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Optimization of pharmacological treatment of acute intestinal obstruction

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Abstract
Indices of lipid peroxidation (LPO), middle weight molecules (MWM), and changes in the structure of the liver and the impact of Reamberin solution on them were analyzed in 202 patients with acute small intestinal obstruction (ASIO). Endogenous intoxication indices were established to increase along with the increase in enteral deficiency. In case of ASIO increase in lipid peroxidation products, MWM in serum, and decrease in ceruloplasmin securities, significant changes in the liver (destruction of granular and smooth endoplasmic reticulum, mitochondria, hepatocytes nuclei) were observed. Surgical resolution of ASIO leads to further temporary deterioration of liver structure, increase in MWM, and indices of lipid peroxidation and decrease in ceruloplasmin levels. Prescription of antioxidant therapy in the postoperative period promotes reparative processes in hepatocytes and leads to normalization of endogenous intoxication indices in blood serum and helps reduce postoperative mortality.

Keywords: acute intestinal obstruction, treatment, intoxication

Introduction
Despite the introduction of modern technologies of diagnostics and surgical interventions, acute small intestinal obstruction (ASIO) is one of actual problems in urgent abdominal surgery which is accompanied by high mortality of 12-25% [1, 2]. Change in secretory, absorption and barrier function of small intestine causes enteral insufficiency syndrome (ESI) which can leads to the development multiple organ failure and death at an early postoperative period [3, 4,7]. Timely resolution of acute intestinal obstruction is important in patients' management. However, many trials have showed acute reperfusion damage of intestine wall develops after liquidation of strangulation and can cause increase in endogenous intoxication [5, 6].

Activation by free radical processes occurs as a result of metabolism disorders in case of ASIO. Lipid peroxidation products accumulate causing oxidative phosphorylation separation and inhibit electron transfer in mitochondrial respiratory chain. As a result, energy-depended functions are inhibited and multiple organ failure develops. Under conditions of intoxication and hypoxia in patients with ASIO, mitochondrial respiratory chain loses its property to receive electrons from other substrates except succinic acid which is intermediate compound of Krebs cycle. Additional exogenic admission of succinic acid enriches energy deficiency in human body [1].

The objective of this research was to study Reamberin solution effects with its antioxidant, antihypoxant and indirect hepatoprotective properties on clinical sings of ileus.

Materials and methods
232 patients were observed including 202 patients with ASIO at the age of 30 to 80 years who were treated at Central City Hospital of Ivano-Frankivsk, Ukraine. The patients included 98 men (48.5%), 104 women (51.5%) and 30 apparently healthy individuals. ASIO reasons included strangulated hernia in 56 (27.7%) patients, including postoperative hernia in 22 (10.8%) patients; strangulated intestinal obstruction in 44 (21.7%) patients, adhesive obstruction in 63 (31.1%) patients, obturation intestinal obstruction in 17 (8.4%) patients. Clinical and biochemical parameters of the functional state of organism as well as histomorphologic parameters of resected section of small intestine were investigated at the preoperative period and on the 1st, 5th and 14th postoperative day.

The material for the study (small intestine of 13 patients) was sampled during small intestine resection. Small intestinal fragments were used as a control. They were taken during autopsy in 9 patients after 3-9 hours of death from diseases not associated with gastrointestinal tract

disorders.

The patients were divided into two groups: main group – 102 persons, and control group – 100 patients. In order to correct metabolic disorders 400-800 ml of Reambein ("Polisan") solution (depending on severity) was introduced to patients of the main group 2 times a day i.v. with the speed of 90 drops per minute before the surgery and during the first 5 days of the postoperative period. Reamberin has antioxidant action causing a positive effect on aerobic processes in the cell reducing the production of free radicals and restoring cells energy potential [2]. The drug is licensed for use by State Pharmacology Center of MPH of Ukraine.

Statistical processing of the results was performed using mathematical program complex for computer based on Microsoft Windows 1985-2005 as well as programs for statistical analysis Analys+Soft, 2007. Verification of samples distribution for normality was performed using Shapiro-Wilk test. Student-Fischer test for normally distributed samples and Wilcoxon-Mann-Whitney test for samples with distribution different from the normal were used to test the hypothesis of averages equality.

Results and discussion

Intensive augmentation of endotoxemia in the body of both patients and animals on the background of intestinal passage violation was established to depend on AOI duration (Table 1).

Table 1: Indices of oxidative-antioxidative balance and EI in patients with ASIO

Groups	Stages of Examination	Indices			
		CP, IU	MWM, IU	DC, IU	MDA, mcmol/l
A) Patients with ASIO					
Norm (control n=8)		29.12±1.04	0.24±0.04	0.38±0.04	3.69±0.16
ASIO before the treatment		*25.47±0.85	**0.46±0.05	**0.53±0.04	***5.22±0.39
After treatment without Reamberin	1-2 days	***23.33±1.02	***0.54±0.06	***0.68±0.07	***5.72±0.61
	5-6 days	26.68±2.05	***0.50±0.02	***0.78±0.03	**1.01±0.52
	11-12 days	***22.29±1.33	***0.54±0.04	**0.57±0.05	***4.86±0.23
After treatment with Reamberin	1-2 days	23.96±0.95	0.69±0.03	0.64±0.10	5.51±0.64
	5-6 days	°°34.45±1.15	°0.44±0.03	°°0.60±0.04	°5.12±0.25
	11-12 days	°°28.13±1.77	°0.45±0.03	°0.40±0.02	°3.75±0.30

Note: Difference compared to norm:* - p<0.05;** - p<0.01;*** - p<0.001.Difference compared to type of treatment:° - p<0.05; °° - p<0.01;°°° - p<0.001

In AOI clinical picture we detected some changes of oxidation-antioxidant balance, EI, depending on the background of observations.

The table shows that CP activity in the serum of patients with ASIO before the treatment and especially in the experiment (II group) compared to the control decreased with further increase and subsequent decrease to critical level on 11th-12th days after curative therapy. This CP dynamics is believed to be the result of increased enzyme rate due to the increase in the substrate of its action with further increase in synthesis of "acute phase protein" liver. Progressive reduction of CP level which occurred in the course of ASIO (II group) without the use of Reamberin is a bad prognostic sign. After ASIO surgery CP level had a slight tendency to normalization.

After ASIO surgery its activity in the serum approached to the normal range on background of Reamberin.

The research of primary (DC) and secondary products of lipid peroxidation (MDA) in serum indicates lipid peroxidation process intensification during the course of ASIO surgery. Toxicity of blood serum correlated with the level of lipid peroxidation products. One of its manifestations is the initiation of free radical oxidation in target organs, especially in the liver [3]. The levels of DC and MDA were higher than the normal level in patients and in experiment at the period of clinical recovery.

Reamberin use for therapeutic purposes caused reduction of lipid peroxidation intensity in ASIO. We observed the typical changes in the liver in cases of ASIO in patients as in the experiment and were approximately in the same direction. Enlargement of the central veins and capillaries, tissue swelling, dyscomplectation of hepatocytes beams with all kinds of degenerative changes and focal necrosis surrounded by histio-lymphocytic infiltrates in the cytoplasm were noted during autopsy in 13 persons who died after surgery for ASIO.

Ultra-thin liver structure was studied in 5 patients with ASIO. Profound changes in the liver parenchyma was established to correlate with disease stage and duration of intestinal obstruction and indicated necrobiotic changes development in all components of the body. Large electron-transparent spaces in hepatocytes cytoplasm were observed. Organelles remains and thin granular substance were occasionally noted there and smooth endoplasmic reticulum was missing. Granular endoplasmic reticulum in the form of short tubules often extended was scattered in the locations of organelles that remained. Hepatocytes nuclei were in a state of pycnosis with density of parietal component. Mitochondria were swollen with structure loss and Disse's spaces were completely destroyed. Necrosis was also observed in endothelial cells and Kupffer sinusoid cells.

In 72 hours after intestinal patency restoration without Reamberin solution prescription, ultrathin elements structure of liver worsened compared to the data before surgical treatment and their partial recovery was observed only in some isolated groups of parenchymal cells. Normalization of the fine structure of hepatocytes majority was observed during the same period in case of Reamberin inclusion to the complex treatment.

The data of morpho-dynamics and ultra-thin structure of liver in patients with ASIO corresponded to the so-called nonspecific reactive hepatitis, the extent of which increased with increase in of EI products levels.

Conclusions

1. Correlation between stages of pathological morphological changes of liver in case of ASIO and intensification of endogenous intoxication in human body was established.
2. Additional use of Reamberin caused energy potential activation in cells, acceleration of intestinal passage and significant decrease in endotoxicosis degree, intensive

decrease in morphology and functional changes in liver and level of endogenous intoxication.

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