ORIGINAL ARTICLE

CONTENTS

Xylate effect on the renal toxicological function with diabetes mellitus complicated by endogenous intoxication syndrome of purulent-septic genesis

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ABSTRACT

Aim: To study xylate effect on the renal toxin-excreting function with diabetes mellitus (DM) complicated by endogenous intoxication syndrome of purulent-septic genesis.

Materials and Methods: The effect of infusions with sorbilact or Ringer's solution in the regimen 3 ml/kg/hour during 3 hours on toxin-excreting function of the kidneys in patients with type 2 DM complicated by EIS is studied.

Results: In the period of the research, xylate increased cleaning blood plasma (extracellular water space) from the total toxicity by 6,0±1,9 ml/min (230±72,3%, Δ p<0,05). Ringer's solution infusion in the fragment of intensive care of the same group of patients (n=53) was determined by increase of clearance of toxic substances by 4,3±1,2 ml/min (165±46,0%, Δ p<0,05). At the same time, xylate infusion decreased the total blood plasma toxicity by 22±4,6 IU/ml (14±2,9%, Δ p<0,05), and Ringer's solution – by 12±3,9 IU/ml (7±2,2%, Δ p Ringer's solution) in patients with Type 2 DM complicated by endogenous intoxication syndrome of purulent-septic genesis. At the same time, xylate infusion reduced the total plasma toxicity by 22±4.6 IU/ml (14±2.9%, Δ p<0.05), Ringer's solution - by 12±3.9 IU/ml (7±2.2%, Δ p<0.05).

Conclusions: Infusion therapy solutions (xylate, Ringer's solution) within the study regimen (3 ml/kg/h for three hours) activate the renal excreting function and reduce the level of toxemia (xylate > Ringer's solution) in patients with Type 2 DM complicated by endogenous intoxication syndrome of purulent-septic genesis. At the same time, xylate infusion reduced the total plasma toxicity by 22±4.6 IU/ml (14±2.9%, Δ p<0.05), Ringer's solution - by 12±3.9 IU/ml (7±2.2%, Δ p<0.05).

KEY WORDS: type 2 DM, renal toxin-excreting function, xylate, endogenous intoxication syndrome of purulent-septic genesis

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INTRODUCTION

Infusion therapy is a basic one in the intensive therapy of biological integrity disorders of a patient organism [1]. It is prioritized due to the content of ingredients essential to maintain homeostasis and correction of its quality. Today, association of diabetes mellitus with endogenous intoxication syndrome (DMEIS) including that of purulent-septic genesis is rather spread nosology [2]. It requires a comprehensive treatment, careful monitoring, individualization of intensive therapy measures considering numerous complications of diabetes mellitus and endogenous intoxication syndrome factors focused on the formation of multiple organ damage [3]. Therefore, the issues concerning the choice of infusion therapy medicines in order to rehabilitate the condition of target organs with diabetes mellitus associated with metabolic disorders initiated by the concomitant syndrome of endogenous intoxication deserve certain attention [4]. One of the answers to this question is within the range of the action of an appropriate drug used for the infusion therapy through the prism of the renal toxin-excreting function. Xylate can be such a drug, since its capabilities correspond to the requirements for the correction of this pathology. Its main component xylitol is a natural intermediate product of carbohydrate metabolism in people and animals. Its pharmacokinetics is not associated with special hormonal or enzymatic transport mechanisms. Its degree of assimilation does not depend on the age of the patient. According to the mechanism of action, it binds the pentose phosphate cycle with uronic acid metabolism. The final product of oxidation is carbon dioxide eliminated by the lungs. Compared to glucose, xylitol is more effective source of energy conversion, and its metabolism does not depend on insulin. It possesses lipotropic and antiketogenic activity, stimulates glycogen synthesis in the liver and insulin secretion, improves microcirculation, normalizes water-salt metabolism and acid-alkaline state, and possesses detoxification action with burn disease, protracted purulent processes and infectious diseases [5].

AIM

The aim of the work was to study xylate effect on the renal toxin-excreting function with diabetes mellitus complicated by endogenous intoxication syndrome of purulent-septic genesis.

MATERIALS AND METHODS

The research is open randomized, prospective and controlled. The patients suffering from type 2 DM complicated by endogenous intoxication syndrome of purulent-septic genesis were examined. Inclusion criteria include type 2 DM, age of patients – 42-65 years, the determined period of the disease – 5-12 years. The previous history: dietary correction, specific regimen, hypoglycemic agents, insulin (9%); actual blood glucose – 8-16 mmol/L, glycosylated hemoglobin > 7%, transient microalbuminuria (30-300 mg/day); different clinical signs of angiopathy and neuropathy are registered without considerable disturbances of the afflicted organs and systems. The course of type 2 DM of these patients was complicated by acute surgical infection after surgical rehabilitation of foci of various localization caused by association of aerobic gram-positive and gram-negative flora. The disease was associated with by endogenous intoxication syndrome of purulent-septic genesis of 20-50 points on the intoxication cellular humoral index scale [6].

All the patients (n=53) received appropriate surgical rehabilitation and a comprehensive standard intensive therapy. Sugar level was corrected in the hospital by insulin in case glucose level > 10 mmol/L. In case of inclusion into the research, the intensive therapy of patients was supplied by infusions of Ringer's and xylate solutions. The indicators characterizing the renal toxin-excreting function were studied in the interval of the test Ringer's solution infusion and 20-24 hours later – xylate. The group characteristics were determined: I-IV groups – type 2 DM including A: indicators of patients before Ringer's solution (I group) or xylate infusion (III group); B – after Ringer's solution (II group) or xylate infusion (IV group). The regimen of solution infusions was 3 ml/kg/hours during 3 hours. After increasing the extracellular space volume with solutions, patients were examined within a 4-hour interval considering the time of infusion load. The parameters of values examined in biological medium including total blood plasma (urine) toxicity [6], concentration of average mass molecules in the blood plasma or urine [7], cellular-humoral intoxication index [6], procalcitonin [8] are presented in the Table. The data obtained were statistically processed by means of Student T-criterion for the dependent (Δ) and independent samples (statistical package Excell, trial version) [9].

RESULTS AND DISCUSSION

The two periods were determined in the course of infusion therapy for the patients with DMEIS (n=53): the first one deals with the examination of Ringer's solution effect (3 ml/kg/hours during 3 hours) on the renal toxin-excreting function (I-II groups); the second one – after 20-24 hours of xylate effect (III-IV group) under the same conditions of the study (Table 1)..

Unicellular receptor systems are sensitive indicators of the total toxicity of the blood plasma (Рт) [10]. As a result of modification [6], it becomes informative as a criterion of activity of the renal toxin-excreting function, balance between toxin formation and toxemia. It enables to evaluate detoxification effect of the solutions in the intensive care (IC) program (Table 1).

Administration of xylate was associated with an increased secretion of toxic substances by 766±118,9 IU/ml (177±27,8%, Δ $p<0,05$). Analysis of this process constituents, that is, concentration characteristics of the total toxicity of urine ingredients – before xylate load and after it (Table 1) with diuresis volume of these patients A – 1,23±0,03 ml/min, B – 3,58±0,08 ml/min, $p<0,05$), is indicative of a prevailing xylate effect on water excretion kidney function and its importance in the formation of the total blood plasma toxicity, since the total urine toxicity decreased.

In the control studies, where Ringer's solution was used (Table 1) excretion of toxic substances increased as well (by 646±117 IU/ml, or by 151±32,6%,Δ $p<0,05$). The volume of excretion of toxic substances by kidney nephrons depends on their filtration ability (filtration fraction), reabsorption, and may be secretion. In its turn, the value of excreted fraction (Table 1) demonstrates a part of toxic substances which is eliminated with urine from the filtration fraction. Xylate infusion in particular, increased excretory fraction by 4,9±0,8%, (Δ $p<0,05$), Ringer's solution by 2,2±0,6%, (Δ $p<0,05$). An increased excretion of toxic substances by the kidney nephrons under conditions of a standardized glomerular filtration rate (based on 100 ml/min of glomerular filtration rate) were 623±144,0 IU/ml, (Δ $p<0,05$) and 531±130,8 IU/ml, Δ $p<0,05$) respectively. Meanwhile, the parameters of excretion of toxic substances are more indicative of the kidney functional state. In order to get an idea of the effectiveness of the used solutions in cleaning the extracellular water space from toxic substances, in particular, in the case of endogenous intoxication syndrome caused by the combination of diabetes mellitus with purulent-septic complications, the clearance characteristics were applied, reflecting the stability of homeostasis (Table 1). Xylate administered during the examination period increased blood plasma (extracellular water sector) clearance from total toxicity

Table 1. Effect of xylate and Ringer's solution on toxin-excreting function of the kidneys with type 2 DM complicated by endogenous intoxication syndrome of purulent-septic genesis

Indices	Diabetes mellitus (n=53) (M±m)			
	I group (A)	II group (B)	III group (A)	IV group (B)
P_T, IU//ml	167±3,6	156±3,7**	161±3,7	140±3,8* **
U_T IU/ml	349±4,2	330±4,3**	352±4,4	335±4,5**
U_TV, IU/min	426±4,8	1070±7,3**	433±4,9	1199±7,5* **
U_TV/GFR*100, IU/min	361±4,1	892±9,3**	360±4,0	983±9,9* **
EF_T, %	2,2±0,04	4,4±0,05**	2,1±0,05	7,0±0,06* **
C_T, ml/min	2,6±0,05	6,9±0,11**	2,6±0,06	8,6±0,12* **
P_{MMM}, IU/ml	0,71±0,019	0,64±0,021**	0,69±0,02	0,57±0,020* **
U_{MMM}, IU/ml	11,7±0,21	9,4±0,19**	11,2±0,22	9,3±0,23**
$U_{MMM}V$, IU/min	14,3±0,32	30,5±0,69**	13,8±0,30	33,3±0,71* **
$U_{MMM}V$/GFR*100, IU/min	12,1±0,16	25,4±0,52**	11,5±0,25	27,3±0,58* **
EF_{MMM}, %	17,2±0,20	39,7±0,59**	17,6±0,21	47,9±0,67* **
C_{MMM}, ml/min	20,1±0,57	47,7±1,22**	20,2±0,59	58,4±1,27* **
CHII, score	47±0,94	42±0,91**	45±0,92	38±0,93* **
BPP, ng/ml	4,3±0,09	4,0±0,11**	4,0±0,09*	3,6±0,13* **

Note: I group - IV group – DM; A – patients before Ringer's solution infusion (I group) or xylate (III group); B – patients before Ringer's solution infusion (II group) or xylate (IV group);
*/p≤0,05 – reliability of indices between I group and III, II and IV groups,
**/p≤0,05 – reliability of indices between I group and II; III group and IV group.
P_T – total toxicity of blood plasma;
U_T – urine toxicity;
U_TV – excretion of toxic substances;
U_TV/GFR*100 – excretion of toxic substances per 100 ml GFR;
EF_T – excreted fraction of toxic substances;
C_T – clearance of toxic substances;
P_{MMM} – MMM concentration in blood plasma;
U_{MMM}– MMM concentration in urine;
$U_{MMM}V$ – MMM excretion;
$U_{MMM}V$ /GFR*100 – excretion of toxic substances per 100 ml GFR;
EF_{MMM} – excreted fraction of MMM;
C_{MMM} – MMM clearance;
CHII– cellular humoral intoxication index;
BPP– blood plasma procalcitonin.

by 6.0±1.9 ml/min (230±72,3%, Δ p<0,05). Infusion of Ringer's solution in IT fragment in the same patients (n=53) was marked by increased clearance by 4,3±1,2 ml/min (165±46,0%,Δ p<0,05). Thus, the effectiveness of the administered solutions demonstrated itself in the form of an integrative indicator change – the total toxicity of the blood plasma (Table 1). Under observation conditions, xylate infusion reduced the total toxicity of blood plasma by 22±4.6 IU/ml (14±2,9%, Δ p<0,05), and Ringer's solution – by 12±3,9 IU/ml (7±2,2%,Δ p<0,05).

Among the numerous factors of endogenous intoxication, which are included in the total toxicity of the blood plasma, medium mass molecules (MMM) are distinguished. They possess high biological activity, in particular, neurotoxic, cardiotoxic, hepatotoxic, nephrotoxic activity. Their organotropic action is stipulated by the property to inhibit biosynthesis of protein and enzymes; separate oxidation and phosphorylation processes; perform toxic action on erythropoiesis etc. [11]. MMMs (300-5000 D) are the components of endotoxicosis with endogenous intoxication syndrome. They are freely filtered by the kidney glomeruli and create a high concentration in the ultrafiltrate of the nephron proximal portion. There, the major amount of MMMs is metabolized by the peptidase system of the nephrothelium to amino acids that are reabsorbed. A part of MMMs is excreted by the kidneys. Therefore, activity of MMMs elimination will depend on the

glomerular filtration rate, proximal metabolism, and activity of reabsorption-secretory processes. Considering the fact that MMMs are one of the known fractions causing EIS development, participation of the kidneys in elimination of toxemia components is an important criterion to assess the course of EIS and determine the tactics of infusion therapy.

One of the integrative parameters characterizing the balance between the intensity of MMMs formation and their elimination from the body is MMM concentration index in the blood plasma (Table 1). After xylate infusion, MMM concentration in the blood plasma decreased 0,12±0,032 IU/ml (17±4,4%, Δ p<0,05). In the group of comparison (Ringer's solution infusion) the dynamics of changes was similar (decrease by 0,07±0,024 IU/ml or 10±3,7%, Δ p<0,05).

Among the mechanisms of cleaning the blood plasma from MMMs certain processes in the kidneys are considered. First of all, it is determination of MMM filtration ability. The latter is indicative of the fact that xylate and Ringer's solution in the nephrons of patients suffering from DMEIS does not increase MMMs flow from the glomeruli to the proximal portion of nephrons, since the administered solutions with this mode of introduction did not practically change glomerular filtration rate (I group A – 118±1,7 ml/min; II group B – 120±1,9 ml/min; III group A – 120±1,8 ml/min; IV group B – 122±1,9 ml/min) and produced hemodilution effect.

However, due to decrease in proximal metabolism and reabsorption, the excreted fraction of MMMs (showing how much MMMs from the filtration fraction is eliminated in the urine after reabsorption) after administration of xylate increased by 2.7 times, and after Ringer's solution infusion – by 2.3 times (Table 1). At the same time, nephron activity concerning MMMs excretion under conditions of the standardized glomerular filtration rate (Table 1), after xylate administration increased by 137±37,6%, (Δ p<0,05), and after Ringer's solution infusion – by 110±35,5%, (Δ p<0,05). Eventually, MMMs excretion by the kidneys increased by 177±27,8%,Δ p<0,05 and 151±32,6%, respectively (Δ p<0,05). This index is a constituent to calculate the effect of solutions on the clearance processes of the extracellular space from MMMs by the kidneys in patients with DMEIS. The findings are presented in the Table 1. It should be noted, that at this stage of the research in the regimen of infusion therapy (3 ml/kg/hours during 3 hours), xylate promoted increase of the volume of extracellular fluid clearance by 38,2±8,1 ml/min (189±40,1%,Δ p<0,05); and Ringer's solution – by 27,6±7,9 ml/min respectively(137±42,0%, Δ p<0,05). The reaction and practical value of the cellular humoral index of intoxication and concentration of procalcitonin in the blood plasma after administration of xylate of Ringer's solution are indicative of the level of their importance with the given course of toxemia in patients with DMEIS (Table 1).

CONCLUSIONS

Infusion therapy solutions (xylate, Ringer's solution) within the study regimen (3 ml/kg/h for three hours) activate the renal excreting function and reduce the level of toxemia (xylate > Ringer's solution) in patients with Type 2 DM complicated by endogenous intoxication syndrome of purulent-septic genesis. At the same time, xylate infusion reduced the total plasma toxicity by 22±4.6 IU/ml (14±2.9%, Δ p<0.05), Ringer's solution - by 12±3.9 IU/ml (7±2.2%, Δ p<0.05).

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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