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SERUM ZINC LEVELS IN CHILDREN WITH GLOMERULONEPHRITIS

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SUMMARY

Key words: zinc, glomerulonephritis, nephrotic syndrome.

The paper presents a study on serum zinc levels of 80 children with glomerulonephritis (GN) at different clinical stages of disease development. During the acute phase of clinical manifestations, in patients with steroid-sensitive nephrotic syndrome (SSNS), serum zinc (Zn) level significantly decreased by 2,8 times, and in steroid-resistant nephrotic syndrome (SRNS) - by 3,4 times, compared to the control group. In remission serum Zn level was increased as compared to the initial level, but was still reduced as compared to the control group. Determination of serum Zn levels could be used to monitor the activity of a pathological process in children with various variants of GN and to assess the effectiveness of therapeutic measures.

РЕЗЮМЕ

УРОВЕНЬ ЦИНКА В КРОВИ У ДЕТЕЙ С ГЛОМЕРУЛОНЕФРИТОМ

Ключевые слова: цинк, гломерулонефрит, нефротический синдром.

Была изучена концентрация цинка (Zn) в крови у 80 детей с гломерулонефритом (ГН) в различные клинические стадии заболевания. В острой фазе клинических проявлений у больных с стероид-чувствительным нефротическим синдромом (СЧНС) уровень Zn в крови достоверно снижается в 2,8 раза, а при стероид-резистентном нефротическом синдроме (СРНС) - в 3,4 раза. В период ремиссии уровень Zn в крови повышается по сравнению с исходным уровнем, но остается сниженным по сравнению с контрольной группой. Определение концентрации Zn в крови может быть использовано для мониторинга активности патологического процесса у детей с различными вариантами ГН, и контроля эффективности лечебных мероприятий.

REZUMAT

NIVELUL SERIC AL ZINCULUI LA COPIII CU GLOMERULONEFRITĂ

Cuvinte-cheie: zinc, glomerulonefrită, sindrom nefrotic.

Lucrarea prezintă un studiu efectuat pe un lot de 80 de copii cu glomerulonefrită (GN) la diferite etape clinico-evolutive ale maladiei, cu determinarea nivelului de zinc (Zn) seric. S-a stabilit că la pacienții cu sindrom nefrotic steroid-sensibil (SNSS), în perioada acutizării, nivelul Zn seric se reduce semnificativ - de 2,8 ori, iar în sindromul nefrotic steroid-rezistent (SNSR) - de 3,4 ori, comparativ cu grupul de control. În perioada de remisiune, nivelul Zn seric a crescut, comparativ cu nivelul inițial, dar a rămas mai redus, comparativ cu grupul de control. Determinarea nivelului de Zn seric este o metodă ce poate fi utilizată pentru monitorizarea activității procesului patologic la copii cu diverse variante ale GN, precum și pentru evaluarea eficacității tratamentului.

Introduction.

Homeostatic processes under normal conditions, and those defined by the pathological conditions are driven by numerous factors, among which an essential role is played by microelements, especially those of transition, such as zinc. Zinc is an essential microelement that is involved in the structure of many enzymes associated with different metabolic processes, including the metabolism of nucleic

acids, carbohydrates and proteins. It is the second most abundant metal in mammalian tissues, after iron, with almost 90% of that found in muscle and bone.

Zinc is required for the normal functioning of the immune system. Thus, zinc deficiency can suppress immunity and affect the body's defense mechanisms [3]. Zinc deficiency (ZnD) is associated with multiple disorders. There are few studies that investigate the level of microelements in NS,

and the results of these studies are contradictory regarding some microelements [4, 5, 7]. Complex information on zinc modifications in the clinical and evolutionary variants of glomerulonephritis is missing.

The aim of the study is to evaluate the concentration of serum zinc level in children with glomerulonephritis at clinical and evolutionary stages of the disease.

Material and methods.

The study included 80 children with glomerulonephritis, including 25 children with acute glomerulonephritis (AGN) nephritic syndrome, 20 children with steroid-sensitive nephrotic syndrome (SSNS) and 15 children with steroid-resistant nephrotic syndrome (SRNS), 20 children with chronic glomerulonephritis (CGN) nephrotic form. The control group consisted of 20 practically healthy children. The examined children were divided into 2 groups according to the response to glucocorticoid treatment: SSNS and SRNS. Nephrotic syndrome (NS) was diagnosed in the presence of edema, massive proteinuria (>40 mg/m²/h or urinary protein/creatinine ratio >2,0 mg/mg) and hypoalbuminemia (<2,5 mg/dl) [2].

Statistical methods were used to estimate the significant difference between the studied indices of the compared groups, by estimating the average arithmetic mean [X], the mean square deviation, and the average error of the average arithmetic mean [$\pm m$]. In addition, the non-parametric statistical test “U Mann-Whitney” and the significance threshold $p < 0,05$.

Results.

The average age of the onset of NS was 6,4 \pm 0,5 years. The clinical manifestations of NS were represented by edema which constituted 92,5 \pm 2,9%, anasarca – 60,0 \pm 5,5%, rare urination – 48,83 \pm 5,6%, headache – 22,5 \pm 4,7%, dyspnea – 1,3 \pm 0,8%. Paraclinical examinations have determined a hypoproteinemia up to 52,9 \pm 0,91 g/l, seric albumins – 34,03 \pm 2,82 g/l, increase of lipid metabolism indices – total lipids increased up to 9,53 \pm 0 98 g/l, cholesterol – 8,48 \pm 0,35 mmol/l, β -lipoproteins – 99,4 \pm 2,75 arbitrary units, serum urea – 6,2 \pm 0,53 mmol/l, creatinine – 0,060 \pm 0,04 mmol/l, proteinuria up to 5,5 \pm 0,66 g/l in urine within 24 hours. Table 1 presents the results of the evaluation of serum zinc levels of the patients with GN in different clinical and evolutionary stages of the disease.

Table 1. Serum zinc levels in patients with glomerulonephritis

Study groups	Zn (μ mol/l)	
	exacerbation	remission
Control (n=20)	15,19 \pm 0,77	
AGN nephritic syndrome (n=25)	8,72 \pm 0,95***	11,12 \pm 0,50*** $p_1 < 0,05$
SSNS (n=20)	5,41 \pm 0,80*** $p_3 > 0,05$	9,94 \pm 0,81*** $p_1 < 0,01; p_3 < 0,01$
SRNS (n=15)	4,51 \pm 0,38*** $p_2 > 0,05; p_3 < 0,01$	-
CGN nephrotic form (n=20)	8,60 \pm 1,40**	13,34 \pm 0,98 $p_1 < 0,01$

Note: statistically significant difference with compared to the control group values: * $p < 0,05$; ** $p < 0,01$; *** $p < 0,001$.

p_1 - the authenticity in comparison with the respective index registered at the acute phase.

p_2 - authenticity when comparing SSNS with SRNS.

p_3 - authenticity when comparing the CGN nephrotic form with SSNS and SRNS.

Steroid-sensitive nephrotic syndrome was dominated by the normalization of urinalysis within 4 weeks rarely 8 weeks after administration of glucocorticoids and installation of complete remission [2].

Steroid-resistant nephrotic syndrome was characterized in the case of maintaining of the level of proteinuria to <3 g/dL over the 8 weeks of treatment with prednisolone at a dose of 2 mg/kg/24 h (no more than 60 mg/24h) and subsequently carrying out pulse therapy with prednisolone 20-30 mg/kg/24h nr. 3 (not more than 1 g during a course) [2].

The determination of serum zinc level was performed using the analysis sets of Elitech (France), according to the instructions attached to the set.

According to the data obtained, the content of Zn in the four forms of GN undergoes changes of orientation and different intensity. Thus, serum zinc levels in all clinical variants of GN was reduced, compared to the values of the control group. More pronounced changes of serum zinc levels were recorded in patients with SRNS, during the onset, where the concentration of this element was reduced by 3,4 times - up to (4,51 \pm 0,38 μ mol/l), whereas in the SSNS group it was reduced by 2,8 times (5,41 \pm 0,80 μ mol/l), compared to the control group (15,19 \pm 0,77 μ mol/l). During the remission period, the serum zinc levels increased compared to the initial values, but remained below the control values.

Discussion.

In this study were obtained significantly lower values of serum zinc concentrations, in all clinical variants of GN, compared to the control group. The results were similar to other studies.

The mean plasma zinc level was significantly lower in patients with severe form rather than in those with mild to moderate nephrotic syndrome. The correlation between plasma zinc level and the nephrotic syndrome severity was significant, which may have implications for improving the prognosis of patients with nephrotic syndrome [6]. In addition, a study by GurgozeMK. et al. concluded that chronic hemodialysis might lead to abnormal plasma zinc levels of trace elements in children with chronic renal failure. The low levels of trace elements, especially zinc, may be associated with prognosis and symptoms in children undergoing chronic hemodialysis [1]. Another study [4] demonstrated that plasma zinc level in NS was significantly reduced compared to the control group.

According to this study, plasma zinc level had a negative correlation with urinary protein during 24 h, which was statistically significant ($r = -0.442$, $p = 0.021$). Thus, if the proteinuria increases, the plasma zinc level drops. Most likely, this is due to the loss of metals - binding proteins. The plasma zinc levels were significantly lower in both active and remission patients (for all $p=0.0001$) [7]. Another cause of hypo-zincemia, found in our research, could be induced by the loss of this microelement in the urinary tract. The study Sherali A R. demonstrated that zinc supplementation was helpful in reducing relapses in nephrotic syndrome [5].

Zhang X. et al. showed that Zinc deficiency (ZnD) enhances diabetic renal interstitial fibrosis, as indicated by an increase in levels of type I collagen, fibronectin, α -SMA and vimentin, which is may occur via the TGF- β /Smad2/3 pathway. These results are the first to demonstrate the effect of ZnD on the pathogenic mechanisms of renal interstitial fibrosis during the development of diabetic nephropathy (DN) [8].

A recent meta-analysis of 15 randomized controlled studies examined the effects of zinc intake on hemodialysis (HD) patients and demonstrated that zinc supplementation was strongly and independently associated with reduced plasma C-reactive protein (CRP) levels, higher superoxide dismutase (SOD) plasma

levels, improved nutrition status, and lower plasma malondialdehyde (MDA) concentrations [9].

Conclusions.

The study showed that the determination of the serum zinc level could be used to monitor the renal pathological processes in children with different variants of glomerulonephritis and control the effectiveness of the treatment applied.

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