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ENZYME BLOOD LEVEL DISORDER AS A MARKER OF METABOLIC PROCESSES SEVERITY IN MULTIPLE SCLEROSIS

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Dynamics of membrane-bound enzymes activity changes in the blood of 67 patients with multiple sclerosis was investigated depending on the variety and duration of the disease. It was noted that the most pronounced enzymatic dysbalance was observed in patients with cerebrospinal multiple sclerosis and in patients with the disease duration over 10 years, which is a marker of disease severity and degree of the pathological process generalization. Decreased CPK level in patients with all varieties of the disease, regardless of multiple sclerosis duration, reflects the degree of reduction of metabolic and energy processes rate in the cells of muscular and nervous tissues, possibly due to increased catabolism and, as a consequence, development of movement disorders.

Key words: multiple sclerosis, enzymes.

At present multiple sclerosis (MS) is the second disabling disorder among nervous system disorders in Ukraine [1]. Medical and social significance of this problem is caused, on the one hand, by steady growth of the number of MS patients, among whom the vast majority are young and middle-aged persons, on the other hand, by the treatment complexity, which, despite significant economic costs, not always allows preserving ability to work and vitality [2–4].

Today the problem of pathophysiology of the demyelinating process is investigated in depth, as the theory, according to which immunological disorders are the dominant factor in myelin damage, undergoes changes. Herein, more attention is paid to other causes of demyelization and axonal damage, including disorders of a number of metabolic processes in neurons and their processes. It is known that when metabolism of proteins, amino acids, hormones is disturbed, the activity of a number of enzymes and the content of certain minerals change [5, 6]. Having a close relationship with macro- and microelements, hormones, vitamins and other biologically active substances, enzymes are indispensable participants of all physiological processes in the organism. The change in their activity suggests of disorders of intracellular metabolic processes and redox reactions. Thus, identification of enzyme dysbalance and determination of its degree in the blood of MS patients may be an indicator of cell dystrophy and have some diagnostic and prognostic significance for assessing severity of neuronal damage in MS.

The purpose of this work was to study the dynamics of the changes in activity of membrane-bound enzymes in the blood of MS patients, depending on the variety and duration of the disease.

This study involved 67 MS patients (main group), of them 28 men and 39 women treated at the neurology department. The mean age was 30.1±9.3 years.

All patients were diagnosed MS according to McDonald's criteria (2010) [7], and underwent MRI investigation which confirmed the presence of demyelinating foci in the central nervous system. Depending on the clinical manifestations cerebral MS was diagnosed in 14 patients, spinal in 5 and cerebrospinal in 48. Mean level of the functional disturbances by EDSS (Expanded Disability Status Scale) [8] in 49 MS patients was under 5 points (moderate signs of disability and moderate dependence) and over 5 points in 18 patients.

At the time of the examination the disease duration under 5 years was present in 21 patients, from 5 to 9 years in 26 patients, and over 10 years in 20 patients.

The controls were 30 healthy age- and sex-matched persons without any nervous system pathology.

Enzymes activity and the content of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), creatine phosphokinase (CPK), gamma-glutamyl transpeptidase (GGT), lactate dehydrogenase (LDH) were studied using enzymatic kinetic method with biochemical analyzer Screen master lab (Hospitex Diagnostics, Switzerland, Italy) using standard procedures.

The obtained data were statistically processed with statistical software package Statistica 6. Mean values and mean error were calculated. Parametric Student's test was used as a criterion for significance of the samples difference; the differences were considered significant at $p < 0.05$.

The performed clinical neurological examination revealed that the study group presented predominantly with pyramidal disorders such as central and hemiparaparesis (91%), cognitive dysfunction (80%), cerebellar ataxic syndrome (74.5%), sensitive disorders (74%), syndromes of the brain stem and cranial nerves lesions (58.5%), visual disorders (44%), sphincter disorders (39.5% of cases).

Mean EDSS values in patients with different varieties and duration of the disease revealed the lowest

rate in patients with cerebral MS (3.0–3.5), and the highest in patients with cerebrospinal MS (4.0–6.0 points). Directly proportional relationship in deterioration of the functional state of MS patients assessed by EDSS and increase of the disease duration were noted. Thus, in patients with disease duration under 5 years, mean values of the functional condition ranged within 3.0–4.0 points, in patients with disease duration of 5–9 years it ranged within 4.0–5.5 points, while at disease duration over 10 years the total on the scale of disability reached 5.0–6.0 points.

The analysis of the values of enzyme activity in MS in the whole showed significant reduction of CPK by 56.5% and elevation of ALT by 38.9% vs. the controls, as well as a tendency to reduction of AST levels (by 12.5%), ALP (by 10.6%) and increased GGT (by 23.9%) (Table 1).

The direction and intensity of enzymatic dysbalance depended on the variety and duration of the disease. Thus, a significant reduction of AST by 32.2% and CPK by 72.3% as well as a tendency to reduction of LDH levels by 16.5%, increase in ALT levels by 50.4% and GGT by 14.4% vs. the controls (Table 2) were revealed in patients with cerebral MS. In patients with spinal MS only a significant reduction in CPK levels by 71.0% was present. Increased activity of AST, ALT, ALP and GGT vs. the controls was not statistically significant, but demonstrated a definite tendency (Table 2).

The most pronounced changes in enzyme activity were observed in patients with cerebrospinal MS, which differed not only from the controls, but also significantly differed from those in other varieties of the disease. Enzymatic dysbalance in these patients was characterized by a significant decrease of activity of ALP, CPK, LDH by 16.9; 67.3 and 16.6%, respectively, 28.9% higher vs. the controls ALT levels (Table 2).

The analysis of the findings on the blood enzymes content depending on MS duration demonstrated that in patients with the disease duration under 5 years ALT level was significantly elevated by 34.5% and CPK was reduced by 55% vs. the controls. Increased GGT (by 43%) and reduced ALP level (by 14.7%) in these patients generally had a clear tendency though not significant. AST and LDH activity values ranged greatly vs. the controls, therefore in general these patients did not have any changes in these values (Table 3).

The analysis of the biochemical findings in patients with MS duration ranging within 5–9 years showed a significant reduction in the levels of AST,

Table 1

The content of membrane-bound enzymes in the blood serum of MS patients

Group	AST	ALT	ALP	CPK	LDH	GGT
Main, $n = 67$	23.16±2.11	24.41±2.23*	189.71±12.54	35.55±6.89*	363.65±26.22	21.82±3.01
Controls, $n = 30$	26.48±1.81	17.58±0.63	212.18±11.07	81.71±9.13	379.78±21.99	17.61±1.18

* $p < 0.05$ as to the controls. The same in Table 2, 3.

Table 2

Enzyme activity dynamics in patients with MS depending on the disease variety

MS variety	AST	ALT	ALP	CPK	LDH	GGT
Cerebral, $n = 14$	17.96±3.74*	26.44±5.26	191.88±24.61	22.61±4.52*	317.01±38.81	20.14±5.39
Spinal, $n = 5$	30.82±11.03	35.15±9.67	242.68±75.65	23.68±6.12*	382.73±31.15	21.88±4.17
Cerebrospinal, $n = 48$	24.04±1.71	22.66±2.21*	176.29±10.98*	26.73±5.49*	316.73±16.21*	21.08±2.89
Controls, $n = 30$	26.48±1.81	17.58±0.63	212.18±11.07	81.71±9.13	379.78±21.99	17.61±1.18

Table 3

Enzyme activity values in patients with MS depending on the disease duration

MS duration	AST	ALT	ALP	CPK	LDH	GGT
Under 5 years, $n = 21$	25.08±3.32	23.65±3.02*	180.92±17.01	36.79±10.59*	343.89±21.85	25.22±5.01
5–9 years, $n = 26$	19.06±2.68*	24.24±4.03	190.57±16.98	28.81±7.57*	301.18±25.31*	19.68±4.21
Over 10 years, $n = 20$	26.73±4.52	12.97±6.24	163.01±12.87*	22.02±3.22*	318.06±29.92	18.19±2.36
Controls, $n = 30$	26.48±1.81	17.58±0.63	212.18±11.07	81.71±9.13	379.78±21.99	17.61±1.18

CPK, LDH by 28; 64.7 and 20.7%, respectively, vs. those in the controls. Further increase in disease duration was accompanied by a progressive reduction in enzyme activity according to significant reduction in the levels of ALP by 23.2% and CPK by 73% vs. the controls and a clear tendency to reduction of ALT (by 26.2%) and LDH (by 16.3%) in patients with MS duration over 10 years (Table 3).

The revealed enzymatic changes suggested of disorders in various intracellular metabolic processes that occurred in MS patients. Herewith, increase of ALT ($p < 0.05$) and GGT ($p > 0.05$) levels in the examined group in total and depending on the variety and duration of the disease reflected destruction of nerve cells and protein metabolism disorder. Marked reduction in CPK activity in all patients regardless of the variety and duration of MS is a marker of inhibition of metabolic and energy processes in the cells, mainly muscular and nerve tissues, which was associated with the restriction and/or a sharp decrease in the motor activity of MS patients due to disorders of the muscular tissue nerve supply. More pronounced enzymatic disorders in cerebrospinal MS compared to other varieties of the disease in the form of increased ALT levels and reduced ALP, CPK and LDH values, were apparently associated with aggravation of disorders in metabolism and redox reactions in the cells during development of the multi-level pathological process. Hypofermentemia elevation with increase in the disease duration reflected aggravation of metabolic disorders associated with predominance of catabolic processes, depletion of reserve capacity of the organism with development and progression of MS and was a poor prognostic sign.

Thus, our findings allow us to draw the following conclusion.

MS patients have a resistant dysfermentemia, severity and direction of which depend on the variety and duration of the disease.

The most pronounced reduction in the activity of the marker membrane-bound enzymes is observed in cerebrospinal MS and at disease duration over 10 years, which is a marker of the condition severity, generalization of the pathological process and depletion of the reserve capacity of the organism.

Reduced levels of CPK in all varieties of the disease, regardless of MS duration reflect the degree of deceleration of metabolic and energy processes in the cells of the nervous and muscular tissue, probably due to the development of motor disturbances.

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ДИСФЕРМЕНТЕМИЯ КАК МАРКЕР ТЯЖЕСТИ ОБМЕННЫХ ПРОЦЕССОВ ПРИ РАССЕЯННОМ СКЛЕРОЗЕ

Е. В. МАРКОВСКАЯ

Проведено исследование динамики изменения активности мембраносвязанных ферментов в крови 67 больных рассеянным склерозом в зависимости от формы и длительности заболевания. Отмечено, что наиболее выраженный ферментативный дисбаланс наблюдается при цереброспинальной форме рассеянного склероза и у пациентов с длительностью заболевания более 10 лет, что является маркером тяжести состояния больных и степени генерализации патологического процесса. Снижение уровня креатининфосфокиназы при всех формах заболевания, независимо от длительности рассеянного склероза, отражает степень уменьшения скорости метаболических и энергетических процессов в клетках мышечной и нервной тканей, возможно, из-за явлений повышенного катаболизма и, как следствие, развития двигательных нарушений.

Ключевые слова: рассеянный склероз, ферменты, маркер обменных процессов.

ДИСФЕРМЕНТЕМІЯ ЯК МАРКЕР ТЯЖКОСТІ ОБМІННИХ ПРОЦЕСІВ ПРИ РОЗСІЯНОМУ СКЛЕРОЗІ

О. В. МАРКОВСЬКА

Проведено дослідження динаміки зміни активності мембранозв'язаних ферментів у крові 67 хворих розсіяним склерозом залежно від форми й тривалості захворювання. Зазначено, що найбільш виражений ферментативний дисбаланс спостерігається при цереброспинальній формі розсіяного склерозу й у пацієнтів із тривалістю захворювання понад 10 років, що є маркером тяжкості стану хворих і ступеня генералізації патологічного процесу. Зниження рівня креатинінфосфокінази при всіх формах захворювання, незалежно від тривалості розсіяного склерозу, відображає ступінь зниження швидкості метаболічних і енергетичних процесів у клітинах м'язової й нервової тканин, можливо, через явища підвищеного катаболізму і, як наслідок, розвиток рухових порушень.

Ключові слова: розсіяний склероз, ферменти, маркер обмінних процесів.

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