IJIMM, Volume 2, Issue 5, 2024 ISSN: 2995-5319
http://medicaljournals.eu/index.php/IJIMM/issue/view/3

INTERNATIONAL JOURNAL OF INTEGRATIVE AND MODERN MEDICINE

Clinical and Experimental Basis of Lymphatic Therapy in the Treatment of Ulcerative Colitis

Akhtam Ruziev
Bukhara State Medical Institute, Uzbekistan

Abstract: This article analyzes the problems of experimental modeling of ulcerative colitis, as well as the management and treatment of patients with ulcerative colitis using lymphotropic therapy in the postoperative period as part of the treatment complex.

Using serial experiments in experimental animals, a model of ulcerative colitis was created. Against the background of the created model and after it, lymphatic drainage in the intestinal mesentery was studied. Based on the results of experimental studies, we used lymphotropic therapy in a clinical setting in 54 patients as part of the treatment of ulcerative colitis in the postoperative period. The obtained results convincingly showed the positive effect of this method. At the same time, intestinal complications in the postoperative period are significantly reduced and the patient's length of stay in the hospital is shortened.

Keywords: ulcerative colitis model, ulcerative colitis, lymphotropic therapy.

Relevance

Currently, the problem of treating inflammatory bowel diseases, including ulcerative colitis, is a very urgent task in coloproctology. According to the International Research Committee, the incidence of ulcerative colitis in recent years has shown a steady increase in all regions of the globe. Over the past decades, the study of this condition has gained rapid progress [1;15].

According to the lymphatic theory, in ulcerative colitis, primary changes develop in the lymph nodes of the mesentery and lymphoid follicles of the intestinal wall. These changes lead to lymphatic edema of the submucosal layer, which ends with destruction and granulomatosis of the intestinal wall [3].

Active research is being conducted on the role of opportunistic microflora in ulcerative colitis, which continuously stimulate the intestinal immune system and lead to a local allergic reaction [7; 9; 10; 11; 13].

It must be emphasized that the peak incidence of ulcerative colitis occurs in the age group that is the most socially active, from 20 to 40 years [7; 13; 14; 15;16].

Despite the fact that the etiology and pathogenesis of ulcerative colitis remains unclear, there has been some progress in these matters, which allows the creation of new treatment agents. New therapeutic strategies are based on established principles of evidence-based medicine [6].

In the modern world, the basis for the treatment of ulcerative colitis is conservative therapy, and surgical interventions are performed only in cases of its ineffectiveness or the development of complications in 10-20% of patients [4; 12]. In the postoperative period, early complications during planned interventions are still about 10%, emergency ones up to 40-45%, and mortality is from 12% to 35% [2; 6].

And yet, to date, morphological criteria that are reliable with the position of evidence-based medicine [5], which could objectively assess the dynamics of the inflammatory process in ulcerative colitis, have not been sufficiently developed. As well as the results of various treatment methods, including after operations. The unresolved nature of these issues makes ulcerative colitis relevant in relation to its treatment.

In this regard, it is important to further study the pathogenesis of ulcerative colitis, as well as the development and preclinical testing of new approaches to diagnosis and treatment. This is only possible under the conditions of experimental modeling of ulcerative colitis [8; 15].

Goal of the work - experimentally create a model of ulcerative colitis, while studying the state of the lymphatic system of the intestinal mesentery before and after modeling. And also in patients to study the importance of lymphotropic therapy in the complex treatment of ulcerative colitis in the postoperative period.

Material and methods

To achieve the goal of the work, serial experiments were carried out on experimental dogs. First, the normal conditions of the intestinal lymphatic system and its mesentery were studied. The experiments were based on the resorption of the dye - Evans blue from the intestinal mesentery of the animal. To do this, part of the loop of the small intestine with the mesentery is brought out and isolated with a sterile swab. 0.1 ml of a 0.1% solution of Evans blue dye was injected subserosally into the intestinal mesentery in three places: the root, the middle part, the marginal part of the intestine and additionally into the intestinal wall, and the time from the moment of its administration was set using a stopwatch. The resorption time of the dye solution introduced at four points was determined visually until their color completely disappeared (Table No. 1).

Table 1. The resorption time of Evans blue from the intestinal mesentery is normal

№ experience	Points of injection of Evans blue and time of its resorption			
	Mesenteric root	Middle part of the mesentery	Marginal part of the intestinal mesentery	Intestinal wall - subserosal part
1	3 min. 22 sec	3 min. 52 sec.	4 min.15 sec.	4 min. 22 sec.
2	3 min.29 sec	3 min. 54 sec.	4 min.17 sec.	4 min. 25 sec.
3	3 min.24 sec	3 min.55 sec.	4 min.21 sec.	4 min. 29 sec.
4	3 min.31 sec	3 min. 57 sec.	4 min.18 sec.	4 min.34 sec.
5	3 min.33 sec	3 min. 52 sec.	4 min.15 sec.	4 min.36 sec.
6	3 min.38 sec	3 min. 59 sec.	4 min.24 sec.	4 min.39 sec.
7	3 min.37 sec	3 min. 53 sec.	4 min.26 sec.	4 min. 19 sec.
8	3 min.31 sec	3 min.50 sec.	4 min.19 sec.	4 min. 34 sec.

The table shows that the time of resorption of Evans blue at different points of the mesentery and subserous layer of the intestine is not the same. In the future, it was necessary to create a model of ulcerative colitis and, using the model, also study the conditions of the intestinal lymphatic system and its mesentery. Important requirements for the model were prostate, speed of delivery and low cost. And at the same time, it should be as close as possible to the clinical, morphological, immunological and hematological picture of ulcerative colitis. From the literature, the most optimal option for modeling ulcerative colitis was identified, a chemically induced model, by rectal administration of 4% and 6% acetic acid. Based on literature data, a series of experiments were conducted to create a model of ulcerative colitis. After cleansing the intestines of the experimental animal, 4% acetic acid was injected rectally into the cavity of the large intestine in an amount of 2-3 ml in fractions. The condition was monitored for 3 days. However, no clinicopathological changes were observed on the part of the experimental animal: clinical signs of intoxication, diarrhea mixed with mucus and blood, loss of body weight. However, after 5 days they decided to operate on the experimental animal. Unfortunately, during the operation they could not visually find clearly pathologically altered areas of the large intestine. Still, they decided to resect that part of the large intestine where 4% acetic acid was injected into its cavity. Histological examination under a microscope of the resected sections of the large intestine revealed no obvious pathological changes.

To create a model of ulcerative colitis, in the second series of experiments, 6% acetic acid in an amount of 2.0 ml was injected rectally into the cavity of the large intestine of an experimental animal,

in fractions. After the manipulation, starting from the third day, minor clinical signs of intoxication and diarrhea mixed with mucus were observed. On day 5, the operation was performed under general intravenous anesthesia. During the operation on the projection of the large intestine, 6% acetic acid was injected into the cavity; from the outside, swelling and hyperemia were detected. This part of the intestine was resected along with areas that were not subject to pathological changes (Fig. 1).

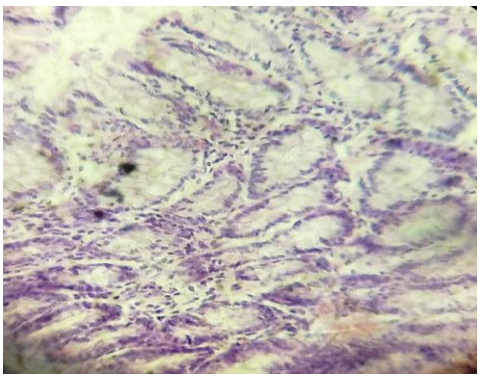

Fig. 1. The intestinal mucosa is normal: the glandular tissues are unchanged.

Staining: hemotoxylin-eosin. Ok.10, vol. 40.

During histological examination under a microscope, necrotic areas of the mucous layer were determined in the area of the pathological focus (Fig. 2).

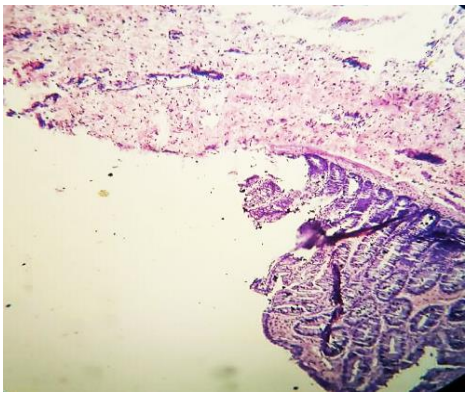

Fig. 2. Acute ulcer, necrosis of the thick mucous layer intestines.

Staining: hemotoxylin-eosin. Ok.10, vol. 40.

It was decided, before resecting part of the large intestine, to determine the time of resorption of Evans's blue against the background of inflammation. A 0.1% solution of Evans blue dye in an amount of 0.1 ml was injected subserously into the mesentery of the pathologically altered part of the intestine in three places: the root, the middle part, the marginal part of the intestine and additionally into the intestinal wall. The time from the moment of administration of the Evans blue dye solution was established. Subsequently, the time of resorption of the dye solution introduced at four points was determined visually using a stopwatch until their color completely disappeared (Table 2).

Table 2. Time of resorption of Evans blue from the intestinal mesentery against the background of the created model of "ulcerative colitis".

№ experience	Points of injection of Evans blue and time of its resorption			
	Mesenteric root	Middle part of the mesentery	Marginal part of the intestinal mesentery	Intestinal wall - subserosal part
1	6 min.39 sec	7 min. 21 sec.	8 min.35 sec.	8 min. 57 sec.
2	6 min.44 sec	7 min. 19 sec.	8 min.37 sec.	8 min. 55 sec.
3	6 min.49 sec	7 min. 43 sec.	8 min.41 sec.	8 min. 59 sec.
4	6 min.35 sec	7 min. 37 sec.	8 min.48 sec.	9 min. 04 sec.

5	6 min.51 sec	7 min. 39 sec.	8 min.35 sec.	8 min. 56 sec.
6	6 min.38 sec	7 min. 29 sec.	8 min.34 sec.	8 min. 59 sec.
7	6 min. 47 sec	7 min. 38 sec.	8 min.46 sec.	8 min. 59 sec.
8	6 min.43 sec	7 min. 41 sec.	8 min.39 sec.	9 min. 05 sec.

The table shows that after modeling ulcerative colitis in experimental animals, a slowdown in lymph circulation in the mesentery and intestines is observed by 2 times or more relative to normal.

Upon completion of the experimental part of the work, we began the clinical part - to apply lymphotropic therapy in the complex treatment of ulcerative colitis in 54 patients in the postoperative period. All operated patients were divided into two groups. The first control group included patients who received generally accepted traditional treatment in the postoperative period (n=43), using parenteral antibacterial therapy. For patients included in the second, main group, complex treatment in the postoperative period was supplemented by the use of endomesenteric lymphatropic therapy according to an algorithm developed in the clinic (n=54). All patients of the main group, upon completion of the main stage of the operation, had a special polyvinyl chloride catheter installed in the intestinal mesentery for endomesenteric lymphatic therapy in the postoperative period. Through which endomesenteric lymphatropic therapy was carried out for 4-5 days, 1 time per day. Lymphatic therapy is carried out after stimulation of the lymphatic system. A solution of glucose 5% - 50 ml + novocaine 0.5% -50 ml with the addition of 5000 units was introduced dropwise. heparin or lasix 64 units. slowly for 40-60 minutes. Upon completion of the manipulation, a selected one dose of antibiotic was connected to the same system, having previously dissolved it in 50 ml of a 0.5% novocaine solution, also by drip.

Results and discussion

The results of the experimental part of the work showed that in the intestinal mesenteries in the model of ulcerative colitis, lymphatic circulation—lymph outflow—slows down significantly, in contrast to the norm. This is a precursor to intestinal complications in the postoperative period with ulcerative colitis.

The results of the clinical part of the work - endomesenteric lymphatic therapy in the postoperative period convincingly showed the high effectiveness of the use of specific measures to prevent the development of functional-dynamic intestinal obstruction in the postoperative period. Endomesenteric lymphostimulation and lymphotropic therapy helped reduce interstitial edema and the concentration of toxins in the intercellular space, blockade of lymphatic flow by toxins, toxic metabolites, bacteria and their breakdown products, which entered the general bloodstream through the lymphogenous route. As well as increasing the drainage function of lymphatic capillaries and normalizing lymph circulation at the level of the abdominal organs. Thus, in the postoperative period, early restoration of intestinal motility was observed in dynamics. This process prevents a number of unwanted complications in the postoperative period.

Conclusions

1. The difference in lymph circulation and drainage in the intestinal wall and its mesentery was determined in normal conditions and in the model of ulcerative colitis, which explains the positive effect of the use of lymphotropic therapy for ulcerative colitis in the postoperative period.
2. The use of lymphotropic therapy in the complex treatment of ulcerative colitis in the postoperative period helps to significantly reduce intestinal complications.
3. When using lymphotropic therapy in the complex treatment of ulcerative colitis in the postoperative period, the material costs of treatment and the number of bed days of the patient in the hospital are reduced.

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