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Essential and toxic microelements in clinical presentation of recurrent pyelonephritis in children

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The study determined content of essential (Zn, Se, Cu) and toxic (Pb, Cd) microelements in blood serum and daily urine in 95 children of 3-15 years of age with recurrent pyelonephritis. It was revealed a statistically significant reduction in the level of essential microelements Se, Cu and Zn in blood serum in comparison with the control group ($p < 0.05$) in the active stage and in the period of decline in activity of pyelonephritis. A statistically significant reduction in Se and Cu urine excretion was registered; at the same time, Zn excretion level was identical to the values in the control group. Study of content of toxic microelements in biological media showed increase in lead concentration in blood serum and urine excretion in children in the period of decline in activity of the disease ($p < 0.05$) and complete clinical laboratory remission ($p < 0.05$) in comparison with the control group. The study did not reveal statistically significant differences in cadmium content in biological media of the examined patients in comparison with the control group. Apparently, deficit of essential microelements in the setting of Pb concentration increase in the body aggravates affection of tubulointerstitial renal tissue resulting in the recurrent course of the disease with brief periods of clinical laboratory remission.

Keywords: microelements, pyelonephritis, children, heavy metals.

INTRODUCTION

Pyelonephritis is one of the most widespread urinary system diseases in children [1, 2]. Many researchers have lately been noting not only a tendency towards pyelonephritis rate increase in children, but also considerable change of its clinical presentation. Increase in the number of scarcely manifested and latent disease course forms complicates timely diagnostics and, therefore, postpones beginning of adequate therapeutic, rehabilitative and preventive measures. This pathology is disposed to chronization, recurrence and progression with formation of nephrosclerosis and development of renal failure, which result in incapacitation of patients [3, 4]. Such severe consequences make further detailed study of etiology and pathogenesis of the disease relevant. Some researchers emphasize an important role of imbalance of essential and toxic microelements for prognosis of course and outcome of microbial-inflammatory nephropathies in children [5-7]. It is well known that kidneys are the primary organ excreting the toxins absorbed by the body. Toxic metals primarily accumulate in cells of proximal tubules causing structural and functional damage [8-10].

The aim of the study is to analyze microelement homeostasis (Zn, Cu, Se, Pb, Cd) in biological media (blood serum, daily urine) in children with recurrent pyelonephritis depending on activity of the pathological process.

MATERIALS AND METHODS

We conducted a complex clinical laboratory examination of 95 children of 3-15 years of age with recurrent pyelonephritis – 68 (71%) girls and 27 (29%) boys: 28 (29.5%) – in the period of maximum activity (group 1), 42 (44.2%) – in the period of decline in activity of the pathological process (group 2) and 25 (26.3%) in the period of remission (group 3). The control group involved 25 healthy children. Duration of the microbial-inflammatory process in tubulointerstitial renal system was 1-10 years in most children, over 10 years – in 9 (9.4%). Diagnosis “pyelonephritis” was verified on the basis of the common standards compiled on the basis of Order #151 of the Ministry of Health of the RF of 7 May 1998 “On time industry medical care volume standards for children”.

Content of chemical elements (Zn, Cu, Se, Cd, Pb) in blood serum and daily urine was evaluated with a method of inversion voltammetry [11] using analyzer TA4 at laboratory “Tomanalyt” (Tomsk). Samples were prepared with a method of wet air oxidation using HNO₃ and H₂O₂ with subsequent burning of the sediment.

The obtained data were statistically manipulated using software package Statistica 6.0 for Windows. Results of biochemical studies are given in the form of a median (Me), upper and lower quartiles (Q1-Q3); statistical significance was evaluated using non-parametric Mann-Whitney test. Differences were considered statistically significant at $p < 0.05$.

RESULTS

Clinical presentation of pyelonephritis exacerbation featured such extrarenal manifestations as intoxication syndrome (79.5%), abdominal pain syndrome (49.4%) and lumbar pain (37.8%). Positive costovertebral angle tenderness was revealed in 49.1% of children, syndrome of dysuric disorders in the form of frequent urination – in 45.2%, enuresis along with neurogenic dysfunction of urinary bladder – in 12%. Rare urination was observed in 15.8% of children, diurnal urinary incontinence – in 4.8%. Urinary syndrome manifested itself with isolated leukocyturia (52.7%) and its combination with hematuria (29.8%) and proteinuria (17.5%). Leukocyturia was neutrophilic in 100% of cases. Proteinuria in daily urine was less than 1 g/l. Symptoms of intoxication, dysuric and pain syndrome were observed considerably rarer in the period of decline in activity of the pathological process. Leukocyturia was observed in many children (75%), while other laboratory manifestations of urinary syndrome were extremely rare.

It is well known that the structure of uropathogens may vary in different regions of Russia. According to our data, *Escherichia coli* was the main causative agent of the renal inflammatory process (51.2%); this corresponds to the results obtained by multicenter trials (L.S. Strachunskiy, 2001), where this causative agent was revealed in 53.1% of cases (varying from 41.3 to 83.3% in different centers of Russia). *Klebsiella pneumoniae* and *Proteus mirabilis* were revealed in the diagnostic titer with approximately the same frequency – 15.6 and 12.2%. It ought to be mentioned that these figures are slightly higher than the Russian average; this may result both from the recurrent course of urogenital infection and microbial peculiarities of the Tomsk region. Other microbes were plated significantly rarer. In total, bacteriuria as reflection of activity of the microbial-inflammatory process in renal tissue was observed in 51.8% of children. Other pathologies were crystalluria (56%), increased oxalate excretion (21.4%), mixed oxalate-urate crystalluria (27.2%) and phosphaturia (8%). Decline in the renal concentration function was revealed in 35% of children with recurrent pyelonephritis.

Children with renal diseases are characterized by a considerable deficit of the main essential elements involved in functioning of antioxidant and immune systems [5, 6, 13, 14]. Microelement homeostasis study results (tbl. 1) indicated that a statistically significant reduction in the level of essential microelements Se, Cu and Zn in blood serum of children was observed in the active stage and in the period of decline in activity of pyelonephritis in comparison with the control group ($p < 0.05$). An especially low Se content was registered in group 1 of children with significant difference from the patients with complete clinical laboratory remission ($p < 0.05$). We

also revealed a statistically significant reduction in excretion of selenium and copper with urine (tb. 2), while the level of Zn excretion did not differ from the control group values. Blood serum Zn content in the stage of complete clinical laboratory pyelonephritis remission did not differ from the control values, while the level of Se and Cu remained reduced ($p<0.05$). Similar dynamics was observed in the study of excretion of these elements with urine. Accumulation of toxic microelements, especially of lead and cadmium, in the body plays a certain role in the change of pathomorphism of microbial-inflammatory renal diseases. It has been shown that lead accumulation in mitochondria of nephron tubular cells results in their functional and ultrastructural changes [9, 10, 12]. The conducted trial revealed lead concentration increase in blood serum and its urinary excretion in children in the stages of decline in activity of the disease ($p<0.05$) and of complete clinical laboratory remission ($p<0.05$) in comparison with the control group. At the same time, we did not reveal statistically significant differences in Pb content in children in the stage of pyelonephritis exacerbation; this indicates its lesser interaction with the degree of activity of renal inflammatory process. However, it is one of the aggregate causes of unfavorable course of the disease. We did not reveal statistically significant differences in cadmium content between biological media of the patients with recurrent pyelonephritis and of the control group.

CONCLUSION

Thus, pathological role both of deficit of essential microelements and of accumulation of toxic microelements in clinical presentation of recurrent pyelonephritis in children is beyond doubt. Zn level reduction in the stage of disease exacerbation and prolonged reduction in concentration of Cu and Se in biological media of patients in different stages of pyelonephritis activity may results from increased consumption of these microelements, especially in the event of pronounced and prolonged activity of renal inflammatory process. Apparently, deficit of essential microelements in the setting of increase of Pb concentration in the body aggravates affection of renal tubulointerstitial tissue and results in the recurrent course of the disease with brief periods of clinical laboratory remission. The obtained results broaden our conception of pathogenesis of persistent infection of upper segments of urinary system in children and may serve as an additional criterion potentiating chronization of infectious-inflammatory process in renal parenchyma.

Tb. 1. Blood serum concentration of microelements in children with recurrent pyelonephritis, Me (Q1-Q3).

Element	Recurrent pyelonephritis n=95			Control group n=25
	Maximum activity stage n=28	Decline stage n=42	Remission stage n=25	
Zn, mg/l	2.92* (0.79-3.99)	3.53* (2.35-4.48)	4.27 (2.76-5.27)	5.68 (4.23-6.97)
Cu, mg/l	0.16* (0.04-0.22)	0.21* (0.08-0.26)	0.16* (0.06-0.23)	0.34 (0.25-0.47)
Se, mcg/l	20.37* (18.2-21.9)	21.74* (28.6-21.03)	41.14* [#] (23.7-58.1)	65.04 (46.12-77.1)
Cd, mcg/l	0.29 (0.23-0.41)	0.43 (0.32-0.89)	0.37 (0.19-0.65)	0.35 (0.14-0.59)
Pb, mcg/l	5.69 (3.51-8.12)	5.87* (3.96-8.96)	7.03* (6.23-9.01)	3.49 (1.47-5.65)

Note. * - $p<0.05$ in comparison with the control group, [#] - $p<0.05$ in comparison with group 1.

Tb. 2. Daily urine concentration of microelements in children with recurrent pyelonephritis, Me (Q1-Q3).

Element	Recurrent pyelonephritis n=95			Control group n=25
	Maximum activity stage n=28	Decline stage n=42	Remission stage n=25	
Zn, mg/l	0.33 (0.19-0.42)	0.21 (0.18-0.23)	0.37 (0.25-0.77)	0.36 (0.22-0.63)
Cu, mg/l	0.023* (0.014-0.067)	0.023* (0.013-0.056)	0.026* (0.015-0.066)	0.013 (0.009-0.021)
Se, mg/l	6.12* (2.93-7.43)	6.01* (2.91-7.4)	7.11* (3.21-9.87)	11.08 (7.42-17.04)
Cd, mcg/l	0.27 (0.18-0.32)	0.23 (0.12-0.37)	0.25 (0.12-0.27)	0.33 (0.12-0.54)
Pb, mcg/l	3.34 (2.89-6.62)	5.42* (3.87-8.96)	4.78 (2.53-5.67)	2.58 (1.97-5.81)

Note. * - $p < 0.05$ in comparison with the control group.

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