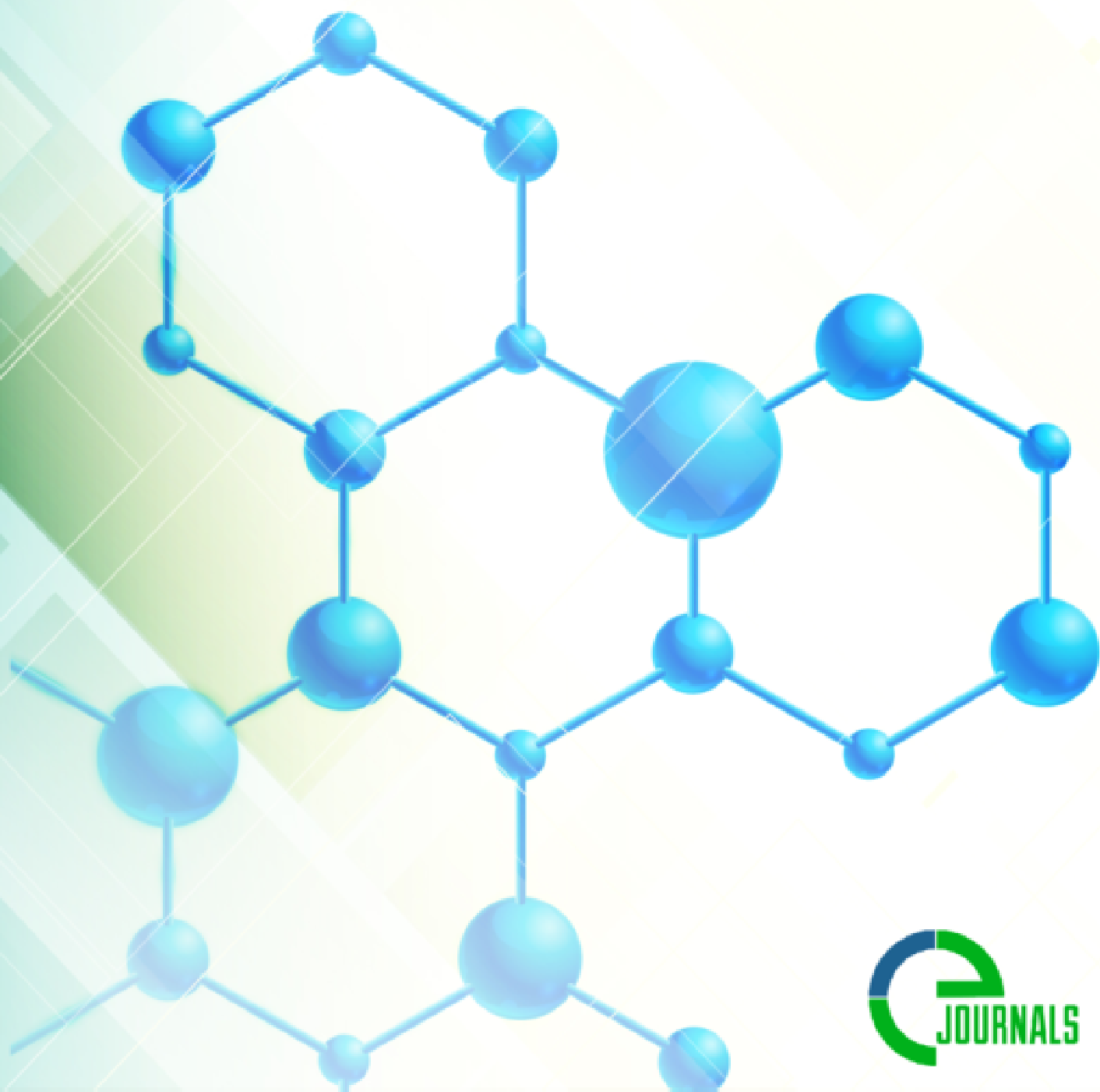


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STUDYING THE FEATURES OF THE MORPHOLOGY OF ADHERENCE FORMATION AND DEVELOPING PREDICTION CRITERIA AND CORRECTION METHODS UNDER THE INFLUENCE OF OZONE IN THE EXPERIMENT

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Abstract: To study the prognostic value of the acetylation phenotype in the formation of intraperitoneal adhesions, 67 children were examined who were admitted with symptoms of adhesive intestinal obstruction and had a history of laparotomy for complicated appendicitis. To perform the acetylation reaction, we used the method for determining free and acetylated norsulfazole in a six-hour urine sample after a single test dose of the drug. The amount of free and total norsulfazole in the urine was determined by the Prebting and Gavrilov method modified by Timofeeva o'10g'.

Keywords: adhesive obstruction, prediction, prevention, experiment, children.

The aim of this work was to study the morphology of adhesion formation under the influence of ozone in the experiment, as well as the development of prediction criteria and methods for correcting increased adhesion in children.

Materials and methods. Experimental studies were carried out on 36 rabbits "Shinshilla" with a body weight of 0.7-1.2 kg., of which 12 animals were included in the control group, which did not carry out ozonation of the abdominal cavity. The main group consisted of 24 rabbits, which were divided into two subgroups (12 animals in each subgroup), which ozonized the abdominal cavity with an ozone-oxygen mixture. In order to study the prognostic value of the acetylation phenotype in the formation of intraperitoneal adhesions, 67 children with symptoms of adhesive intestinal obstruction were examined.

Results. The results of experimental studies showed that in animals of the control group there was the formation of massive adhesions. The basis of adhesions is connective tissue with a significant number of fibroblasts, blood vessels and collagen fibers. In animals of the main group, sharp inhibition of adhesion formation, a delay in the differentiation of fibroblasts and inhibition of their synthetic function were revealed. Acetylation phenotype was determined in 58 patients with appendicular peritonitis. 30 (51%) children turned out to be slow acetylators, and in 28 (49%) patients the phenotype of fast acetylation was established. The results of the study allowed us to isolate fast acetylators as a risk group for excessive adhesion formation and timely start therapeutic and preventive measures.

Introduction. One of the urgent problems facing medical science is purulent infection. In pediatric surgery, it is often necessary to deal with the most severe forms of purulent infection, one of which is appendicular peritonitis, which accounts for 50-90% of all purulent peritonitis in children [1,2,6,12]. The mortality rate remains very high and reaches 1.6-20% [3,15,18,23,15,18,23]. In addition, purulent peritonitis causes a large number of severe intra-abdominal complications. At the same time, the course of complicated purulent peritonitis is much more severe and the mortality rate reaches 20-35% [5,7,16,19]. One of the most serious complications after surgical interventions for appendicular peritonitis is adhesive intestinal obstruction [3,9,10,9,], which is the reason for repeated surgical interventions.

Prediction and prevention of excessive adhesions, especially postoperative adhesive intestinal obstruction, is also one of the unresolved problems of pediatric abdominal surgery [8,11,24,11,]. Since adhesions are excessive formation of connective tissue in the surgical area, in our opinion, it would be interesting to study the features of adhesions in connection with the phenotypic features of patients with surgical pathology [17,2,02]. This opens up new opportunities for identifying individuals predisposed to intra-abdominal adhesions and timely pharmacological regulation of connective tissue formation processes in the field of surgical intervention [3,9,1,3,9,1]. In recent years, the results of scientific studies on the successful use of ozone in clinical practice in patients with surgical and general therapeutic profiles have begun to appear in the medical literature [4,2,1,2]. In addition to the pronounced bactericidal, anti-inflammatory, and antihypoxic effects of medical ozone, a number of researchers note its properties to accelerate regenerative processes [14, 22].

Purpose of the study. To study the morphological features of spike formation under the influence of ozone in the experiment, as well as to develop criteria for predicting and correcting increased spike formation in children.

Materials and methods. Experimental studies were carried out on 36 Chinchilla rabbits with a body weight of 0.7-1.2 kg, of which 12 animals were included in the control group, which did not undergo ozonation of the abdominal cavity. To create an experimental model for studying the development of postoperative adhesive complications, the Shade method was used Shade[10].

The main group consisted of 24 rabbits, which were divided into two subgroups (12 animals in each subgroup). Rabbits of subgroup " A " after appendectomy and deserosis underwent sanitation of the abdominal cavity, stump of the appendix and deserotoc areas of the peritoneum with an ozone-oxygen mixture using the AUTRY-1 device for 5 minutes with an ozone concentration of 5-8 mg/l.

Rabbits of subgroup " B " were additionally injected with 20 cm³ (100 mcg) of ozone per parietal peritoneum in order to create a drug depot.

Animals of both groups were kept in a vivarium under the same conditions, under constant observation, and were removed from the experiment 7, 14, 21, and 30 days after appendectomy under ether anesthesia by instant decapitation (three rabbits for each term). After opening the abdominal cavity, the relative position of the intestinal loops, the condition of the process stump, as well as the presence of adhesions between the stump, visceral and parietal peritoneum were evaluated. Histological examination was performed on samples of peritoneum and adhesions.

Results and discussion.

7 days after the operation, the animals of the control group showed the presence of a pronounced adhesive process. The adhesions were located mainly between the caecum dome and the parietal peritoneum, as well as in the area of the process stump. The spikes were of various lengths (from 0.2 to 1 cm) and shapes (planar, ribbon-like, and

similar).

Histological examination revealed that the basis of adhesions is loose connective tissue, consisting of thin bundles of collagen fibers, between which fibroblasts and a few capillaries are located. From the side of the visceral peritoneum, smooth muscle cells grow into the thickness of the adhesions, the source of which is the middle shell of the cecum and the stump of the process. Small numbers of macrophages, lymphocytes, and neutrophilic leukocytes are detected in the spikes. The surface of the adhesions is lined with mesothelial cells (Fig..

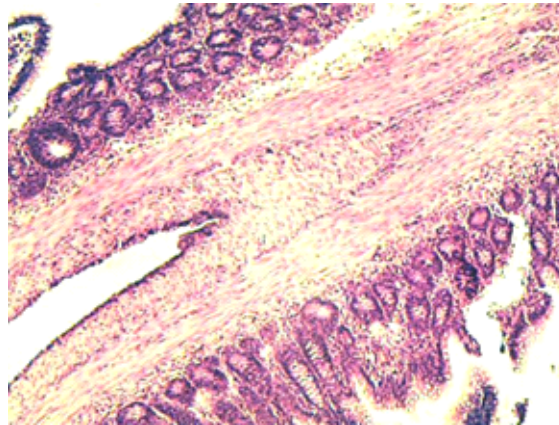


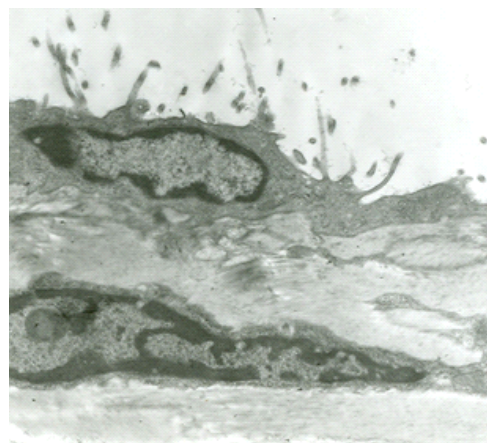
Fig. 1. Adhesion of intestinal loop walls at the site of "demesothelization" and formation of adhesions. Day 7 of peritonitis. G-E. 10 x 10.

In some cases, leukocytic infiltration of the mucous membrane in the stump area is noted.

On the 14th day, the adhesive process increases, the length of the adhesions reaches 3-4 cm. In some cases, adhesions squeeze the intestines, resulting in swollen and collapsed areas. The content of collagen fibers increases, their bundles become thick and coarse. The presence of tissue detritus, leukocyte and macrophage infiltration is noted.

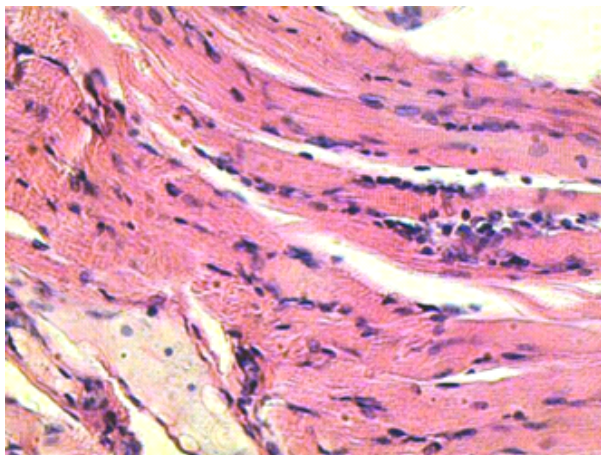
After 21 days, the process of adhesion formation continues. The basis of adhesions is coarseko-fibrous connective tissue with a few fibroblasts, macrophages and lymphocytes. The presence of smooth muscle cells is characteristic.

On the 30th day of the experiment, violations of the topographic and anatomical relationships between intestinal loops are noted due to a large number of adhesions. Most of them have a dense consistency. The basis of adhesions is made up of coarse bundles of collagen fibers, compactly adjacent to each other. There are few cellular elements (Fig. 2).



2. Smooth muscles and collagen fibers in the thickness of the mesothelium-covered junction. 30 days of peritonitis. TAM x 8000.

7 days after appendectomy, rabbits of subgroup "A" have single thin (2-3) adhesions up to 1 cm long. The basis of adhesions is loose connective tissue. The number of fibroblasts and capillaries is significantly lower than in the control group. Neutrophilic leukocytes and macrophages infiltrate around the process stump (Fig. 3).



**3.Reduced changes in the inflammatory-dyscirculatory nature in the peritoneum.
7 day of peritonitis. G-E. 10x 40.**

After 14 days, the number and size of adhesions increased slightly, they are easily torn. There are signs that indicate a decrease in the synthetic activity of fibroblasts: the cell size is reduced, their number is reduced, and the content of collagen fibers is also reduced. In contrast to the control, there is no germination of smooth muscle cells in the thickness of the adhesions. In the area of the process stump, the maturation of connective tissue is slowed down, and at the same time, intensive processes of detritus resorption to macrophages are observed.

After 21 days, single thin loose adhesions are observed in the abdominal cavity. The stump lies freely in the thickness of the adhesions, there are few fibroblasts and capillaries, as well as collagen fibers (Fig. 4).

After 30 days of observation, the loops of the small intestine lie freely. Individual flat spikes are noted, they are fragile and easily torn. The basis of adhesions is mature connective tissue from compactly arranged bundles of collagen fibers. The number of fibroblasts and capillaries is less than in the control group.

Table 1
The number of fibroblasts in the connective tissue of adhesions formed after appendectomy and peritoneal deserosis

Groups of animals	Study time (day)			
	1	14	21	30
1. Control	panel	13,0±0,51	5,7±0,32	4,0±0,54
2.Main:		3,6±0,42*	2,0±0,17*	2,6±0,43
subgroup "A"	6,7±1,45*			
subgroup "B"	5,6±0,27*	2,6±0,32*	3,0±0,52*	2,1 ±0,3 8

Note: * - differences are statistically significant compared to the control group (P<0.001).

One of the causes of pathological adhesions is a violation of collagen metabolism, the synthesis of which begins in fibroblasts and ends in the extracellular space. Stabilization of collagen chains is carried out with the participation of lysyl oxidase, the activity of which is directly related to the activity of the enzyme N - acetyltransferase, which catalyzes the process of inactivation of toxic metabolic products. A link was established between the body's acetylation capacity and the incidence of intraperitoneal adhesions. In "slow acetylators", the rate of fibrin catabolism outstrips the rate of fibroblast proliferation along its filaments, which inhibits the formation of adhesions. In "fast acetylators" there is an inverse picture of the ratio of fibroblast proliferation and the rate of fibrin catabolism with the development of excessive adhesion.

Fast acetylators include individuals with an acetylation rate of 76% or higher, while slow acetylators are less than 76%.

Rapid acetylation phenotype was established in 51 (76.6%) patients, 33 (63.8%) of them were admitted with an acute form of adhesive intestinal obstruction, which was eliminated surgically. In 18 (36.2%) patients, intestinal obstruction was resolved by conservative methods.

16 (23.4%) patients were slow acetylators. Four of them were operated on (27.2%), the operation revealed that the cause of intestinal obstruction was technical errors of the previous surgical intervention. Other patients were diagnosed with intestinal colic and coprostasis.

The results obtained show that the determination of the acetylation phenotype is quite informative in predicting the development of excessive adhesion formation.

Based on this, we determined the acetylation phenotype in 58 patients with appendicular peritonitis. 30 (51%) children were slow acetylators, and 28 (49%) patients had a phenotype of rapid acetylation.

The level of sialic acids at admission to the hospital in both fast and slow acetylators was at the same level (2.1 ± 0.3 ; 2.2 ± 0.2 mmol / l). Starting from 1 day after surgery, the level of sialic acids increases in fast acetylators (3.1 ± 0.3 mmol/l), compared with slow acetylators (2.3 ± 0.2 mmol/L), reaching a maximum value by 10-14 days (3.8 ± 0.4 mmol/L), in slow acetylators (2.0 ± 0.3 mmol/l). An increase in the level of sialic acids in fast acetylators indicated an active inflammatory process and was regarded by us as an indirect evidence of accelerated collagen synthesis.

The results of the study allowed us to identify fast acetylators as a risk group for excessive adhesion formation and to start medical and preventive measures in a timely manner. For this purpose, we used intraperitoneal administration of a dry ozone-oxygen mixture, cuprenyl, and electrophoresis with collalazine

Ozone therapy was used according to the following scheme: intraoperative blowing of the abdominal cavity with a dry ozone-oxygen mixture with an ozone concentration of 5-8 mg / l for 10 minutes, three times intraperitoneal administration of a dry ozone-oxygen mixture with the same ozone concentration, through a microirrigator of 150-200cm³ 1 time a day. The use of ozone therapy leads to a decrease in sialic acids.

Kuprenil was used in tablets per os in age-related dosages during the first 10 days of the postoperative period.

Electrophoresis with collalesin was prescribed from 4-5 days of the postoperative period to the area of the postoperative wound for 10 days.

Thus, the determination of the acetylation phenotype is a simple and affordable method of forecasting, and the use of ozone, cuprenyl, and collalesin electrophoresis can be used as a means of preventing excessive adhesion.

Conclusion.

1.Introduction of ozone into the abdominal cavity in the experiment has a positive effect on the morphological characteristics of the peritoneum, significantly inhibits the adhesive process by suppressing the synthetic function of fibroblasts and vasculogenesis, which indicates the effectiveness and prospects of ozone therapy in the prevention of postoperative adhesive complications.

2.Determination of the acetylation phenotype makes it possible to predict postoperative excessive adhesion, and the combined use of ozone therapy, cuprenil, and collalesin electrophoresis can be used as a means of its prevention.

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