Condition and Consequences of Zinc Metabolic Disorder in Patients with Neurosurgical Pathology Requiring Intensive Care

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ABSTRACT

Introduction: diseases that require neurosurgical intervention for many years constitute the major cause of disability and death in the world. These patients develop the disorder of zinc supply which is a universal bioregulator.

The aim of the research is the assessment of zinc metabolism and effects of its disorder in patients with neurosurgical disorders that require intensive care.

Materials and methods: observational analytical retrospective research («Case control study» type) of zinc exchange status in 60 patients was conducted. Study group included 40 patients of neurosurgical profile who needed intensive care. Control group consisted of 20 conventionally healthy volunteers. Presence of clinical and laboratory signs of zinc deficiency, presence or absence of gastrointestinal failure, level of consciousness, need for mechanical ventilation, and severity of patient's condition were assessed. Statistical analysis of the results was performed using the methods of descriptive statistics, nonparametric comparison of two groups in terms of qualitative and quantitative indicators, establishing correlation relationships.

Results and conclusions: in neurosurgical patients requiring intensive care, on the third day of treatment reduction in plasma zinc was observed, causing the clinical signs of zinc deficiency, even without achieving the minimum diagnostically significant threshold of its content in blood of 13 mcM/l. Zinc deficiency contributes to gastrointestinal, cerebral and immune insufficiency, increases the need for artificial lung ventilation and aggravates the severity of patient's condition. At the same time, high mortality of neurosurgical patients requiring intensive care is not directly related to the level of zinc in the blood plasma.

KEY WORDS: zinc, neurosurgery, intensive care.

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INTRODUCTION

Diseases that require neurosurgical intervention for many years constitute a major cause of disability and death in the world, and their main components – stroke and traumatic brain injury – have been tending to increase [1, 2].

Neurosurgical patients in most cases require treatment in intensive care unit (ICU) due to the disorders of basic vital functions. 24-89% of these patients develop gastrointestinal failure (GIF) [3, 4], which causes disruption of nutrients intake, including zinc.

Zinc is a universal member of metabolism for all biological objects. It is involved in the regeneration of the mucous membranes and regulation of motility of the gastrointestinal tract; it is a part of salivary glands secretion; it regulates the balance between cellular and humoral immunity, acts as a protector in free radical reactions, stabilizes cell membranes against the effects of viral infections and toxins, reduces the release of biologically active substances, stabilizes the permeability of blood-brain barrier [5-11]. That is why zinc plays an important role in the system bioregulation of patients in critical conditions, and of neurosurgical profile in particular.

AIM OF THE STUDY

The aim of the research is the assessment of zinc metabolism and effects of its disorder in patients with neurosurgical disorders that require intensive care.

MATERIALS AND METHODS

Observational analytical retrospective research («Case control study» type) of zinc exchange status in 60 patients was conducted. Study group included 40 patients of both sexes who underwent treatment at ICU of Poltava. The criteria for inclusion in the study group were: patients above the age of 18, presence of acute cerebrovascular disorders of hemorrhagic type, open and closed head injuries (rubrics of International Diseases Classification of X review «Vascular Brain Syndromes of Cerebrovascular Diseases» (G46) and «Head Injuries» (S00-S09), respectively), and the need for prosthetics of vital functions in the context of ICU. Exclusion criteria for this group were as follows: history of gastrointestinal diseases, microelementosis, dermatological diseases, treatment at ICU for less than 3 days. The assessment of monitored parameters in the study group was performed on the third day of stay at ICU.

Control group consisted of 20 conventionally healthy volunteers. The representations of study and control groups did not differ in terms of age and gender.

Before the study, signed acts of informed consent to participate in the research were obtained from patients or their legal representatives. During the study, patients' rights were respected in accordance with requirements of Helsinki Declaration of 1975, as amended in 2005.

Presence of clinical signs of zinc deficiency [12, 13] was assessed: hair loss at tension test; white spots on the nails,

their fragility; dry skin; glossitis; diarrhea.

Complete blood count was conducted using hematology analyzer «Hemascreen 13» of Nospitex Diagnostics (Italy). Content of zinc in plasma was determined via colorimetric method without deproteinization by reaction with a specific complexing agent 5-Br-PARS using biochemical set of Sentinel (Italy). The amount of 13-20 mcM/l was considered as normal zinc in blood plasma [12-14].

The presence or absence of GIF was evaluated on the scale proposed by A. Reintam et al. [15].

The severity of patient's condition was evaluated using the original simplified scale for assessment of physiological disorders (Original Simplified Acute Physiology Score, SAPS) [16].

The level of consciousness in patients was measured on the scale for evaluation of impaired consciousness or brain death (Full Outline of UnResponsiveness, FOUR) [17].

Statistical analysis of the results was performed using the software package Microsoft Office Excel 2003 and Statistica 6.0. The research applied the methods of descriptive statistics, nonparametric comparison of two groups in terms of qualitative and quantitative indicators, establishing correlation relationships. In describing the results of the study the calculations of arithmetic average (m), coverage error (m), and median (me) were used. The comparison of the two groups in terms of qualitative indicators was performed by calculating the compliance with Pearson's c2; comparison of quantitative indicators was performed via calculation of Wilcoxon-Mann-Whitney test (U). Establishing correlations between the phenomena was performed by using Spearman's correlation coefficient (R). In conducting the statistical data, P=0.95 was considered as minimum level of faultless prognosis and $p \leq 0.05$ as the level of error probability, respectively.

RESULTS

In persons of the study group, zinc level was 13.5±0.3 mcM/l (Me=13.9) as against 16.9±0.7 mcM/l (Me=17.9) in those of the control group (U=264; p<0.001). Hypozincemia frequency (below 13 mcM / l) in patients of the study relative to the control group was significantly lower. Hence, in the study group deficiency in plasma was detected in 14 people (35%), and in the control group – in 1 person (5%) (χ^2=6.4; p=0.02).

Severity of clinical manifestations of zinc deficiency in persons of the study group depending on the presence of hypozincemia is represented in Table I.

Correlation relationships in patients of the study group between zinc level in plasma and manifestation of clinical signs specific to its deficiency are shown in Table II.

In complete blood count, lymphocyte level in the study group significantly decreased to 11±0.5% (Me=11) as against the control group, where the figure was 25.7 ± 1.2% (Me=26, U=300; p<0.001). The level of lymphocytes reduction 11±0.5% (Me=11) in studied individuals had a statistically significant inverse relationship with the level of laboratory plasma zinc (R=0.65; p=0.002).

In the study group, a significant increase in the level of white blood cells to 10.4 ± 0.4 x 109/l (Me=9.7) was observed as against the control group, where it reached 5.4 ± 0.2 x 109/l (Me=5, 4; U=1225; p<0.001). The reverse correlation between the level of plasma zinc and white blood cells of studied individuals (R=-0.57; p=0.007) was detected.

Patients of the study had signs of GIF in 40% of cases (n=16), which has never been observed in patients of the control group (χ2=10.9; p=0.002). Manifestations of GIF had reliable reverse correlation with laboratory parameters of plasma zinc (R = -0.8; p<0.001). The statistically significant relationship with the formation of GIF and increasing levels of white blood cells (R=-0.8; p<0.001) was also found.

In the study group, 65% of patients (n = 26) required artificial lung ventilation (ALV), whereas in the control group the respiratory function was not affected in any person (χ2=22.9; p<0.001). The need for replacing the respiratory function with ALV apparatus had a close relationship with the level of zinc deficiency in plasma (R=-0.8; p<0.001).

The level of impaired consciousness on the FOUR scale in the study group amounted to 10.3 ± 0.5 points (Me = 11), in the control group level of consciousness of the studied persons was not impaired and amounted to 16 ± 0 points (Me=16, U=1242; p<0.001). Assessment via FOUR scale was directly dependent on the level of zinc in plasma (R=0.7; p<0.001).

In persons of the study group, the severity of physiological disorders on SAPS scale was 9.1 ± 0.5 points (Me=9), as against 1.2 ± 0.2 points in the control group (Me=1; U=1082.5; p<0.001). The severity of physiological disorders of the body in traumatic brain injury had invert correlation with zinc deficiency in the body of neurosurgical patients (R=-0.7; p<0.001).

Mortality in the study group was 14 people (35%), in the control group there were no deaths (χ2=9.13; p=0.002). The level of mortality had no significant correlation with the level of plasma zinc (R=0.2; p=0.07).

DISCUSSION

The study found that on the third day of the disease neurosurgical patients requiring intensive care had lower plasma zinc as against healthy individuals. Thus, 35% of neurosurgical patients at ICU had clinically significant zinc deficiency, which is its concentration in the blood less than 13 mcM/l [12-14]. In neurosurgical patients with low levels of zinc in plasma clinical signs of deficiency were observed: dry skin, brittle nails, their depigmentation, hair loss, diarrhea, which are considered as clinical markers of zinc deficiency [12-13], and the frequency of their development (except for diarrhea) is directly dependent on the severity of zinc deficiency according to the laboratory tests. It should be noted that in persons of the study group clinical signs of zinc deficiency were observed without reduction of its level in plasma below 13 mcM/l.

In neurosurgical patients requiring intensive care systemic disorders of vital functions were naturally observed (high severity of clinical condition, formation of GIF, changes in

Table I. Clinical manifestations of zinc deficiency in persons of the study group depending on the presence of hypozincemia (n = 40)

Clinical signs	Persons with hypozincemia (n= 14)	Persons without hypozincemia (n= 26)	c	p
Glossitis	4 (28.6%)	0 (0%)	8.3	0.005
White spots on the nails	10 (71.4%)	0 (0%)	24.8	<0.001
Nails fragility	8 (57.1%)	2 (7.7%)	8.4	0.005
Dry skin	12 (85.7%);	4 (15.4%)	18.8	<0.001
Hair loss	8 (57.1%)	2 (7.7%)	8.4	0.005
Diarrhea	2 (14.3%)	0 (0%)	3.8	0.06

Table II. The relationship between the frequency of clinical manifestations of zinc deficiency in neurosurgical patients and decreased zinc content in their blood plasma

Clinical signs	n= 40		
	n (%)	R	p
Glossitis	4 (10%)	-0.52	0.02
White spots on the nails	10 (25%)	-0.59	0.005
Nails fragility	10 (25%)	-0.67	0.001
Dry skin	16 (40%)	-0.71	<
Hair loss	10 (25%)	-0.67	0.001
Diarrhea	2 (5%)	-0.37	0.1

laboratory parameters of immune cells, impaired consciousness, need for ALV), which naturally was not observed in healthy individuals. However, attention is drawn to the fact that these systemic changes have statistical relationship with indicators of zinc supply. Moreover, formation of GIF correlated with the tendency to leukocytosis.

The relationship between changes in the immune system and organ lesions is known [18]. In particular, it is known that GIF promotes bacterial translocation, which is one of the main factors in the formation of systemic immune responses. In view of the above mentioned correlations between the development of GIF and zinc levels in blood plasma, it can be assumed that the formation of these processes is zinc-dependent. Published data [3, 4, 13] show a decrease of zinc in systemic inflammation and its ability to influence the regeneration of intestinal mucosa. Therefore, in these patients there is probably the formation of a vicious circle: in GIF there is decreased zinc supply and systemic immune responses that are enhanced by zinc deficiency. This causes its high consumption in the process of interleukin proinflammatory cascade [8], which lowers the existing zinc level in the body, and this, in turn, inhibits the regeneration of the intestinal mucosa, causing further decrease of exogenous zinc.

It is also probable that the absolute value of zinc content in the blood plasma of neurosurgical patients on the third day of stay at ICU did not reach the initial level due to the inability of providing normal volume of food that is associated with delay in full use of enteral nutrition in these patients because of tissue hypoperfusion and centrogenous motor disturbances of gastrointestinal system [3, 13].

It should be noted that a significant mortality of patients in the study was not directly related to the level of zinc supply.

Thus, zinc deficiency occurs in the development of critical states in neurosurgical patients, which can be caused by the effects of multisystem lesions due to severe course of neurosurgical pathologies. Zinc deficiency, in its turn, promotes the development of GIF, immune and increased neurological insufficiency, affects the need for artificial pulmonary ventilation and increases the severity of patient's condition on the principle of forming a vicious circle.

These facts justify the need for exogenous correction of zinc deficiency in neurosurgical patients by prescribing zinc-containing medications, as well as prospects for further research in determining their effectiveness.

CONCLUSIONS

In neurosurgical patients requiring intensive care, on the third day of treatment the reduction in plasma zinc is observed as against relatively healthy people. Reduction of this trace element causes clinical manifestations of zinc deficiency, even without achieving the minimum diagnostically significant threshold of its content in blood of 13 mcM/l. Zinc deficiency contributes to gastrointestinal, cerebral and immune insufficiency, increases the need for artificial pulmonary ventilation and aggravates the severity of patient's condition. At the same time, high mortality of neurosurgical patients requiring intensive care is not directly related to the level of zinc in the blood plasma.

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