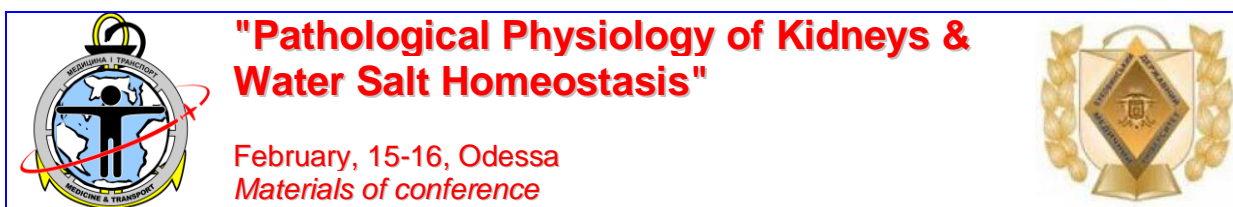


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FEATURES OF SORBILACT-L-ARGININE-COMBINED ACTION ON THE KIDNEYS' VOLUMOREGULATORY FUNCTION OF PATIENTS WITH PURULENT-SEPTIC COMPLICATIONS

N. O. Maksymchuk, V. M. Konovchuk

Higher State Educational Institution of Ukraine «Bukovinian State Medical University»,
Chernivtsi

Abstract

The purpose of the work is to investigate the effect of combined use of sorbilact and L-arginine on the kidneys' volume-regulatory function of patients with endogenous intoxication syndrome (EIS) of purulent-septic origin in the period of stabilization of secondary toxic autoaggression.

Methods. Indicators of kidney volume receptor 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). The second group (II) consisted of 22 patients with EIS who were treated according to Surviving Sepsis Campaign 2016 (standard therapy) [9]. The third group (II) consisted of 24 patients with EIS, who received sorbilact in addition to standard therapy. The fourth group (IV) included 21 patients with SEI 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). Data was obtained and results gathered on the application of drugs in the period of stabilization of secondary toxic autoaggression (fourth day of drugs’ application).

Findings. In the period of stabilization there is a restoration of the volume-regulatory function of the kidneys under standard therapy of endotoxemia of purulent-septic genesis. The use of sorbilact with standard therapy activates the volume-regulatory function of the kidneys (in terms of sodium clearance by 31%, $p < 0,05$) in the period of stabilization of toxic autoaggression. The combination of sorbilact with L-arginine increases the activity of sodium clearance by 12% ($p < 0,05$) induced by sorbilact.

Conclusions. The investigated features of basic adjuvant therapy with L-arginine and sorbilact can be recommended for use in order to restore the volume-regulatory function of the kidneys in cases of endotoxemia of purulent-septic genesis.

Key words: sorbilact, L-arginine, volumoregulatory function.

Introduction

Purulent-septic complications remain a pressing problem of clinical medicine [1]. They cause endotoxemia and multiple organ damage. Kidneys are the main homeostatic organ whose functions undergo intensive strain of various circumstances of multiple organ failure, especially in the event of an initiated toxic aggression.

In this context, attention should be paid to the relevant regulatory framework of their functions, including volume-regulatory; consider the possibility of adjuvant-standard therapy for renoprotection and optimization of functional affiliation [2, 3].

Infusion therapy is the basis for treatment of purulent-septic complications and secondary toxic auto aggression [4]. Among infusion solutions sufficiently promising are preparations of polyhydric alcohols, in particular sorbitol-based [5]. It expands the prospects for using adjuvant therapy, in particular, the combination of solutions of polyhydric alcohols with L-arginine [6]. However, the effect of combined use of sorbilact with L-arginine on renal function remains unknown.

The purpose of the work is to investigate the effect of combined use of sorbilact and L-arginine on the kidneys’ volume -egulatory function of patients with EIS of purulent-septic genes in the period of stabilization of secondary toxic autoaggression.

Methods. The following groups of patients were included in clinical trials:

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 22 patients with EIS of purulent-septic genesis, and were sorted by level of cell-mediated and humoral intoxication index (CHIII) [7] with 20-60 points, who were treated according to Surviving Sepsis Campaign 2016 (standard therapy) [9].

The third group (II) was 24 patients with EIS of purulent-septic genesis with 20-60 CHII points, who received sorbilact in addition to standard therapy.

The fourth group (IV) included 21 patients with SEI of purulent-septic genesis with 20-60 CHII points, who received standard therapy as well as Sorbilact and L-arginine.

During the entire treatment period (from the first to the fourth day of observation), patients received standard complex therapy (surgical sanitation of the source of infection, antibiotic therapy, infusion therapy, rheological, metabolic and inotropic support, etc.). Medications with a diuretic effect were not used in the period of the study. 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).

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

The exclusion criteria was 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 secondary toxic autoaggression according to the volume-regulatory function. Investigation of renal functions was carried out according to generally accepted methods [8]

The statistical analysis of the data was performed using Student's t-test for dependent (Δ) and independent samples using IBM Packs SPSS Statistics 8.

Results

The study of the sodium format reflects the state of the volume-regulatory function of the kidneys (Table).

The obtained data show that in the period of stabilization of toxic autoaggression with standard therapy in patients with EIS the following indicators increased: $U_{Na}V$ (by 9%, $p < 0,05$), EF_{Na} (by 36%, $p < 0,05$) and I_{Na} (by 76%, $p < 0,05$).

Kidney volume-regulatory function in patients with purulent-septic complications

Indicator, units of measure	Investigation groups			
	Group I, SIRS (31 patients)	Group I, EIS+s.t. (22 patients)	Group I, EIS+s.t.+ sorbilact (24 patients)	Group I, EIS+s.t.+ sorbilact+L-arginine (21 patients)
GFR, (ml/min)	118±2,7	73±2,5*	87±2,4*	102±2,3* **
P _{Na} , (mmol/L)	138±1,2	134±1,5*	146±1,4*	140±2,3* **
U _{Na} , (mmol/L)	111±4,4	128±5,3*	135±5,1	129±5,3
U _{Na} V, (μmol/L)	106±4,0	116,5±4,7*	165±4,2*	178±4,8* **
P _{Na} GFR, (μmol/min)	16,2±0,27	9,8±0,29*	12,7±0,28*	14,3±0,30* **
R _{Na} , (%)	99,23±0,04	98,96±0,06*	98,70±0,05*	98,63±0,07**
EF _{Na} , (%)	0,77±0,03	1,05±0,05*	1,3±0,04*	1,4±0,06**
C _{Na} , (ml/min)	0,77±0,02	0,87±0,04*	1,14±0,03*	1,28±0,05* **
C _{Na} ^{H₂O} , (ml/min)	0,18±0,005	0,04±0,007*	0,08±0,006*	0,11±0,008* **
I _{Na} , (mmol/min)	90±3,3	159±3,9*	190±3,9*	175±4,1* **

Note:

*– statistically significant difference between parameters I-II, II-III and III-IV groups; ** – statistically significant difference between parameters II-IV groups; s.t. – standard therapy; P_{Na} – the concentration of sodium in the blood plasma; U_{Na} – concentration of sodium in urine; P_{Na} GFR – sodium filtration fraction; U_{Na}V – sodium excretion; R_{Na} – sodium reabsorbed fraction; EF_{Na} – sodium excreted fraction; C_{Na} – sodium clearance; C_{Na}^{H₂O} – clearance of sodium-free water; I_{Na} – the intensity of sodium excretion at 100 ml GFR.

In essence, the considered parameters determine the clearance of sodium (C_{Na}). C_{Na} is the main indicator that characterizes the state of the kidney volume-regulatory function and shows how much volume they reduce from the volume of the extracellular fluid in the given period of time and in these circumstances, or characterizes the conditional amount of protein-free fluid that is excreted by the kidneys, where sodium concentration corresponds to the sodium concentration in plasma. In patients with EIS, C_{Na} increased by 13% (p<0.05) compared with patients with SIRS.

The clearance of sodium-free water in patients of group II decreased (by 4-5 times, p<0.05) compared to group I, which may indicate a decrease in distal sodium reabsorption. The indicated changes were most likely the basis for some reduction of sodium concentration (p<0,05) in blood plasma (Table). It should be noted that on the first day of the study C_{Na} was 0.42 ± 0.04 ml/min, which means that by the fourth day of the study (Table), this figure increased by 104 ± 37.2% (Δp<0.05).

The research has established changes in the volume-regulatory function in patients with EIS when they were treated by standard therapy and sorbilact. The evaluation and comparison of the data revealed an increase P_{Na} (by 8%, $p < 0,05$), P_{Na} GFR (by 29%, $p < 0,05$), $U_{Na}V$ (by 42%, $p < 0,05$), EF_{Na} (by 24%, $p < 0,05$), and I_{Na} compared with the second group, indicating sorbilact-dependent activation of the volume-regulatory function. In the study period C_{Na} in group III exceeded the value of group II by 31%, $p < 0,05$, and the dynamic changes (on the first day C_{Na} was $0,48 \pm 0,03$ ml/min) were $140 \pm 37\%$, $\Delta p < 0,05$.

As a result of the obtained data analysis of the combined use of sorbilact and L-arginine in addition to standard therapy, an L-arginine-dependent activation of the volume-regulatory function was observed. C_{Na} increased by 12%, ($p < 0,05$) compared with the third group, and by $140 \pm 37,9\%$, ($\Delta p < 0,05$) compared with the indicator of this group on the first day. The base of these changes was the growth of P_{Na} GFR and the dynamic changes of R_{Na} . Accordingly, there is an increase in $U_{Na}V$ compared with the group where only sorbitolact was used.

Conclusions

1. In the period of stabilization there is a restoration of the volume-regulatory function of the kidneys under standard therapy of endotoxemia of purulent-septic genesis.
2. The use of sorbilact with standard therapy activates the volume-regulatory function of the kidneys (in terms of sodium clearance by 31%, $p < 0,05$) in the period of stabilization of toxic autoaggression.
3. The combination of sorbilact with L-arginine increases the activity of sodium clearance by 12% ($p < 0,05$) induced by sorbilact.

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