Use of Enterosgel in the treatment of patients with terminal stage of chronic renal disease with dialysis therapy

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In the recent decades, a steady increase in the number of patients with end-stage chronical kidney disease (CKD) has been observed all over the world. This makes the problem of CKD treatment one of the central in modern nephrology. Considerable progress of renal replacement therapy (RRT), scientific and technical achievements in the field of hemodialysis, widespread introduction of clinic peritoneal dialysis and kidney transplantation have created real conditions for the successful solution of this problem. Bad life prognosis and the inevitable disablement have gone, as well as necessity of absolute avoidance from active social and professional activity [7,11]. At the same time it has become clear that it is important not only to extend life, but also to ensure its high quality.

Today, more than 1.7 million patients in the world are still alive thanks to renal replacement therapy, of them 2/3 cases of chronic hemodialysis. In the developed countries the number of patients on the program hemopdialysis ranges from 600 to 1.100 per million.

The steady increase in the population receiving hemodialysis is connected both to an increase in their life duration (often more than 30-40 years), and the revision of many criteria managing selection of patients [7, 4].

The capabilities of the gastrointestinal tract (GIT) in excretion of uremic toxins (UT) in CKD has been long proved [8.14]. Over the years, new methods of detoxification were searched for, based on the GIT ability to excrete UT. Thus, Young T. et al. performed intestinal dialysis by forced hyperosmotic diarrhea, with replacement of fluid loss with polyion isotonic solution [15, 16]. The authors noted good tolerance of the procedures and significant symptomatic improvement. However, in a retrospective generalization of experience of osmotic diarrhea E.A Fridman pointed out that the prospects for clinical application of this technique were very low [12]. Attempts to use enteric dialysis using a two-pass probe also cause some doubts about their effectiveness, complexity of performance and manipulation (sensing jejunum) and inevitable loss of nutrients during the prolonged use [6]. More than 30 years ago, T.M. Chang suggested to use polymeric materials capable of transmitting certain types of substances as a membrane envelope of the cells. [10] Thus, for the treatment of uremic state compositions of sorbents and enzymes was supposed to provide. A drug was created, including urease that decomposed urea to ammonia, and zirconium phosphate absorbing ammonia. Setala K. (1978) used nonpathogenic soil bacteria enzymes capable of converting urea, creatinine derivatives, guanidine and other nitrogen compounds into amino acids to remove products of nitrogen metabolism through the digestive tract in the cases of uremia [13]. However, the experiments were carried out on animals and clinical observation of patients with CKD did not receive further development. In modern literature there are abundant data on the use of enterosorption for correcting CKD uremia. High efficiency of SCN sorbent has been proved [3]. Enterosorption mechanism is reduced to UT fixation on the surface in the small intestine, reducing the possibility of their re-absorption in the blood of the colon. Significant role among the sorbents belongs to Enterosgel - methylsilicic acid hydrogel with a maximum sorption spectrum at medium-weight toxic metabolites and microorganisms, 400 - 3000 times more active than charcoal [9]. The structure of the material is a matrix rigidly "crosslinked" with siloxane bonds between the silicon atoms. Unlike other sorbents (charcoal, polyphepanum, aerosil), chemical basis of Enterosgel not hydrophilic - it is a hydrated, hydrophobic, porous structure having si = o = si globules and organic radicals consisitng from 17 - 35 fragments, saturated with water dipoles. Thus it is important that maximum action of Enterosgel

is concentrated on the harmful substances with medium molecular weight from 70 to 1000 (urea, bilirubin, cholesterol, bile acids, middle molecules). Substances having molecular weight less than 70 (metal ions, inorganic salts) and more than 1000 (common proteins, vitamins, immunoglobulins) are practically not sorbed [9]. Most of the previously used methods have become outdated (intestinal lavage, oral administration of oxiamylum, oxycellulose, forced diarrhea, etc.). Some of them did not enter clinical practice because of low efficiency, poor tolerability and possible complications. Nonetheless, the relevance of the development of new methods of UT detoxification in CKD, aimed at extension and improvement of the quality of life of patients, exists as well.

It has been proved that Enterosgel has a general detoxifying effect on intestinal adsorption of toxic substances and products of incomplete metabolism from the blood. At the same time the sorbent improves liver, renal and intestinal function, forming normal blood and urine values, promotes the removal of incorporated radionuclides, coats the stomach and the intestine, promotes regenerative processes, has beneficial effects on the colonization of normal intestinal microflora [9].

MATERIALS AND METHODS

The study included 31 patients aged from 28 to 63 years with CKD, grade V, receiving hemodialysis program in the hemodialysis department with extracorporeal detoxification of healthcare institution "Grodno Regional Clinical Hospital". The average length of dialysis experience of the patients was 4.7 years. All patients 3 times a week received bicarbonate hemodialysis (arteriovenous variant) on devices *Fresenius 4008B*, Germany («Fresenius Medical Care») using polisulphone membranes. Vascular access was provided via the native arterio-venous fistula. Blood flow velocity was 250-280 ml / min, the duration of a session - 240-270 min. All patients were divided into 2 groups: patients undergoing program hemodialysis (n = 14) and a group of patients who, along with sessions of program hemodialysis received Enterosgel (n = 17). All the patients received a weekly course (45 g / day) of treatment with Enterosgel, administered orally 3 times per day (15 g / dose).

Table 1 Dynamics of endotoxemia aspects on administration of Enterosgel in patients with chronic kidney disease grade V, receiving program hemodialysis (M ± m)

Study parameter	Group without Enterosgel, n=17		Group receiving Enterosgel, n=14	
	Initial period	Seven days later	Initial period	Seven days later
Urea before hemodialysis, mmol/l	30,8±2,3	25,4±2,6	31,0±1,8	26,4±2,1
Urea after hemodialysis, mmol/l	13,5±2,1	11,0±0,9	12,2±1,1	10,1±0,6
Creatinine before hemodialysis, µmol/l	1026,5±73,5	919,6±64,3	1112,8±39,2	850,1±53,8
Creatinine after hemodialysis, µmol/l	477,2±43,6	421,4±27,1	519,3±36,4	363,2±30,0*

* – $p<0.05$ compared with the identical stage of the group without use of Enterosgel

Table 2 Dynamics of hemodialysis adequacy and level of medium molecular weight substances on the background of application of Enterosgel in patients with chronic kidney disease, grade V, receiving program hemodialysis (M ± m).

Study parameter	Group without Enterosgel, n=17	Group receiving Enterosgel, n=14
Kt/V before treatment	1,13±0,07	1,08±0,06
Kt/V 7 days after treatment	1,07±0,03	1,17±0,06*
Medium-weight molecules before treatment, U	739,5±67,3	745,9±28,4
Medium-weight molecules 7 days after treatment, U	633,3±55,4	518,3±23,6*

* – $p<0.05$ compared with the identical stage of the group without use of Enterosgel

The level of urea and creatinine was determined by biochemical method on the unit *Architect® c8000 System* (USA), with reagents of «Human» company (Germany). The level of medium-weight molecules (MWM) was examined using spectrophotometry. Adequacy of dialysis was calculated by Kt / V index.

The test parameters were studied before treatment and 7 days before and after hemodialysis. Statistical processing of the results was performed using software package "*Statistisa 6.0 for Windows*» (Stat Soft Inc, USA). The distribution pattern was evaluated by Kolmogorov-Smirnov and Liljefors tests for normality. Given that the nature of the distribution of the overwhelming majority of the investigated data was abnormal by the above criteria, nonparametric Mann-Whitney test was used for statistical data analysis. The critical level of significance (p) on checking statistical hypotheses was assumed to be 0.05.

RESULTS AND DISCUSSION

On studying biochemical parameters (Table. 1) reflecting endotoxemia expression in CKD, grade V and efficiency of dialysis therapy, the positive trend in reduction of urea in blood plasma should be noted after hemodialysis of patients receiving Enterosgel. Moreover, a significant decrease of creatinine from 519.2 ± 36.4 to 363.2 ± 30.0 (by about 29%) took place in the group with the study sorbent by day 7 of the treatment.

Table 2 shows evaluation of the adequacy of hemodialysis for Kt / V value, as well as dynamics of the level of mdium-weight molecules. Application of the most widely used dialysis membrane (low-flux), that takes place in the present study does not mean removal of UT with medium molecular weight. In this regard, detoxification effect of the procedure can be strengthened by administration of Enterosgel.

On the background of the treatment with Enterosgel, a significant increase in the Kt / V index was noted within 7 days in the patients with CKD grade V, receiving hemodialysis program, as well as a significant decrease of medium-weight molecules from 745.9 ± 28.4 to 518.3 ± 23.6 (about 30%). The obtained positive data on reduction can be the reason for a more serious research, not previously described in the available literature. A significant decrease in the concentration of urea, creatinine and medium-weight molecules in the plasma is achieved by UT back passage from the blood to the intestine with subsequent deactivation and purification of reabsorbed digestive secretions (bile, enzymes) (15-20 l / day).

Clinical effects observed against application of Enterosgel in patients receiving hemodialysis program included reduction of the skin itching, dyspeptic signs and paresthesia, as well as improved sleep and overall life quality. It is also important that the patients did not report any adverse effects of the sorbent.

A study of pharmacoeconomics of the use of Enterosgel in the treatment of this category seems interesting, which can reduce the cost of treatment by reducing the time of dialysis and / or provide an increase in intradialytic intervals. It is known that during the year a patient with CKD, grade V receives an average of 150 hemodialysis sessions, with average length of one procedure of 4 hours (600 hours per year). In inadequate dialysis and prolonged procedure (one hour longer) the number of dialysis hours of increases up to 150 per year.

Using of complex therapy with Enterosgel on the background of program hemodialysis improves its adequacy in terms of Kt / V from 1.08 ± 0.06 to 1.17 ± 0.06 (average of 8%), as shown in this study. This improvement is unique in children for direct reduction of the cost of treatment per patient.

Thus, by analyzing the above results, it should be noted that the application of Enterosgel in patients receiving program hemodialysis gives a positive trend towards UT reduction and improves the adequacy of hemodialysis, which in turn leads to improved life quality of dialysis patients, reduces uremic polyneuropathy and enteropathy, as well as gives the possibility to lengthen the intradialytic intervals or not to increase hemodialysis duration. In this connection, Enterosgel is a safe and effective enterosorbent that can be used in the complex therapy of patients on hemodialysis program

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