Clinical efficacy of enterosorption in treatment of microbial-inflammatory and immunocomplex kidney diseases in children

Authors: *I.V. Bagdasarova, Institute of Nephrology AMS of Ukraine, O.I. Osadchaya, A.M. Boyarskaya, Institute of Hematology and Transfusiology AMS of Ukraine, B.S. Sheyman, N.A. Voloshina, L.I. Medved Institute of Ecohygiene and Toxicology, the Ministry of Health of Ukraine.*
Subjects: *Nephrology, Pediatrics / Neonatology*
Chapters: *Clinical investigations*

Introduction

Intoxication is the main pathological syndrome requiring intensive therapy for inflammatory diseases in children. It is caused by accumulation of four groups of metabolites: bacterial exo- and endotoxins, tissue antigens, toxic organic substances (lactic acid, urea, keto acids), biological amines and inflammatory mediators (histamine, serotonin, prostaglandins, leukotrienes) [2, 3]. As a result, the intoxication represents a non-specific response of the body to specific infectious effect during inflammatory diseases.

A number of authors attribute an important role to the peptides of the average mass in the development of intoxication syndrome in children suffering from inflammatory diseases. These compounds are capable of inhibiting phagocytic activity of leukocytes, tissue respiration. The content of the average mass molecules (AMM) in peripheral blood correlates with the severity of clinical manifestations of intoxication [2-4, 6]. Many researchers pay special attention to the studying the effectiveness of various methods of detoxification during inflammatory diseases in children [5, 6, 8]. Among these methods, enterosorption takes a very prominent place.

Objective

Comparative study of the influence of enterosorption with the medicine Enterosgel on activity of the factors of natural antitoxic resistance in children with acute glomerulonephritis and pyelonephritis.

Characteristics of the examined patients and study methods

A total of 30 children with acute pyelonephritis (APN) and 30 children with acute glomerulonephritis (AGN) were examined. The examined children were from 5 to 14 years of age. All the children were examined for cytolytic activity of autologous serum and its fractions in relation to their own white blood cells - as an indicator of the severity of endogenous intoxication, toxin-binding ability of blood serum proteins, results the of ethanol test were studied as a measure of the accumulation of tissue degradation products, AMM content, the functional activity of neutrophilic granulocytes (NG) and monocytes (M) in the NBT test (spontaneous and stimulated with lipopolysaccharide).

The trials were conducted twice: on admission of children to the hospital, and upon the completion of treatment by Enterosgel. The conventional scheme of combination therapy of acute APN and AGN included Enterosgel in age-specific dosage variances for 14 days in all the examined children.

Results and discussion

The study of cytolytic activity of autologous serum revealed that in children with acute APN the development of endogenous intoxication owes to the accumulation in the peripheral blood of toxins of microbial origin (10-200 nm) which have a direct damaging effect (Table 1).

Table 1. Indicators of cytological activity and the ability of autologous serum to bind toxins in children with acute APN (M ± m, n – 30)

Studied indicators	Unit of measure	Duration of the study		Indicators of healthy individuals
		Prior to treatment	After treatment	
Whole autologous serum	%	49.2 ± 1.2*	44.5 ± 1.3*,**	20.5 ± 0.7
Albumin fraction of blood serum	%	34.2 ± 1.1*	32.2 ± 1.4*	22.55 ± 1.20
Globulin fraction of blood serum	%	34.4 ± 1.3*	34.5 ± 1.2*	22.7 ± 1.5
Fraction of medium-sized adhesions (10 - 200 nm) of blood serum	%	56.7 ± 2.3*	42.3 ± 1.2*,**	20.2 ± 1.2
Toxin binding capacity of serum proteins	c.u.	0.058 ± 0.007**	0.072 ± 0.007*	0.095 ± 0.010
Ethanol test	Number of positive results	45.34 ± 3.33*	40.57 ± 4.02*	1.07 ± 0.03

Note: * - veracity of differences in relation to the indices of healthy individuals ($p < 0.05$); ** - veracity of differences in relation to initial indices ($p < 0.05$).

The primary study of AMM content in children with acute APN revealed 0.93 ± 0.07 units of optical density (indicators of healthy individuals – 0.56 ± 0.06 units of optical density). There was also a significant increase in the content of the hydrophobic AMM fraction that exceeded the indices of healthy individuals ($p < 0.05$). The hydrophobic fraction of AMM was in plasma and almost completely in the bound state - in the form of complexes with albumin and low density lipoproteins.

It is hydrophobic protein degradation products that possess the most severe toxic properties as they are easily bound to membranes of blood cells and intracellular proteins by altering their structure, increasing the membrane permeability and inhibiting enzyme activity, particularly NG. Herewith, there was a notable decline in the indices of toxin binding capacity of blood serum in relation to those of healthy individuals ($p < 0.05$) and the accumulation of tissue destruction products, attested by a significant specific gravity of positive results of ethanol test.

The study of the group of children with AGN showed that a considerable damaging effect in realizing cytolytic activity of autologous serum in relation to own leukocytes was exercised by globulin fraction of blood serum (Table 2).

Table 2. Indicators of cytological activity and the ability of autologous serum to bind toxins in children with acute AGN (M ± m, n – 30)

Studied indicators	Unit of measure	Duration of the study		Indicators of healthy individuals
		Prior to treatment	After treatment	
Whole autologous serum	%	59.7 ± 1.5*	52.2 ± 1.7*,**	20.5 ± 0.7
Albumin fraction of blood serum	%	35.7 ± 1.5*	33.5 ± 1.2*	22.56 ± 1.20
Globulin fraction of blood serum	%	54.3 ± 1.2*	45.2 ± 1.3*, **	22.7 ± 1.5
Fraction of medium-sized adhesions (10 - 200 nm) of blood serum	%	34.7 ± 1.5*	30.5 ± 1.7*,**	20.2 ± 1.2
Toxin binding capacity of serum proteins	c.u.	0.057 ± 0.007**	0.070 ± 0.007*	0.095 ± 0.010
Ethanol test	Number of positive results	71.56 ± 4.11*	65.07 ± 5.22*,**	1.07 ± 0.03

Note: * - veracity of differences in relation to the indices of healthy individuals ($p < 0.05$); ** - veracity of differences in relation to initial indices ($p < 0.05$).

Concurrently, this group of patients demonstrated high AMM content due to an increase of the hydrophobic fraction. AMM content stood at 0.95 ± 0.07 units of optical density, exceeding the indices of healthy individuals ($p < 0.05$). A reduction in the ability of blood proteins to bind toxins was observed, as well as the accumulation of tissue degradation products, as evidenced by the large proportion of positive ethanol test results. These substances have a significant damaging effect and determine high autosensitization of the body.

The use of Enterosgel medication in complex treatment of children in both groups led to a reduction in the severity of endotoxemia. Herewith, children with APN showed a decrease in cytolytic activity of the fraction of medium-sized toxins of microbial origin, correlating with a drop in AMM content, which attests to the functioning of antimicrobial resistance systems at the subcompensated level and the reduction of the risk connected with infectious complications on later stages of the disease.

Enterosorption treatment of children with AGN promoted a decrease in cytolytic activity of globulin fraction of blood serum, as well as medium-sized fractions of toxins of microbial origin. Upon that, a tendency towards a rise in toxin binding capacity of blood serum proteins and shrinkage of AMM content was educed, against a backdrop of a declining share of positive ethanol test results. This data testifies that the use of enterosorbent Enterosgel in children with AGN reduces the number of auto-aggressive substances of direct damaging effect that determines reduction of the risk of autoimmune complications.

The study of the functional activity of NG and M of peripheral blood in children with PN in NBT test discovered a significant improvement of its performance in relation to the indices of healthy individuals ($p < 0.05$). Additional stimulation of NG with lipopolysaccharide E.coli cell wall resulted in a remarkable decrease in activity indicators of NG and M in NBT test against both the spontaneous reaction and that of healthy individuals ($p < 0.05$) (Table. 3).

Table 3. Activity index dynamics of NG and M in NBT test in children with APN (M ± m, n – 30)

Studied indicators	**Unit of measure**	**Duration of the study**		**Indicators of healthy individuals (n = 40)**
		Prior to treatment	**After treatment**	
Neutrophilic granulocytes				
Spontaneous NBT test	%	22.33 ± 0.22*	15.45 ± 0.67*,**	11.57 ± 0.34
Induced NBT test	%	7.23 ± 0.45*	9.74 ± 0.59*, **	12.33 ± 0.47
Stimulation index	Units	-15.12	-5.70	0.76
Monocytes				
Spontaneous NBT test	%	5.22 ± 0.77*	9.75 ± 0.22*,**	11.34 ± 0.34
Induced NBT test	%	3.23 ± 0.23*	5.02 ± 0.45*, **	12.23 ± 0.45
Stimulation index	Units	-1.99	0.77	1.09

Note: * - veracity of differences in relation to the indices of healthy individuals ($p < 0.05$); ** - veracity of differences in relation to initial indices ($p < 0.05$).

The study of the functional activity of NG and M in children with AGN revealed a decrease of the given index in relation to the indicators of healthy individuals ($p < 0.05$) (Table 4). The activity of NG in children of this group was observed on the stage of subcompensation during the whole study, while the spontaneous reaction of M was dramatically reduced and extra stimulation entailed further inhibition of functional activity of M.

Table 4. Activity index dynamics of NG and M in NBT test in children with AGN (M ± m, n – 30)

Studied indicators	**Unit of measure**	**Duration of the study**		**Indicators of healthy individuals (n = 40)**
		Prior to treatment	**After treatment**	
Neutrophilic granulocytes				
Spontaneous NBT test	%	15.22 ± 0.22*	15.24 ± 0.93*	11.57 ± 0.34
Induced NBT test	%	9.22 ± 0.47*	10.27 ± 0.65	12.33 ± 0.47

Stimulation index	Units	-8.00	-4.97	0.76
Monocytes				
Spontaneous NBT test	%	5.17 ± 0.29*	6.07 ± 0.31*	11.34 ± 0.34
Induced NBT test	%	2.56 ± 0.11*	4.11 ± 0.22*, **	12.23 ± 0.45
Stimulation index	Units	-2.61	-1.96	1.09

Note: * - veracity of differences in relation to the indices of healthy individuals ($p < 0.05$); ** - veracity of differences in relation to initial indices ($p < 0.05$).

Spontaneous NBT test with intact NG and M is known to represent the degree of functional stimulation of phagocytic in vivo cells, as an indirect indicator of the state of homeostasis, while induced in the presence of stimulator NBT test characterizes the potential activity of NG and is regarded as a biochemical test of their readiness for phagocytosis completion. Increased rates of spontaneous NBT test indicate a violation of the internal environment of the organism and can serve as a prerequisite for identifying the factor behind the change in the reactivity of cells, and a decline in indices of induced NBT test NG allows diagnosing blockade of production of oxygen-bactericidal factors (possibility of activation of the oxygen dependent phase of phagocytosis).

Obtained on admission, the results of the study of the functional activity of NG in NBT test in response to antigenic stimulation show significant function decompensation of phagocytic cells, and an inability to form adequate response to microbial antigens. Herewith, the inhibition of the functional activity of M as the main component of immune cell antigen presentation constitutes a violation of the presentation mechanisms and regulation of the immune response in general and determines the possibility of developing autoimmune reactions.

Upon completion of the Enterosgel medication course, children with APN demonstrated a downward trend in activity indicators of NG and M in the spontaneous NBT test with respect to baseline characteristics ($p <0.05$). At the same time, a boost in NG and M activity indices was observed in the induced NBT test in relation to the initial indicators, attesting to retention of the functional activity of NG and M in children with APN at subcompensated level.

The use of enterosorption in children with AGN promotes perdurance of M's activity at subcompensated level, providing the opportunity to preserve the mechanisms of antigen presentation at an adequate functional level and to lower the risk of development of autoimmune complications in the given category of patients.

Conclusions

1. The undertaken trials revealed that acute pyelonephritis and acute glomerulonephritis in children are accompanied by development of severe endotoxemia due to the accumulation of medium-sized toxins (10-200 nm). During pyelonephritis, endotoxemia is caused mainly by the accumulation of microbial toxins, and during glomerulonephritis – by auto-aggressive substances and tissue degradation products.

2. During acute pyelonephritis and acute glomerulonephritis, children showed decompensation in function of phagocytic cells as the primary cell factor of organism's anti-toxic antimicrobial resistance. In children with acute pyelonephritis dysfunction of these cells is associated with inhibition of the functionality of neutrophils, while in children with acute glomerulonephritis – with damage of the monocyte function.

3. The use of enterosorption with Enterosgel medication in combination therapy of children with acute pyelonephritis reduces the toxic load on the neutrophilic granulocytes and contributes to the preservation of functional activity of the given cells at subcompensated level, reducing the risk of generalization of infection and the development of associated complications.

4. The use of Enterosgel medication in combination therapy of children with acute glomerulonephritis promotes preservation of the functional activity of monocytes and optimization of their participation in the mechanisms of antigen presentation to immune cells, which reduces the risk of autoimmune complications.