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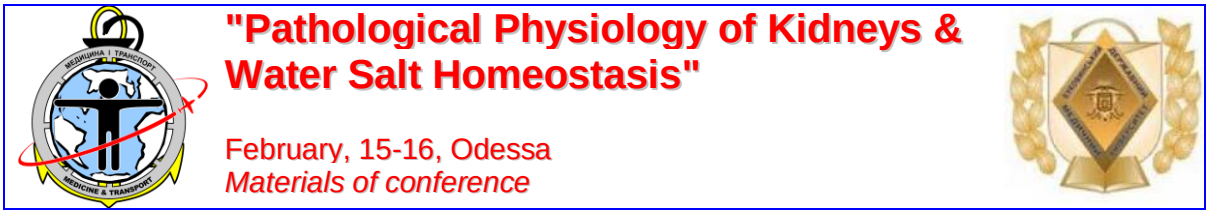

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THE EFFECT OF REOSORBILACT ON VOLUMETRIC AND OSMOREGULATORY RENAL FUNCTIONS IN PATIENTS WITH DOPAMINE-DEPENDENT COMPENSATION FOR SEPSIS-INDUCED HYPOTENSION

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Abstract

Objective to study the response of volumetric and osmoregulatory renal functiona to the action of Reosorbilact in dopamine-dependent compensation of sepsis-induced hypotension.

Materials and methods. Inclusion criteria - patients with purulent-septic complications in dopamine-dependent compensation (5-10 μg / kg min) according to the initial values: MAP> 70 mmHg, APs> 95 mmHg, CVP> 4 mmHg, diuresis> 30 ml / h. Control studies - Patients with Systemic Inflammatory Response Syndrome (SIRS) who met the criteria of ICD-10 classification: SIRS, ICD-10: R-65.2. The patients were divided into 4 groups: I gr. and II gr. - control studies (SIRS, n = 25); III gr. and IV gr. - severe sepsis (n =

28). The patients from groups II and IV received an infusion load of Reosorbilact in the amount of 7-8 ml / kg at a rate of 18-20 ml / min.

Results. The results of studies on the influence of Reosorbilact on volumetric and osmoregulatory function of the kidneys in patients with severe sepsis in case of dopaminergic hemodynamic compensation (a comparison between groups III and IV) have been presented. The following results were obtained: diuresis, due to a reduction of water reabsorption, increased by 224 ± 58,9% (Δ, P <0,05), sodium clearance by 317 ± 52,5% (Δ, P <0,05), clearance of osmotically active substances - by 240 ± 68,6% (Δ, P <0,05); glomerular filtration rate by 54 ± 11,7% (Δ, P <0,05), the reabsorbed sodium fraction decreased by 1,58 ± 0,29% (Δ, P <0,05), and the reabsorbed fraction of osmotically active substances by 4.2 ± 1.40% (Δ, P <0.05).

Conclusions. In dopamine-dependent compensation of sepsis-induced hypotension, there is a decrease in the level of values of glomerular filtration rate (by 41%, P <0.05), sodium clearance (by 17%, P <0.05) and osmotically active substances (by 16% , P <0.05) compared to those in patients with SIRS, which is indicative of the depression of the volumetric and osmoregulatory function. The infusion load with Reosorbilact in patients with compensated sepsis-induced hypotension is realized by increasing the filtration fractions of sodium and osmotically active substances, reducing their reabsorption in the renal tubules, compensatory restoration of volume-dependent reactions characterizing volumetric and osmoregulatory functions of the kidneys.

Key words: **volumetric and osmoregulatory renal functions, Reosorbilact, severe sepsis.**

ВПЛИВ РЕОСОРБІЛАКТУ НА ВОЛЮМО- ТА ОСМОРЕГУЛЯТОРНУ ФУНКЦІЇ НИРОК У ХВОРИХ ІЗ ДОФАМІН-ЗАЛЕЖНОЮ КОМПЕНСАЦІЇ СЕПСИС-ІНДУКОВАНОЇ ГІПОТЕНЗІЇ

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Мета роботи – дослідити реакцію волюмо- та осморегуляторної функції нирок на дію Реосорбілакту при дофамін-залежній компенсації сепсис-індукованої гіпотензії.

Матеріал та методи. Критерії включення – пацієнти з гнійно-септичними ускладненнями з дофамін-залежною компенсацією (5-10 мкг/кг·хв) за стартовими показниками: САТ >70 мм.рт.ст., АТс >95 мм.рт.ст., ЦВТ >4 мм.рт.ст., діурезу >30мл/год. Контрольні дослідження – пацієнти з синдромом системної запальної відповіді (ССЗВ), котрі відповідали класифікатору МКХ-10: SIRS, ICD-10: R-65.2. Пацієнти були розподілені на 4 групи: I гр. та II гр. – контрольні дослідження (ССЗВ, n=25); III гр. та IV гр. – тяжкий сепсис (n=28). Пацієнти II гр. та IV гр. отримували інфузійне навантаження Реосорбілактом в кількості 7-8 мл/кг зі швидкістю 18-20 мл/хв.

Результати. Представлені результати досліджень впливу Реосорбілакту на волюмо- та осморегуляторну функції нирок у хворих на тяжкий сепсис (порівняння між III гр. та IV гр.) за умови дофамінергічної компенсації гемодинаміки. Отримані наступні результати: діурез, за рахунок зменшення реабсорбції води, збільшувався на 224±58,9% (Δ, P<0,05), кліренс натрію – на 317±52,5% (Δ, P<0,05), кліренс осмотично активних речовин – на 240±68,6% (Δ, P<0,05); швидкість клубочкової фільтрації – на 54±11,7 % (Δ, P<0,05), реабсорбована фракція натрію зменшувалася на 1,58±0,29% (Δ, P<0,05), а реабсорбована фракція осмотично активних речовин – на 4,2±1,40% (Δ, P<0,05).

Висновки. При дофамін-залежній компенсації сепсис-індукованої гіпотензії спостерігається зниження рівня значень показників швидкості клубочкової фільтрації (на 41%, P<0,05), кліренсів натрію (на 17%, P<0,05) та осмотично активних речовин (на 16%, P<0,05) від даних у пацієнтів із ССЗВ, що свідчить за депресію волюмо- та осморегуляторної функції. Інфузійне навантаження Реосорбілактом хворим з компенсованою сепсис-індукованою гіпотензією реалізується підвищенням фільтраційних фракцій натрію та осмотично активних речовин, зменшенням їх

реабсорбції в канальцях нирок, компенсаторним відновленням об'єм-залежних реакцій, що характеризують волюмо- та осморегуляторну функції нирок.

Ключові слова: **волюмо- та осморегуляторна функції нирок, Реосорбілакт, тяжкий сепсис.**

ВЛИЯНИЕ РЕОСОРБИЛАКТА НА ВОЛЮМО- И ОСМОРЕГУЛЯТОРНЫХ ФУНКЦИИЙ ПОЧЕК У БОЛЬНЫХ С ДОФАМИН-ЗАВИСИМОЙ КОМПЕНСАЦИИ СЕПСИС-ИНДУЦИРОВАННОЙ ГИПОТЕНЗИИ

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Цель работы - исследовать реакцию волюмо- и осморегуляторных функций почек на действие Реосорбилакта при дофамин-зависимой компенсации сепсис-индуцированной гипотензии.

Материал и методы. Критерии включения - пациенты с гнойно-септическими осложнениями со дофамин-зависимой компенсацией (5-10 мкг / кг · мин) по стартовым показателям: САД> 70 мм, АДс> 95 мм, ЦВД> 4 мм, диуреза> 30 мл / ч. Контрольные исследования - пациенты с синдромом системного воспалительного ответа (ССВО), которые отвечали классификатору МКБ-10: SIRS, ICD-10: R-65.2. Пациенты были разделены на 4 группы: I гр. и II гр. - контрольные исследования (ССВО, n = 25); III гр. и IV гр. - тяжелый сепсис (n = 28). Пациенты II гр. и IV гр. получали инфузионная нагрузка Реосорбилакт в количестве 7-8 мл / кг со скоростью 18-20 мл / мин.

Результаты. Представлены результаты исследований влияния Реосорбилакта на волюмо- и осморегуляторных функций почек у больных на тяжелый сепсис (сравнение между III гр. и IV гр.) При условии дофаминергической компенсации гемодинамики. Получены следующие результаты: диурез за счет уменьшения реабсорбции воды, увеличивался на 224 ± 58,9% (Δ, P <0,05), клиренс натрия - на 317 ± 52,5% (Δ, P <0,05), клиренс осмотически активных веществ - на 240 ± 68,6% (Δ, p <0,05) скорость клубочковой фильтрации - на 54 ± 11,7% (Δ, P <0,05), реабсорбованая фракция натрия уменьшалась на 1,58 ± 0,29% (Δ, P <0,05), а реабсорбованая фракция осмотически активных веществ - на 4,2 ± 1,40% (Δ, P <0,05).

Выводы. При дофамин-зависимой компенсации сепсис-индуцированной гипотензии наблюдается снижение уровня значений показателей скорости клубочковой фильтрации (на 41%, P <0,05), клиренс натрия (на 17%, P <0,05) и осмотически активных веществ (на 16% , P <0,05) от данных у пациентов с ССВО, что свидетельствует за депрессию волюмо- и осморегуляторных функций. Инфузионная нагрузка Реосорбилакт больным с компенсированной сепсис-индуцированной гипотензии реализуется повышением фильтрационных фракций натрия и осмотически активных веществ, уменьшением их реабсорбции в канальцах почек, компенсаторным восстановлением объем зависимых реакций, характеризующие волюмо- и осморегуляторных функций почек.

Ключевые слова: волюмо- и осморегуляторные функции почек, Реосорбилакт, тяжелый сепсис.

Introduction. The current approaches to the intensive infusion therapy for sepsis are focused on recommendations for giving priority to the use of crystalloid drugs [1, 6]. Due to some symptoms, the erythrocyte mass, albumin and gelatin drugs are administered [2]. Derivatives of Hydroxyethilstarch, according to multicenter studies, cause complications and have side effects that limit their use significantly [3]. Taking into account the polymorphism of the sepsis pathogenesis, multiple organ effect, mutual aggravation and possible secondary comorbidity, such an arsenal of intensive care should be considered as not being able to satisfy the pathogenetic substantiation of the basic component of the program for the sepsis intensive therapy [2].

In this connection, attention was paid to the properties and spectrum of the derivatives of polyhydric alcohols action, namely sorbitol. Nephroprotection, which is due to the improvement of rheology, hemodilution, increased renal blood flow, increased glomerular filtration, the effect of osmotic diuresis is an evidence base for the use of drugs [4]. In this regard, taking into account the homeostatic value of the kidneys, namely its functions - volumetric and osmoregulatory ones, relevant studies were conducted in patients with severe sepsis.

Objective. To study the effect of Reosorbilact on volumetric and osmoregulatory renal function in dopamine-dependent compensation of sepsis-induced hypotension (severe sepsis).

Materials and methods. The studies are open, randomized, prospective, and controlled. Inclusion criteria - patients with purulent-septic complications with dopamine-

dependent compensation (5-10 μg / kg · min) according to the starting values: MAP >70 mm Hg, APs >95 mm Hg, CVP> 4 mmHg, diuresis> 30 ml / h. Control studies - Patients with Systemic Inflammatory Response Syndrome (SIRS) who met the criteria of ICD-10 classification: SIRS, ICD-10: R-65.2. The patients were divided into 4 groups: Groups I and II - control studies (SIRS, n = 25); Groups III and IV - severe sepsis (n = 28). The patients from groups II and IV received an infusion load with Reosorbilact in the amount of 7-8 ml / kg at a rate of 18-20 ml / min. For statistical analysis of the data, the Student's t-criterion for dependent (Δ) and independent choices (statistical package - Excell) was used.

Results and discussion

The methodology of the study objectivization of renal function suggests the stability of hemodynamics during the observation. Correction of hemodynamics with the growth of septic hypotension is based on the principles of rapid fluid resuscitation and using the infusion of adrenergic agents to restore the vascular tone. It should be noted that the initial volume-dependent infusion correction of sepsis-induced hypotension was 30-45 ml / kg of body weight (control: MAP, CVP, diuresis) by keeping hemoglobin in the plasma at the rate 100-120 g/l, packed cell volume – 30-35%, whole protein– 60-65 g/l. The indications for dopamine infusion were a decrease in MAP (up to 70 mm Hg) and APs (up to 90-95 mm Hg) with proper volume liquid support. After obtaining a satisfactory compensation, after 8-12 hours, the requirements of the study were met, namely, the action of Reosorbilact in the selected mode (provided by the IT program) on the volumetric and osmoregulatory function of the kidneys (Table). Implementation of the research project took place after the creation of a hemodynamic plateau, for example, for MAP.

The table presents the main values characterizing volumetric and osmoregulatory functions of the kidneys in patients with SIRS (group I) and sepsis-induced hypotension with corrected dopaminergic support (group III). The glomerular filtration rate (GFR) is the integrative index among them. Its variability in severe sepsis is due to numerous factors of endotoxicosis and the state of the central and peripheral hemodynamics [5, 6]. Although the depression of GFR in patients from group III was 41% (P <0.05), the excreted water fraction exceeded the control value by 57% (P <0.05), and diuresis reached 91% (P> 0.05) from those of the comparison group. The explanation is in the aspect of different activity of reabsorption, namely: in group I R_{H2O}=99,19±0,13%, and in group III R_{H2O}=98,73±0,12% (P<0,05). The main figure that characterizes the state of volumoregulatory function of the kidneys is the clearance of sodium rate. It shows how much the volume of the extracellular fluid reduces in a given period of time and under these circumstances or characterizes the conditional amount

of protein free fluid that is excreted by the kidneys, where the concentration of sodium corresponds to the concentration of cation in the blood plasma.

Table

The effect of reosorbilact on volumetric and osmoregulatory renal functions in patients with dopamine-dependent compensation for sepsis-induced hypotension

Values	**SIRS (n=25)**		**Severe sepsis (n=28)**	
	Group I (A)	Group II (B)	Group III (A)	Group IV (B)
V, ml/min	0,92±0,06	2,82±0,12**	0,84±0,06	2,71±0,11**
EF_{H2O}, %	0,81±0,02	2,20±0,03**	1,27±0,04*	2,63±0,03** *
GFR, ml/min	114±2,3	129±2,4**	67±2,2*	103±2,3** *
P_{Na}, mmol / l	138±0,7	143±0,8**	136±0,5*	144±0,7**
P_{Na}·GFR, mmol / l /min	15,7±0,38	18,5±0,39**	9,1±0,29*	14,8±0,35** *
U_{Na}, mmol / l	114±5,1	142±6,8**	105±5,3	141±6,4**
$U_{Na}V$, µmol / min	105±4,6	400±7,9**	88±4,4*	382±7,7**
C_{Na}, ml/min	0,77±0,03	2,80±0,07**	0,64±0,04*	2,66±0,06**
EF_{Na}, %	0,68±0,04	2,17±0,09**	0,99±0,05*	2,59±0,06** *
$C_{Na}^{H_2O}$, ml/min	0,16±0,008	0,02±0,003**	0,21±0,007*	0,05±0,008** *
P_{osm}, mosm / l	294±2,2	301±2,3**	302±2,0*	308±2,3** *
U_{osm}, mosm / l	839±22,1	887±23,9	785±19,7	852±20,9**
$U_{osm}V$, mcosm / min	772±32,2	2501±87,7**	659±31,9*	2309±47,3** *
C_{osm}, ml/min	2,6±0,09	8,3±0,15**	2,2±0,09*	7,5±0,12** *
EF_{osm}, %	2,3±0,11	6,5±0,17**	3,3±0,08*	7,5±0,11** *
T^c_{H2O}, ml/min	1,7±0,05	5,5±0,16**	1,4±0,04*	4,8±0,09** *

Note: Groups I and II – Systemic inflammatory response syndrome (SIRS; Groups III and IV – severe sepsis (SS); IEFV – increased extracellular fluid volume by means of Reosorbilact; A – patients before IEFV, B – patients after IEFV; */P≤0,05 – reliability of values between groups I and III, II and IV, **/P≤0,05 – reliability of values between the conditions A and B; V – diuresis, EF_{H2O} – Fractional excretion of water, GFR – glomerular filtration rate, P_{Na} – sodium concentration in the plasma, P_{Na}·GFR – fractional excretion of sodium, U_{Na}- sodium concentration in urine, $U_{Na}V$ – sodium excretion with urine, C_{Na} – sodium clearance, EF_{H2O} – fractional excretion of sodium, $C_{Na}^{H_2O}$ – sodium-free water clearance, P_{osm} – plasma OAS concentrationy, U_{osm} – urine OAS concentration, $U_{osm}V$ – OAS excretion with urine, C_{osm} – OAS clearance, EF_{osm} – OAS fractional excretion, T^c_{H2O} – reabsorption of osmotically free fluid.

With septic endotoxicosis and dopaminergic support, clearance of sodium is 83% (P <0.05) of the control level (SIRS). The main reason is the reduction of the filtration fraction of sodium, since cation reabsorption by the parameters of the excreted fraction and the calculation of sodium excretion by 100 ml of GFR (92 ± 3.1 μmol / min – group I; 131 ± 4.1 μmol / min – group III, (P <0.05) was less than the control values. If we take into account the increase in the clearance of sodium-free water, it should be noted that the distal reabsorption of sodium was elevated (group III). Changes (depression) in the osmoregulatory function of the kidneys were the same; in particular, the OAS clearance was 84% of the control one. The excreted fraction (due to a decrease in reabsorption and an increase in the secretion of OAS) was elevated, and its equivalent - the intensity of excretion of OAS per 100 ml of GFR was 984 ± 28.4 mc / min in group III and 677 ± 31.8 mCsm / min in group I, P <0.05). In addition, the value T^{c}_{H2O} is indicative of a decrease in the reabsorption of osmotically free fluid in the distal parts of the nephrons. The intensity of the reabsorption of osmotically free fluid in distal nephron departments depends on the size of the tubule cytokine volume in the distal regions, the magnitude of the osmotic gradient in the medullary substance of kidney and the permeability of the nephron peripheral department for water. Thus, with the condition of toxic endotoxicosis and forced dopaminergic support of hemodynamics without stimulation with reosorbilact, the depression of the volumetric and osmoregulatory function of the kidneys is observed in the clearance characteristics. The regulatory principles of process dynamics in distal nephron departments are aimed at increasing sodium reabsorption and reducing reabsorption of osmotically free fluid.

The table presents the results of studies on the effect of Reosorbilact on volumetric and osmoregulatory function of the kidneys in patients with severe sepsis (comparison between groups III and IV) under dopaminergic hemodynamic compensation. The corresponding values of these changes are characterized by the following figures: diuresis, due to the reduction of water reabsorption, increased by 224 ± 58,9% (Δ, P <0,05), sodium clearance by 317 ± 52,5% (Δ, P <0 , 05), clearance of osmotically active substances - by 240 ± 68,6% (Δ, P <0,05); the glomerular filtration rate by 54 ± 11,7 (Δ, P <0,05), the reabsorbed sodium fraction decreased by 1,58 ± 0,29% (Δ, P <0,05), and the reabsorbed fraction of osmotically active substances - by 4.2 ± 1.40% (Δ, P <0.05). The significant decrease in clearance of sodium-free water indicates the inhibition of sodium reabsorption in the distal nephron, and the $\mathbf{T^{c}_{H2O}}$ value shows activation of the osmotically free fluid transport.

In this regard, consideration of the comparative characteristics of the values between groups II and IV (the reaction of volumetric and osmoregulatory function of the kidneys in

patients with SIRS and severe sepsis for the introduction of Reosorbilact) is important. After increasing the extracellular fluid volume (IEFV) by means of reosorbilact, the glomerular filtration rate remains lower and is 80% compared to group II (P <0.05). Due to more intensive compensatory inhibition of reabsorption of water, sodium and OAS by their excretory fractions (an increase in Δ, P <0,05), clearance of sodium and OAS after IEFV in group IV patients approached the values of group II, and their differences were 5% (P> 0.05) and 9% (P <0.05) respectively while their diuresis was 4% (P> 0.05). According to the rate of clearance of sodium-free water after IEFV in patients with SIRS and severe sepsis, distal reabsorption of sodium decreased, and that of osmotically free fluid increased.

Conclusions

1. With dopamine-dependent compensation for sepsis-induced hypotension, there is a decrease in the values of the glomerular filtration rate (by 41%), sodium clearance (by 17%) and osmotically active substances (by 16%) compared to those in patients with systemic inflammatory response syndrome, which testifies to the corresponding depression of the volumetric and osmoregulatory function.

2. The infusion load with Reosorbilact in patients with compensated sepsis-induced hypotension is realized by increasing the filtration fractions of sodium and osmotically active substances, reducing their reabsorption in the renal tubules, compensatory restoration of volume-dependent reactions characterizing volumetric and osmoregulatory functions of the kidneys.

3. The obtained results indicate that Reosorbilact should be considered as a means of nephroprotection in severe sepsis.

Prospects for further research. The obtained results can serve as an aid in drawing up the program of intensive care, studying the effects of other infusion agents, studying the osmotic and volumetric and regulatory functions of the kidneys in severe sepsis.

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