

# IMPROVING THE RESULTS OF TREATMENT OF STEROID-DEPENDENT AND STEROID- RESISTANT FORMS OF NON-SPECIFIC ULCERATIVE COLITIS USING PLASMAPHERESIS

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**Abstract:** The paper analyses clinical material based on the results of complex examination and treatment of 102 patients with confirmed diagnosis of nonspecific ulcerative colitis. Positive dynamics of general clinical, laboratory parameters and endoscopic picture in patients with steroid-dependent and steroid-resistant forms of nonspecific ulcerative colitis when using for their treatment a course of operations of extracorporeal plasmapheresis testifies to its effectiveness for exacerbation of the disease. Despite the use of minimal doses of corticosteroids during plasmapheresis sessions, in comparison with standard therapy, patients with steroid-dependent and steroid-resistant forms of nonspecific ulcerative colitis achieve remission more often (from 22% to 96%), complications from long-term corticosteroid use are significantly reduced, the possibility of complete cancellation of supportive therapy is achieved, which ultimately leads to an improvement in the quality of life of this category of patients.

**Keywords:** Non-specific ulcerative colitis, steroid-dependent and steroid-resistant forms, plasmapheresis.

**Introduction.** According to epidemiological studies, there is currently an increase in the incidence of nonspecific ulcerative colitis (NUC) worldwide. By severity of course, frequency of complications and lethality, NUC occupies one of the leading places in the structure of gastrointestinal tract diseases. The number of patients with hormone-resistant and hormone-dependent forms is growing(4).

Chronic recurrent course of NNC, development of life-threatening complications (perforation, toxic dilatation of the intestine, peritonitis, tumour transformation, etc.), extraintestinal lesions, predominantly affecting people of working age, insufficiently effective and often expensive treatment of NNC determine the relevance of this problem (1,3).

These groups were almost identical in terms of the localisation of the process in the colon and the severity of the process. Thus, according to the localisation and degree of process prevalence in the colon in the main group the patients were distributed as follows: 11 (23%) patients had total lesion of the colon, 15 (32%) patients had left colon lesion, 17 (36%) patients had proctosigmoiditis, 4 (9%) patients had ulcerative proctitis. In the control group 13 (22,5%) patients had total lesion of the colon, 18 (31%) patients - lesion of the left sections, 21 (36%)

patients - proctosigmoiditis, 6 (10,5%) patients - ulcerative proctitis.

Severe course of the inflammatory process in the main group was diagnosed in 13 (27,5%) patients, moderately severe - in 29 (62%) patients, mild - in 5 (10,5%) patients. In the comparison group severe course of inflammatory process was diagnosed in 16 (27,5%) patients, moderate - in 33 (57%) patients, mild - in 9 (15,5%) patients.

In the main group, out of 47 patients hormonal dependence and/or resistance developed in 10 (21%) patients after the first attack of the disease, in 15 (30%) patients - with the duration of the disease 1 year, in 17 (34%) patients - with the history of the disease up to 5 years, in 7 (15%) patients - within 10 years.

In the control group, hormone dependence and/or resistance developed in 14 (24%) patients after the first attack of the disease, in 16 (31%) patients - with a disease duration of 1 year, in 15 (31%) patients - with a disease history of up to 5 years, in 8 (14%) patients - within 10 years.

On the basis of endoscopic criteria we diagnosed minimal (Fig. 1), moderate (Fig. 2) and expressed activity of the inflammatory process (Fig. 3).



Figure 1. Patient G. 28 years old. Endophoto: there is hyperaemia, edema of the intestinal mucosa, no vascular pattern, weakly expressed contact bleeding



Figure 2. Patient D. 41 years old. Endophoto: there is severe contact bleeding of the mucosa, presence of small ulcerative defects and erosions



Figure 3 Patient C. 39 years old. Endophoto: there are confluent superficial ulcers with fibrinous plaque, a lot of blood, mucus, pus in the intestinal lumen

Endoscopic examination of the colon and terminal ileum was carried out with the help of fibrocolonoscope on admission and on the 20th day, which corresponded to the end of treatment by plasmapheresis, on indications - in other various terms, then - during a year, also on indications, and in the absence of exacerbation clinic control terms were 6 and 12 months.

Two groups of drugs were basic in the treatment of NPC: - 5-aminosalicylic acid preparations (sulfasalazine, mesalazine); - glucocorticosteroids (GCS).

Taking into account that non-specific ulcerative colitis is a chronic disease of the large intestine and its basis is an inflammatory process that affects all layers of the intestinal wall, in severe cases - with destruction up to perforation with the presence of antibodies to the structures of the mucous membrane of the colon, circulating immune complexes, excess inflammatory mediators and as a consequence - maintenance of endogenous intoxication and further stimulation of autoimmune inflammation, we included plasmapheresis in the treatment complex in the main group of patients.

The use of therapeutic plasmapheresis allows to quickly eliminate from the vascular bed pathogenic agents that support chronic inflammatory process in the intestine.

Plasmapheresis was carried out on the apparatus "Hemofenix".

In non-specific ulcerative colitis it is necessary to remove about one third of the volume of circulating plasma, and for reimbursement to use only crystalloid solutions in the ratio to the volume of removed plasma 1.5:1. In most of these cases, especially in autoimmune conditions, donor plasma and other protein preparations are generally contraindicated.

Given the need for plasma replacement in discrete plasmapheresis of donor plasma, which is highly undesirable in autoimmune diseases, which includes NNC, we improved the method of plasmapheresis, providing for the exfusion of plasma with its detoxification and transfusion of detoxified autoplasm. Detoxification of blood plasma was carried out by indirect electrochemical detoxification of the patient's blood plasma and additional ozonisation.

The patients underwent therapeutic plasmapheresis in the volume of 1200-1400 ml of plasma extraction. Exfused blood plasma under aseptic conditions was collected in sterile vials of 0.9% NaCl solution in calculated volumes.

In compliance with aseptic rules, 0.12% (1200 mg/l) sodium hypochlorite solution (sodium hypochlorite was obtained at the electrochemical unit EDO-4 by oxidation of isotonic sodium chloride solution) was added by syringe to the exfused plasma in a 10:1 ratio (i.e. 40 ml NaClO was added to 400 ml of plasma). The precipitate (50-70 ml) was removed from a 500 ml glass vial using a plasma extractor or by aspiration.

From the detoxified plasma container, 10 ml of plasma was taken for biochemical studies. Making sure that it is sufficiently detoxified (effective albumin concentration increases more than 1.9 times), decided on the possibility of reinfusion of this autoplasm as a plasma replacement medium during the subsequent session of programmed plasmapheresis. Criteria of detoxification of the exfused plasma, making possible its reinfusion were determined according to N.M. Fedorovsky (2004).

**Results and their discussion.** Clinical course of the disease was assessed subjectively at admission, on the 8th day from the beginning of treatment and on the 20th day. The studies showed that, in general, during the course of plasmapheresis, the clinical course of NNC with steroid-dependent and steroid-resistant forms was more favourable, achievement of remission was observed in more patients and in shorter terms.

One of the leading symptoms of NNC is frequent liquid stools. The frequency of stools, depending on the severity of the course of the disease, ranged from 3-4 to 20 times a day. In the main group treated by plasmapheresis, on the 8th day, i.e. after 2 sessions, symptoms in the form of frequent stools persisted in 9 (19%) out of 49 patients, including 1 (2%) out of 5 patients with mild course of the disease, 2 (4%) out of 29 patients with moderately severe course and 6 (13%) out of 13 patients with severe course of NNC. In the comparison group this symptom was observed in 27 (47%) out of 53 patients: in 2 (4%) out of 9 patients with mild course of NNC, in 10 (17%) out of 33 patients with moderate course and in 15 (26%) out of 16 patients with severe course.

On the 20th day, i.e. after the end of plasmapheresis treatment, in the main group only 2 (4%) out of 13 patients with severe course of NNC complained about frequent liquid stools up to 4-5 times a day, in contrast to the control group, where in the same terms of treatment 4 (7%) out of 33 patients with moderate course of inflammatory process had stools up to 4-5 times a day, in 9 (15%) out of 16 patients with severe course of colitis the frequency of stools was 7-9 times a day.

On the 8th day of treatment in the main group 3 (6%) out of 13 patients with severe

course of NSCLC had blood in stools. In the control group on the 8th day blood in the faeces was observed in 4 (7%) out of 33 patients with moderately severe course of inflammatory process and 11 (19%) out of 16 patients with severe course of NNC. After the last, 4th session of plasmapheresis, which corresponded to the 20th day of treatment, all patients of the main group had no blood in the stool, in contrast to the control group, in which stool with blood was observed in 8 (14%) patients.

Most patients had abdominal pain of a contraction-like character. All patients noted pain intensification before stools and subsiding after defecation. At carrying out 2 sessions of plasmapheresis, already on the 8th day of treatment, pain sensations and tenesms in patients of the main group were absent. In patients of the control group in the same terms the pain syndrome remained expressed in 13 (22 %) from 58 patients, tenesmus - in 9 (16 %) from 58 patients, on the 20th day that corresponded to terms of termination of a course of plasmapheresis, abdominal pain bothered 6 (10 %) from 58 patients, tenesmus - 4 (7 %) from 58 patients.

An important criterion of the general reaction of the organism to the development of inflammatory process in the large intestine is an increase in the general body temperature. On admission in the main group, elevated body temperature was observed in 29 (62%) out of 49 patients, including subfebrile temperature in 16 (34%) out of 29 patients with moderately severe course of NNC, febrile temperature in 13 (28%) out of 13 patients with severe course (Fig. 5). In the control group elevated temperature was noted in 37 (64%) out of 53 patients, of which subfebrile temperature was registered in 21 (36%) out of 33 patients with moderately severe course of colitis and febrile temperature - in 16 (27,5%) out of 16 patients with severe course. By the 8th day of treatment in all patients of the main group the temperature normalised. Against the background of the standard scheme of medical treatment in 8 (14%) of 16 patients of the control group with a severe course of inflammatory process elevated body temperature was kept more than 8 days of treatment and in 4 (7%) patients remained by the 20th day of treatment.

Already after 2 sessions of plasmapheresis, in the main group clinical remission was achieved in 38 (81%) of 49 patients, including 4 (9%) of 5 patients with a mild course of the disease, in 27 (57%) of 29 patients with a moderate course and in 7 (15%) of 13 patients with severe course of NNC; by the end of the course of plasmapheresis - in 45 (96%) of 49 patients, including 11 (23%) of 13 patients with severe course of colitis. In the control group clinical remission on the 8th day of treatment was achieved in 31 (53 %) of 58 patients, including 7 (12 %) of 9 patients with mild course of the process, in 23 (40 %) of 33 patients with moderate course and in 1 (2 %) of 16 patients with severe course of NNC; on the 20th day - in 45(78%) out of 58 patients, including 29(50%) out of 33 patients with a moderate course of the inflammatory process and 7(12%) out of 16 patients with a severe course of NNC, which is presented graphically in Fig. 7

Thus, when plasmapheresis was used in the complex treatment of the main group of NNC patients, 45 (96%) patients managed to achieve clinical remission, in contrast to the control group, where 13 (22%) patients still had clinical signs of the disease against the background of massive corticosteroid and cytostatic therapy.

When studying non-specific markers of the inflammatory process activity, such as leukocytes level, COE and C - reactive protein on the 20th day of treatment, statistically significant decrease with reaching the norm was found in the patients of the main group, in contrast to the control group, where they remained elevated.



**Conclusions.** Positive dynamics of general clinical, laboratory parameters and endoscopic picture in patients with steroid-dependent and steroid-resistant forms of nonspecific ulcerative colitis when using a course of operations of extracorporeal plasmapheresis for their treatment testifies to its effectiveness for acute exacerbation of the disease.

2. Despite the use of minimal doses of corticosteroids in plasmapheresis sessions, compared with standard therapy, in patients with steroid-dependent and steroid-resistant forms of nonspecific ulcerative colitis achieving remission occurs more often (from 22% to 96%), significantly reduced complications from long-term corticosteroid use, achieved the possibility of complete withdrawal of supportive therapy, which ultimately leads to improved quality of life in this category of patients.

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