status of monoaminergic systems [2-5,10,11]. Pronounced activation of serotonin and dopamine oxidative deamination by MAO was revealed in different brain structures during postischemic (acute) stage of the experimental IS [7,10,12]. Change in MAO activity is probably a pathogenetic factor affecting neuroplasticity during IS, but we found no clinical trials on this issue. Direct study of MAO activity in the brain of patients with IS is impossible. Human blood platelets are known to be used as a model of peripheral serotonergic and dopamine synapses in CNS [12,13]. Despite certain limitations, analysis of MAO activity in platelets allows indirect evaluation of CNS processes (*e.g.* particular oxidative deamination) [3,12,13].

Here we studied MAO activity in platelet in the acute period of IS in patients with different degree of neurological function recovery and estimated possible prognostic value of MAO activity for regression of neurologic deficit.

MATERIALS AND METHODS

Clinical and biochemical study of 25 patients (14 females, 11 males, mean age 67±10 years) with verified IS in carotid system was conducted. The severity of neurological deficit in patients with IS was assessed by clinical examination data and with the NIHSS (The National Institutes of Health Stroke Scale, 1989) and the Barthel indexes (1965). The major etiological factors of IS in 64% cases (19 patients) were atherosclerosis and arterial hypertension and 30% cases were associated with heart diseases (11 patients). Clinical symptoms and the therapy were described previously in detail [4].

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TABLE 1. Platelet MAO Activity in Patients in the Acute Period of IS and in Clinically Healthy Subjects

MAO, nmol benzaldehyde/mg protein/h	Median	Standard deviation	Value		Percentiles	
			minimum	maximum	10	90
Control (*N*=17)	8.70	0.78	10.2	7.96	7.96	10.2
Patients with IS (*N*=25)	16.10	8.5	7.00	35.7	9.5	30.1

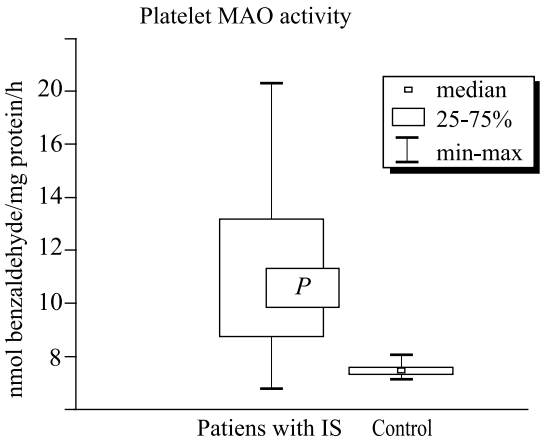

Fig. 1. Comparative analysis of MAO activity in platelets of patients with IS on days 3-5 of the disease and in the group control. $p<0.00002$.

The control group comprised 17 age- and sex-matched healthy persons without signs of CNS pathology and chronic cerebrovascular insufficiency. The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from each participant.

Biochemical assay was carried out on days 3-5 of IS. MAO activity in platelets was measured as described previously [1].

Statistical analysis was performed by parametric and nonparametric tests assessing differences and consistency of variables using Statistica software. Differences were considered significant at $p<0.05$.

RESULTS

On days 3-5 of IS, a significant increase in platelet MAO activity was revealed in 80% patients. The values for the two groups are presented in Table 1 as median and the 10th and 90th percentiles. On day 3-5 of the disease, patients with IS showed sharp increase in platelet MAO activity versus control group at the maximum significance level (Mann–Whitney *U* test, $p<0.00002$; Fig. 1). These results demonstrate pronounced activation of deamination due to increased monoamine activity in patients with IS. Similar results were obtained in experimental studies on various models of IS [7,9-11]. The levels of dopamine and serotonin deamination products are shown to increase greatly in the postischemic period during brain reperfusion. A correlation between the levels of monoamines and glutamate was demonstrated experimentally. The role of glutamate in excitotoxicity and apoptotic neuronal death during local cerebral ischemia is well documented [2,9,10].

Thus, enhanced MAO activity in the acute period of IS is a compensatory response aimed at stabilization of homeostasis. Significant association between MAO activity and regression of neurological deficit revealed by dynamic monitoring of patients with IS confirms this assumption. On day 21 of the disease (end of acute period), 80% patients showed moderate or good recovery of neurological functions against the backgrounds of treatment, while 5 patients (20%) demonstrated minimal functional recovery, and in all cases MAO activity was reduced or normal. Logistic regression revealed a negative correlation between MAO activity at days 3-5 of acute cerebrovascular disease and the severity of neurological deficit (NIHSS score) on day 21 of IS. The chi-square test for association between two variables yielded $(\chi^2\text{-}1)=7.47$ ($p=0.005$) with odds ratio 1.29. A strong positive correlation was revealed between the total values of MAO activity and Bartel index scores: MAO on days 3-5 of IS/ Bartel on day 21 of IS: $r=+0.66$, $p<0.05$.

Thus, the revealed pathogenetic relationship between MAO activity and regression of neurological deficit allows considering this enzyme activity as a possible biomarker of functional post-stroke recovery.

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