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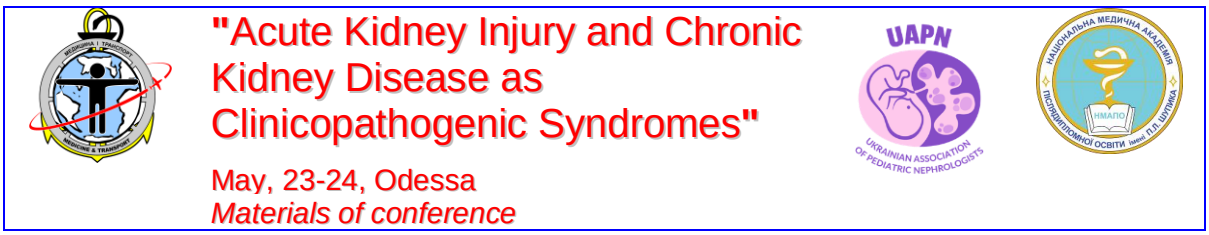

Peculiarities of the influence of sorbilact and its combination with L-arginine on the level of toxemia and detoxification function of the kidneys in the period of development of endogenous intoxication syndrome

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Abstract

Kidney injury in case of endogenous intoxication syndrome of purulent-septic genesis necessitates nephroprotective therapy.

The aim of the work was to determine effects of combined use of sorbilact and L-arginine to levels of toxemia and the detoxification function of the kidneys in endogenous intoxication syndrome during the period of it's development.

Methods. Kidneys' detoxication function have been studied in patients of the following groups.

The first group (I, control) consisted of 31 patients with systemic inflammatory response syndrome (SIRS, ICD-10: R-65.2).

The second group (II) consisted of 27 patients with endogenous intoxication syndrome

who were treated according to Surviving Sepsis Campaign 2016 (standard therapy) [9].

The third group (III) consisited of 29 patients with endogenous intoxication syndrome, who received sorbilact in addition to standard therapy.

The fourth group (IV) included 30 patients with endogenous intoxication syndrome who received sorbilact and L-arginine in addition to standard therapy.

Sorbilact infusion to patients of III and IV groups was performed at a rate of 6-7 ml/kg body weight, intravenously dripping at a rate of 7-8 ml/min. After the end of infusion of sorbilact, patients of IV group were infused with 4.2% solution of L-arginine ("Tivortin" intravenous drip according to the instructions). Data were obtained and results gathered on the application of drugs in the period of stabilization (according to the state of volumoregulatory and osmoregulatory function) of secondary toxic autoagresion (fourth day of drugs' application).

As a single-celled receptor-effector system, the Paramecium caudatum culture was used. Low Molecular Weight Proteins (LMWP) concentration in blood and urine were determined using a modified method.

Results. Development of the syndrome of endogenous intoxication was accompanied by a manifestation of kidney injury. Infusion of sorbilact as a part of complex intensive therapy of endogenous intoxication syndrome has allowed to find out its influence on detoxification functions of the kidneys after a single administration. Under these conditions, sorbilact regulates the ability of the kidneys to excrete toxic substances ($p<0,05$).

Conclusion. Combination of sorbilact with L-arginine according corresponding indicators of total clearance of toxic substances and Low Molecular Weight Proteins after the first infusion leads to the potentiation of the detoxication effect of sorbilact.

Key words: sorbilact, L-arginine, endogenous intoxication syndrome, kidneys.

Introduction

Despite considerable progress, the issue of treating sepsis remains the focus of clinical medicine [1]. Sepsis is inextricably linked to the development of multiple organ disfuntion syndrome, which results in the accumulation of endotoxins and, accordingly, the development of toxemia [2]. Kidneys, as one of the main organs of the detoxification system, are always involved in the clinical and pathophysiological changes, so they require nephroprotection [3]. Nephroprotective therapy requires the use of markers of renal function. Using of additional indicators of endogenous intoxication syndrome (EIS) as well as conventional markers of renal function, allows much better characterize the functional status of the kidneys in

pathology and the effect of therapeutic measures to them [4].

Along with surgical treatment, antibiotic therapy, elimination of water-electrolyte, coagulation and rheological disorders, the correction of endotoxicosis remains the main pathogenetic method of these patients treatment.

Infusion therapy remains the basis of complex intensive care in those cases [5]. Important place among the preparations with detoxification properties belongs to solutions that include polyhydric alcohols, in particular sorbilact. The drug has a wide range of positive characteristics [6], and its effectiveness is established clinically [7]. The use of L-arginine with sorbilact constitutes a significant potential for positive effects on the kidneys.

The aim of the work was to determine effects of combined use of sorbilact and L-arginine on the level of toxemia and the detoxification function of the kidneys in endogenous intoxication syndrome during the period of it's development.

Methods

The study included patients with surgical infection of the Chernivtsi Regional Clinical Hospital. Patients were randomized into groups:

The first group (I, control) consisted of 31 patients with systemic inflammatory response syndrome (SIRS, ICD-10: R-65.2).

The second group (II) consisted of 27patients with EIS of septic genesis, and were sorted by level of cell-mediated and humoral intoxication index (CMHII) according to Konovchuk VM [8] with 20-60 points, who were treated according to Surviving Sepsis Campaign 2016 (standard therapy).

The third group (III) was 29 patients with EIS of septic genesis with 20-60 CMHII points, who received sorbilact in addition to standard therapy.

The fourth group (IV) included 30 patients with SEI of septic genesis with 20-60 CMHII points, who received standard therapy as well as Sorbilact and L-arginine.

Sorbilact infusion to patients of III and IV groups was performed at a rate of 6-7 ml/kg body weight, intravenously dripping at a rate of 7-8 ml/min. After the end of infusion of sorbilact, patients of IV group were infused with 4.2% solution of L-arginine ("Tivortin" intravenous drip according to the instructions).

Inclusion criteria to groups II-IV were acute surgical infection of different localization due to the association of aerobic gram-positive and gram-negative microorganisms with the subsequent development of secondary toxic autoaggression on the scale of CHII more than 40 points; more than 2 points on the SOFA scale with stable hemodynamics; 1 stage of acute kidney damage by the classification of KDIGO; no signs of artificial ventilation.

During the entire treatment period (from the first to the fourth day of observation), patients received standard complex therapy according to Surviving Sepsis Campaign (2016) (surgical sanitation of the source of infection, antibiotic therapy, infusion therapy, rheological, metabolic and inotropic support, etc.), with what the scheme of therapy was coordinated with the practical recommendations of KDIGO. Medications with a diuretic effect were not used in the period of the study.

The circumstances of the termination of the study were regulated by the inclusion criteria (a decrease of CHII below 20 points).

The exclusion criteria were the emergence of one or more circumstances that were not included in the inclusion criteria, in particular: supplementing the intensive therapy with hemodialysis, plasmapheresis, artificial ventilation, hyperbaric oxygenation; a significant deterioration of the general condition due to the activation of comorbid diseases or the progression of complications, which required the use of intensive care measures that were not subject to inclusion criteria.

Blood and urine collection was performed 4 hours (±10 min) from the beginning of infusion of sorbilact on the fourth day of observation (in the period of stabilization of the volume-regulatory function).

CHII was determined by the scale described by Konovchuk VM (2016) [8]. The total concentration of toxic substances was determined using cellular receptor-effector systems (Paramecium caudstum) according to Ershov IuA (1999). LMWP were determined by a modified technique for V. Kamyshnikov (2009) [9]. For statistical data processing, Student's t-criterion for independent samples was used (IBM SPSS Statistics 8).

Results

Development of the syndrome of endogenous intoxication was accompanied by a manifestation of kidney injury. The complex of indexes of kidneys' detoxication function on the first day of observation was investigated (Table 1).

The effect of sorbilact on the detoxification function of the kidneys of patients with EIS is characterized by a sanation effect. The statistically significant increase of the excreted fraction of toxic substances and the intensity of excretion of toxic substances per 100 ml of GFR shows that sorbilact activates the detoxification of the kidneys by increasing the load on the active nephron.

Table 1

Indicators of EIS and kidneys' detoxification function

Indicator, units of measure	Investigation groups			
	Group I, SIRS (31 patients)	Group I, EIS+s.t. (27 patients)	Group I, EIS+s.t.+ sorbilact (29 patients)	Group I, EIS+s.t.+ sorbilact+L-arginine (30 patients)
P_t, toxicity units / ml	103±4,1	172±5,3*	167±5,1	159±5,5**
U_t, toxicity units / ml	290±8,9	346±8,1*	359±7,9	367±7,7**
U_tV, toxicity units / min	275±5,1	222±5,3*	263±5,2*	279±4,9***
EF_t, %	2,3±0,05	1,9±0,05*	2,1±0,04*	2,2±0,04**
C_t, ml / min	2,7±0,06	1,3±0,05*	1,6±0,04*	1,76±0,04***
$U_tV/GFR \cdot 100$ ml, toxicity units / min	234±4,2	337±6,1*	351±5,5*	345±5,1**
P_{LMWP}, cond. units / ml	2,9±0,02	2,1±0,04*	2,2±0,03*	2,3±0,02**
P_{LMWP} GFR, cond. units / min	0,27±0,011	0,75±0,026*	0,68±0,021*	0,63±0,022**
U_{LMWP}, cond. units / ml	4,5±0,13	12,1±0,39*	12,7±0,40	12,9±0,39
U_{LMWP} V, conditional units / min	31,47±0,71	50,1±1,09*	51,7±0,69	51,1±0,65
RF_{LMWP}%, %	4,22±0,18	7,68±0,20*	9,31±0,17*	9,80±0,16***
EF_{LMWP} %, %	14,41±0,35	16,05±0,38*	18,01±0,33*	18,99±0,29***
C_{LMWP}, ml / min	15,91±0,69	10,29±0,73*	13,70±0,65*	15,6±0,59***
U_{LMWP} V/GFR ·100 ml, conditional units / min	3,60±0,16	11,7±0,21*	12,4±0,17*	12,1±0,13.

*– statistically significant difference between parameters of I-II, II-III and III-IV Groups;
** – statistically significant difference between parameters of II-IV groups;
P_t total toxicity of blood plasma; U_t total toxicity of urine; U_tV – excretion of toxic substances; EF_t – excreted fraction of toxic substances; C_t – clearance of toxic substances; $U_tV/GFR \cdot 100$ ml – standardized excretion of toxic substances per 100 ml of GFR; P_{LMWP} – Low Molecular Weight Proteins of blood plasma; P_{LMWP} GFR – excretion of Low Molecular Weight Proteins; U_{LMWP} – Low Molecular Weight Proteins of urine; U_{LMWP} V – excretion of Low Molecular Weight Proteins; RF_{LMWP} % – reabsorbed fraction of Low Molecular Weight Proteins; EF_{LMWP} % – excreted fraction of Low Molecular Weight Proteins; C_{LMWP} – clearance of Low Molecular Weight Proteins; U_{LMWP} V/GFR ·100 ml – standardized excretion of Low Molecular Weight Proteins; s.t.– standard therapy.

Investigation of LMWP makes it possible to elaborate the mechanisms of renoprotection of sorbilact. Given the fact that the filtration fraction was in line with the

control value, and the excretion, clearance and excreted fraction of LMWP increased, the explanation for the effect of sorbilact is reduction the reabsorption of LMWP in the proximal parts of the nephrons. The final effect is a LMWP decrease in plasma.

Comparison and analysis of indicators characterizing the detoxification function of the kidneys at levels of total concentration of toxic substances and LMWP (excretion, clearance) indicates that L-arginine activates it.

Conclusion. Combination of sorbilact with L-arginine according corresponding indicators of total clearance of toxic substances and Low Molecular Weight Proteins after the first infusion leads to the potentiation of the detoxication effect of sorbilact.

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