

PHARMACOECONOMIC EVALUATION OF THE USE OF A NEW DETOXICANT IN PATIENTS WITH ACUTE PANCREATITIS

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Annotation. *In a clinical study, a new combination of sodium hypochlorite and taurine for detoxifying activity was evaluated in patients with acute pancreatitis. Thus, the efficiency in the main group of subjects who received the drug Neoreodes was 91.67%, which is significantly higher than the efficiency in the control group - 60.4%. Therefore, the hypothesis about the advantages of treatment effectiveness in the main group of subjects in comparison with the control was confirmed. Calculations of pharmacoeconomic evaluation according to the methodology of "cost-effectiveness" showed that the use of "Neoreodesis" in the pharmacotherapeutic treatment regimen is inferior to the combination of Sodium chloride 0.9% + glucose solution 5% in economic terms: CERneoreodesis 22.2 UAH / ef and CERstand. ter. 14.5 UAH / ef. However, it is important to note that in the group using Neoreodesis, a shorter stay of patients in the intensive care unit was registered compared to the group receiving standard therapy.*

Key words: *fixed combination of sodium and taurine hypochlorite, Neoreodesis, acute pancreatitis, "decision tree", cost-effectiveness of treatment.*

One of the problems of the modern clinics is chronic endotoxycosis, the manifested by typical pathological process, are determined by organ and systemic reactions in the patient's body. The mechanisms of cytotoxic damage as a result of exposure to toxic products of lipid peroxidation (LPO) and due to the imbalance of the chains of immunological reactivity are closely related, which causes changes in the resulting cellular reactions that form the pathological process [1].

It is known that modern methods of extracorporeal detoxification, namely, hemodialysis and hemosorption, are insufficiently effective in removing hydrophobic toxins. It is known that the use of sodium hypochlorite is accompanied by a simultaneous decrease in both components of toxemia, and the severity of the effect increases as the syndrome of endogenous intoxication progresses. We first evaluated the detoxifying properties of a fixed combination of low-concentration sodium hypochlorite solution and taurine under conditions of endotoxycosis on the background of acute pancreatitis [2, 3].

It is known that acute pancreatitis is one of the most serious urgent diseases of the abdominal cavity. In terms of the share of treatment, it ranks third, second is acute appendicitis and cholecystitis. It accounts for up to 5-10% of urgent pathology of the abdominal cavity. At the same time, every fourth patient develops aseptic necrotic

pancreatitis, the overall mortality of which even in specialized clinics around the world remains consistently high (level of evidence A, B), ranging from 2.1% to 15% [4]. In the infected form of pancreatic necrosis, mortality reaches 30-70%. In Ukraine, the incidence of acute pancreatitis is 102 per 100,000 population, the overall mortality ranges from 4 to 15% reaching 24-60% in the necrotic form, and postoperative mortality is 70%. Pathogenetic changes in acute pancreatitis are very diverse, covering many body systems. This explains the severity of the clinical course of the pathological process and in many cases - the emergence of severe multiorgan failure on the background of endotoxemia [5, 6].

Therefore, the search for a new detoxifier today is an urgent problem for modern surgery.

The aim of the study was to determine the clinical and cost effectiveness of the new detoxifying agent "Neoreodesis" in patients with acute pancreatitis.

Research methods. Research design - open, randomized comparative, parallel.

The clinical study included 96 patients with acute pancreatitis. Patients based on the method of randomization in a ratio of 1: 1 were divided into the main group - 48 patients and control - 48 patients. All patients received basic therapy (antispasmodics, proton pump inhibitors, protease inhibitors, somatostatin drugs, antibiotics). In addition, patients in the main group were prescribed an experimental infusion solution with the working name "Neoreodesis" for 3 days.

The effectiveness of treatment was evaluated by changes in the level of total bilirubin, blood amylase, urine diastase after 3 days of treatment compared with baseline. Treatment was considered successful if the level of at least two of the three evaluated indicators decreased by 35% from baseline or more. The safety of the drug was assessed on the basis of monitoring data on the patient's condition, frequency and nature of adverse reactions, laboratory data, assessment of the patient's subjective condition.

Pharmacoeconomic evaluation was performed using the "decision tree" model based on the cost-effectiveness indicator.

When performing the study, known clinical and statistical methods were used: quantitative analysis, variation statistics, comparison of efficiency between groups, determination of the efficiency unit [7].

Research results. Among the patients included in the clinical study there were 44 female and 52 male patients. The distribution of patients by sex are presented in table 1. To assess the homogeneity on the basis of gender the chi-square Person criterion was used, taking into account the correction for continuity.

The diagnosis of acute pancreatitis was confirmed by assessment of blood amylase and urine diastase. Data from the initial assessment of the of blood amylase and urine diastase levels by methods of descriptive statistics are presented in table 2.

Table 1

Distribution of patients by sex

Gender	Main Group		Control group		Total	
	n	%	n	%	n	%
Male	27	56,25	25	52,08	52	54,17
Female	21	43,75	23	47,92	44	45,83
Total	48	100,0	48	100,0	96	100,0

Table 2

Analysis of the initial homogeneity of groups according to the assessment of blood amylase and urine diastase

Index	Group	N	Arithmetic mean	Median	Standard deviation	Min	Max
blood amylase, mg/(g*ml)	Main	48	90,48	85,0	28,00	42	192
	Control	48	94,48	86,0	25,29	70	189
urine diastase, g/g*l	Main	48	230,85	207,0	104,73	126	800
	Control	48	237,08	219,0	67,86	119	410

Baseline levels of blood amylase and urine diastase were significantly elevated. Based on the results of statistical analysis, we can conclude that the groups did not differ significantly according to the initial data of the assessment of blood amylase and urine diastase.

To assess the degree of endogenous intoxication the method of molecules of the medium weight (MMW) determining was used. The evaluation was performed by spectrometry in different modes X = 254 nm and X = 280 nm. In addition, the level of malonic dialdehyde (MDA) was determined at the screening stage, which is a clinical and laboratory marker of oxidative stress and blood pH. Data estimates of the level of molecules of medium weight, and blood pH at the stage of screening by methods of descriptive statistics are given in table. 3.

Thus, in most subjects of the main group the level of total bilirubin, blood amylase and urine diastase by 35% or more was managed to reduce compared to the baseline.

During the clinical study, no adverse reactions that could be associated with the administration of the studied drug were reported. During the clinical study, a daily examination and interview of patients was performed to identify possible adverse reactions. Examination and interview of patients of the main group did not reveal any complaints, unexpected side effects, complications or intolerances of the drug Neoreodesis when prescribed for 3 days. Patients did not complain and did not experience any unpleasant sensations that could be associated with the action of the study drug. It did not have a negative effect on blood pressure, heart rate and body temperature: at the

end of the clinical study there were no negative changes in these indicators compared to baseline before treatment in patients of the main group.

Table 3

Analysis of the initial homogeneity of groups according to the assessment of the medium molecular weight peptides level, MMW and PH blood

Index	Group	N	Arithmetic mean	Median	Standard deviation	Min	Max
MMW in X = 254 nm	Main	48	0,04	0,04	0,02	0,01	0,10
	Control	48	0,05	0,05	0,04	0,01	0,24
MMW in X = 280 nm	Main	48	0,08	0,07	0,13	0,01	0,98
	Control	48	0,10	0,07	0,36	0,01	2,59
MDA	Main	48	3,02	2,87	0,94	1,24	5,92
	Control	48	3,27	3,04	0,95	1,28	6,48
Blood PH	Main	48	7,38	7,38	0,04	7,31	7,47
	Control	48	7,39	7,38	0,04	7,32	7,48

Laboratory parameters did not change negatively in any case, in most number of patients the level of leukocytes in the blood and the rate of erythrocyte sedimentation decreased, which indicates a decrease in the severity of the inflammatory reaction. Tolerability of treatment with the study drug in all cases was regarded as good.

Thus, the use of the drug "Neoreodes" as part of basic therapy significantly increases the effectiveness of treatment in patients with acute pancreatitis compared with the administration of basic therapy alone.

Thus, the efficiency in the main group of patients who received the drug Neoreodes was 91.67%, which is significantly higher than the efficiency in the control group - 60.4%. The hypothesis about the advantages of treatment effectiveness in the main group of subjects in comparison with the control was confirmed [8].

In assessing the economic component of the use of "Neoreodesis" in patients with endotoxiosis on the background of acute pancreatitis, a model of the "decision tree" was used.

Cost analysis was performed from the perspective of a patient who pays for a course of intoxication therapy. The modeling horizon is equal to the duration of the course of pharmacotherapy of peritonitis.

Calculations of pharmacoeconomic evaluation according to the methodology of "cost-effectiveness" showed that the use of "Neoreodesis" in the pharmacotherapeutic treatment regimen is inferior to the combination of Sodium chloride 0.9% + glucose solution 5% in economic terms: CERneoreodesis 22.2 UAH / ef and CERstand. ter. 14.5 UAH / ef. However, it is important to note that in the group using Neoreodesis, a shorter stay of patients in the intensive care unit (ICU) was registered compared to the group receiving standard therapy (Fig. 1).

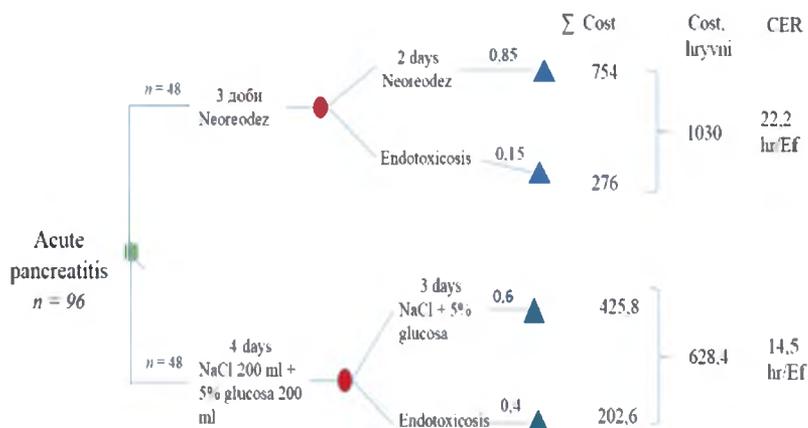


Fig. 1. Model "decision tree" for pharmacoeconomic evaluation of the course of detoxification therapy of acute pancreatitis.

If the cost of the patient's stay in the ICU was taken into account when constructing the "decision tree" model, the financial burden was more significant for patients receiving standard therapy.

Conclusions. When analyzing the indexes of clinical efficacy and total costs in monetary terms for the course of detoxification therapy, namely, infusion solutions, the advantages of using a new combination of sodium hypochlorite in combination with taurine ("Neoreodesis") were determined.

Prospects for further research. In future, we plan further studies of the use of "Neoreodesis" in clinical practice under different conditions of endotoxiosis, such as peritonitis.

References:

1. Hauben M, Hung E.Y. (2016). Revisiting the reported signal of acute pancreatitis with rasburicase: an object lesson in pharmacovigilance. *Ther Adv Drug Saf.*;7(3):94-101.
2. Dronov S.N. (2014) The detoxifying properties and acute toxicity of a fixed combination of low-concentration solution of sodium hypochlorite and taurine intended for parenteral administration. *Farmakolohiia ta likarska toksykolohiia.* 2014;4-5(40):32-9.
3. Berezhnysky YaS, Fomin PD. (2010) Standards of organization and professionally-

oriented protocols for providing medical care to patients with urgent surgical pathology of the abdominal organs. Kyiv: Doctor of Media; 470 p. [Ukrainian]

4. Bilenkyi G.Z. (2016) Estimation of changes in biochemical parameters of blood and urine plasma. against the background of long-term administration of "Neoreodesis" / Bilenky GZ // Proceedings of the international scientific-practical conference "Medical and pharmaceutical sciences: analysis of the present and forecast of the future", Dnipro, November 11-12; - P. 12-16. [Ukrainian]

5. Mamchur V.I, Dronov S.M, Bilenkyi G.Z. (2016) The influence of intravenous solution "Neoreodez" on the course of experimental endotoxemia and evaluation of the regenerative properties of drug in the condition of application. Medychni perspektyvy. Vol.3:15-20 [Ukrainian].

6. Bilenkyi G.Z. (2018) Peculiarities of tolerability of a new detoxifier in healthy volunteers. Bulletin of problems of biology and medicine. Vol. 3 (145); P. 88-91. [Ukrainian].

7. Bilenkys G.Z. (2018) Clinical efficacy and tolerability of sodium hypochlorite in combination with taurine on the background of basic therapy in patients with acute pancreatitis. Medical perspectives. Vol. XXIII, №3; P. 53-58. [Ukrainian].

8. The statistical analysis program. WEB-resource. Available from: www.analystsoft.com/ru.