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# *Serological markers of cognitive deficit development in the acute period of traumatic brain injury*

Markery serologiczne rozwoju deficytu poznawczego w ostrym okresie pourazowego uszkodzenia mózgu

## INTRODUCTION

Traumatic brain injury is one of the most important causes of invalidisation all over the world. Cognitive deficit appears in 70 % of patients who survived craniocerebral trauma. Success in the treatment of posttraumatic dementia mainly depends on the early diagnostics and appropriate pathogenic therapy. Diagnostic criteria of early posttraumatic cognitive deficit are still unclear. There are a number of neuropsychological tests which nowadays are used for diagnostics of cognitive decline in different patients but most of them need additional application of objective criteria for the verification of early cognitive deficit [1]. A number of serological markers such as protein S-100, Tau-protein and others failed the test for the applicability as clinical diagnostic markers of the development of posttraumatic dementia [1].

Long-term oxidative and nitrosative stresses are believed to be one of the major contributing factors in progression of neuronal degeneration and decline of cognitive function in posttraumatic period. Compensative activation of antioxidant defense system is one of the most important mechanisms of adequate systemic regeneration after the trauma. Experimental data showed retardation in mental development in animals with impaired function of superoxide dismutase (SOD), catalase, glutathione-transferase [1]. Nitric oxide is implicated in the processes of memory and learning both as neuromediator and endocrine regulator of neurophysiological processes. Under the condition of oxidative stress, development excessive production of NO results in the formation of toxic peroxinitrite anion and nitrosative stress development.

The aim of our work was to investigate the state of cognitive functions in patients in acute period of mild and moderate traumatic brain injury according to the standard tests of neuropsychological diagnostics and to evaluate the sensitivity of assay of lipid peroxidation activity, SOD and catalase activities and NO-metabolites concentration as serological tests for the routine diagnostics of early posttraumatic cognitive deficit.

## MATERIAL AND METHODS

We examined 27 patients in the acute period of mild and moderate craniocerebral trauma. The state of cognitive functions was examined with the use of standard test – FAB (frontal assessment battery) [2] and MMSE (mini-mental state examination) [3]. Parameters of prooxidant-antioxidant metabolic status and nitric oxide metabolites were estimated in erythrocyte hemolysate and blood plasma. Concentration of $NO_2^-$ was measured with the method [5], activity of SOD by [4], activity of catalase by [7] in erythrocyte hemolysate, concentration of MDA in blood serum by [8].

## RESULTS AND DISCUSSION

It was revealed that 83% of the examined patients have posttraumatic cognitive deficit. The correlation analysis showed that in the scoring between the scales of FAB and MMSE) and MDA concentrations there is a negative correlation average force ($r = -0.37$ scale for MMSE, $p < 0.05$, and $r = -0.48$ scale for FAB, $p < 0.05$). The same strength and directivity correlation was typical of the activity of catalase ($r = -0.31$, $p < 0.05$, and $r = -0.33$, $p < 0.05$, for the scale and MMSE FAB, respectively). A strong positive correlation was determined between SOD activity and the amount of points by the FAB in both clinical groups of patients. Regression analysis of changes in SOD activity according to the degree of the loss of cognitive functions by MMSE scale was the same for directivity (positive), but the average force. Superoxide dismutase is one of the most effective metabolic mechanisms for the inactivation of reactive oxygen species. Elevated SOD activity can be therapeutically useful by protecting against oxidative stress-induced neurotoxicity. It was found that mice with genetic overexpression of SOD do not show the aging-induced decline in learning and memory that control, wild type mice show [1].

A strong negative correlation was revealed between the growth of total $NO_2^-$ concentrations in serum of patients and total score on the scale of FAB is a ($r = -0.84$). A significant negative correlation is also observed when comparing the total score for the MMSE scale and the content of serum nitric oxide metabolites, but the strength of the relationship between these parameters is much lower ($r = -0.30$).

## CONCLUSIONS

The combination of neuropsychological testing with scale FAB and laboratory determination of $NO_2^-$ and SOD activity can be a useful diagnostic tool for posttraumatic patients who require extra attention from neuropsychologists for more adequate treatment in the acute period of craniocerebral trauma. The choice of the mentioned markers is pathogenically substantiated and can be used in routine clinical practice for precise diagnostics of posttraumatic cognitive deficit.

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## SUMMARY

The aim of our work was to investigate the state of cognitive functions in patients in acute period of mild and moderate traumatic brain injury according to the standard tests of neuropsychological diagnostics and to evaluate the sensitivity of assay of lipid peroxidation activity, SOD and catalase activities and NO-metabolites concentration as serological tests for the routine diagnostics of early posttraumatic cognitive deficit. The combination of neuropsychological testing with scale FAB and laboratory determination of $NO_2^-$ and SOD activity can be a useful diagnostic tool for posttraumatic patients who require extra attention from neuropsychologists for more adequate treatment in the acute period of craniocerebral trauma. The choice of the mentioned markers is pathogenically substantiated and can be used in routine clinical practice for the precise diagnostics of posttraumatic cognitive deficit.

*Keywords:* traumatic brain injury, cognitive deficit, nitric oxide, superoxide dismutase

## STRESZCZENIE

Celem badań było określenie stanu funkcji poznawczych u pacjentów w ostrym okresie niewielkiego i umiarkowanego pourazowego uszkodzenia mózgu w odniesieniu do standardowych testów stosowanych w diagnostyce neuropsychologicznej i dla określenia czułości oznaczeń aktywności procesów peroksydacji lipidów, aktywności SOD i katalazy oraz stężenia metabolitów NO jako testów serologicznych rutynowej diagnostyki wczesnego pourazowego deficytu poznawczego. Kombinacja testów neuropsychologicznych ze skalą FAB i oznaczeniami laboratoryjnymi stężenia $NO_2^-$ i aktywności SOD mogą być pomocnym narzędziem diagnostycznym u pacjentów pourazowych, którzy wymagają wyjątkowej uwagi neuropsychologów w kierunku wdrożenia bardziej adekwatnego leczenia w ostrym okresie urazu czaszkowo-mózgowego. Wybór wspomnianych markerów jest patogenicznie uzasadniony i mogą być one stosowane w rutynowej praktyce klinicznej w celu precyzyjnej diagnostyki pourazowego deficytu poznawczego.

*Słowa kluczowe:* pourazowe uszkodzenie mózgu, deficyt poznawczy, tlenek azotu, dysmutaza ponadtlenkowa