VOLUME 1, 2011

CONSERVATIVE THERAPY OF INFLAMMATORY DISEASES OF LARGE INTENSTINE

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ABSTRACT

The target of research was the implementation of the comparative analysis of conservative therapy of preparation of basic therapy and also new methods of treatment (anticytokine therapy). Appointment of salofalk - in twos tablets (0, 5) 3-4 times a day per os, and also 2,0 gr in the form of a rectal enema unitary for a period of seven days, then had transferd the patients to reception 2,0 gr salofalk per os, allowed to achieve substantial improvement patients' clinic-laboratory and endoscopic symptoms with a heavy intensification of ulcer colitis variation, providing full clinic-labaratory remissions achievements of disease at 8 (34 %) patients. In the Minister of the Uzbek Public Health of the Republican Science Coloproctological Center at 10 patients with the IDI have spent the therapy remicade, 7 of them had NUC and 3 patients had the Crohn's disease. Therefore, all patients no longer than on the first week after introduction of remicade had improvement of a course disease which was expressed in defering stool, extinction or reduction of pathological impurity in excrement and subsidence bellyaches. During colonoscopical inspection, in 12-18 weeks after the first infusion at 80% of the patients had observed disappearance of ulcers and erosion. In terms of 6 months of supervision of relapse of disease was not noted. All new directions in treatment of the IDI, apparently, are perspective, but while are proved only theoretically and had no practical development. Unique and enough effective and safe method at the IDI and already has clinical acknowledgement is remicade.

UDC Code & KEYWORDS

■ 613.3 ■ CROHN'S DISEASE■ NONSPECIFIC ULCEROUS COLITIS ■ SALOFALK ■ REMICADE ■

INTRODUCTION

The Crohn's disease and nonspecific ulcerous colitis – inflammatory diseases of intestines (IDI) recurrent disposition, the etiology of them is not known yet [3, 4]. The main symptoms of the IDI are caused by inflammation of intestines, the therapy is directed on cut off of inflammation. Basic therapy of the IDI includes three groups of medical products: corticosteroid hormones, medicines 5- amine salicylic acids (5- ASA) and immunosuppressors [1]. There are also used medicines against diarrhea, transfusion and general health-improving preparations. In the case of inefficiency of conservative therapy, as a rule, surgical treatment is applied. The IDI is the disease to the whole life which lead to decrease the quality of life,caused by as both disease,as treatment by itself.

In the present time among the principal etiological factors identified the genetic, the immunological and the environment factors side by side with an infection [4, 6]. In this case, the medicament us therapy used at given disease, is reduced to influence on an inflammation. At these acute intestinal diseases inability of the immune system associated with a mucous membrane of an intestine is accurately traced to supervise inflammatory process. The significant genesis inflammation of immune's system plays cytokines – low-molecular substances of the albuminous nature regulating various aspects of intercellular interactions.

The fundamental moment in immunopathogenesis of the IDI is predominance of proinflammatory cytokine (IL-1, TNF - α, IF-y, chemokinesis, IL 6, IL 7, IL 12, IL 16, IL 17, IL 18) over antiinflammatory (IL 4, IL 10, IL 11, IL 13, the transforming factor of growth β). Among cytokines with inflammatory action one of the most active is FNO - α. It is considered as the key in the course of inflammation. This cytokine exists in two kinds: in the transmembrane form and in the form of soluble trim tab.

Insufficient efficiency of existing basic therapy of the IDI and necessity of improvement the results of conservative treatment of these diseases, overcoming of steroid resistance put in the forefront searches of new approaches on therapy [2]. Progress in the treatment of the IDI consists in development of essentially new "biological" medical strategy. This direction is based on the use as medical products or chimeric biological active molecules blocking various stages of inflammatory reaction in a tissue [4, 5]. Within the limits of biological strategy, the most perspective strategy for today is inhibition of the necrosis factor represented by a tumor; this cytokine is as the basic, to one of the leaders in inflammation development of the IDI.

Nowadays, the recombinant medicine has entered into clinical practice infliksimab (Remicade) which represents chimeric monoclonal mouse antibodies to FNO - α, amalgamated with human antibody G1 (25 % of mouse protein and 75 % of a human antibody).

Therefore, clinical tests of remicade, have spent on the Crohn's disease in the various Western countries, and in particular Russia, have proved its high efficiency and safety. Remicade was registered in Uzbekistan in 2004 under two basic indications – the rheumatoid arthritis and the Crohn's disease, similar with mechanisms developments of an inflammation. There were no any scientific works concerning applications of remicade about the Crohn's disease and nonspecific ulcer colitis in Uzbekistan till now.

The target of research was the implementation of the comparative analysis of conservative therapy of preparation of basic therapy and also new methods of treatment (anticytokine therapy).

We have done the assessment of clinical efficiency in use of мesalazine (salofalk®) at an aggravation ulcer colitis. Under supervision there were 45 patients of different ages from 18 till 56 years (38 women, 7 men), suffering from ulcer colitis (the diagnosis is established with clinical, endoscopic and histologic methods). It was marked,three patients had total defeat of a thick gut, 25 patients had left-sided defeat, 15 of them had process which localized in a straight line and sigmoid gut, and 2 patients – had in a rectum, and duration of disease exceeded during 3 years. At endoscopy process, 4 patients with proctitis are revealed a hypostasis, hyperaemia and the raised vulnerability of a mucous membrane. In other cases, irrespective of localization, there were erosions, haemorrhages, individual ulcers, contact and

■ European Medical, Health and Pharmaceutical Journal ■ ISSN 1804-5804 ■

spontaneous hemophilic mucous membrane of a thick gut. The observed have been divided on two groups. To the patients of the 1st group (23 persons) have been done salofalk medicines - in twos tablets (0, 5gr) 3- 4 times a day per os, and also 2,0 gr in the form of a rectal enema unitary in a seven days period, then patients were transfered on reception 2,0 gr of salofalk. The patients of the 2nd group (22 persons) were spent treatment with sulfazaline, - in twos tablets (1, 0) 3-4 times a day. Simultaneously, all patients were alloted astringent, adsorbing preparations, vitamins B, C, PP groups, spasmolytics and enzymes.

As a rule, we have carried out parenteral therapy with fiber solutions and electrolits. Treatment was continued for 4 weeks. At arrival and after to all patients we did colonoscopy or rectoromanoscopy and the duration was 14 and 28 days. In order to estimate the activity of ulcer colitis we used the modified mark system offered by Rachmilewitz (1989), taking into account factor of the importance of each of estimated symptoms.

The given system of estimation includes 10 kliniko-laboratory and 5 endoscopic signs of ulcer colitis (table1), and each of them which depending on expressiveness value from 0 to 5 is appropriated. According to this method, the remission of ulcer colitis corresponds to numerical sum value less than 5, at incomplete remission the total sum of points tremble in a range from 5 to 15 points, the aggravation of easy extent is characterized by values from 16 to 25 points, the medium-weight aggravation – from 26 to 50. If the score of the patient exceeds 50, that case is regarded as aggravation of heavy degree.

RESULTS OF RESEARCH

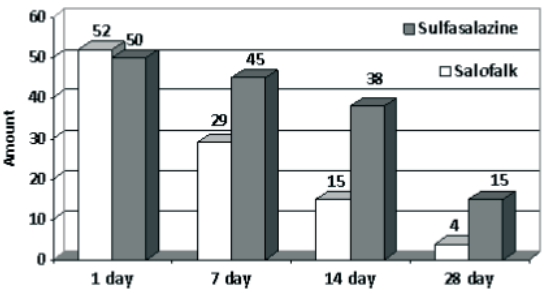
To estimate the effectiveness of the ulser colitis treatment we have spent the comparative search work of dynamics of a reduction on semiology with different methods of treatment.

The received results are showed on fig. 1. During the treatment with salofalk - in twos tablets (0, 5) 3- 4 times a day and 2,0 gr in the rectal enema form one time in a duration of 7 days (the 1st group), the general mark indicator has decreased on 44,23 %, differences are significant .

Table 1: Study

1.	Frequency of the stool in a day	
	< 3	0
	40666	1
	40792	2
	>9	3
2.	Additive of blood in the stool:	
	absent	0
	not great	2
	high	4
3.	The general state of health	
	good	0
	perturb	1
	bad	2
	very bad	3
4.	Stomach ache	
	absent	0
	weak	1
	temperate	2
	strong	3
5.	Heart rate	
	60-80 ictus/min	0
	> 80 ictus/min	2
	< 60 ictus/min	4
6.	Arterial Tension	
	195 - 205	0
	> 205	2
	< 195	4
7.	Temperature of the body (fever, assisted with colitis), °C	
	37	0
	> 38	3
8.	Abenteric display	
9.	iritis	4
	gangliform erythema	4
	arthritis	4
10.	Haemoglobin	
	130	0
	101	1
	70	2
	< 69	3
11.	ESR (erythrocyte sedimentation rate)	
	12-50 millimeter/hour	0
	50-100 millimeter/hour	2
	> 100 millimeter/hour	3
	Endoscopic indication	
12.	Granulation of surface area mucous cover diffract reflected light	
	no	0
	yes	2
13.	Vascular picture	
	normal	0
	diffused / inadequate	1
	generally not traced	2
14.	Vulnerability mucous cover	
	default	0
	slightly increased (contact bleedings)	2
	sharp increased (spontaneous bleedings)	4
15.	Incrustation on mucous cover (crypt cell production, fibrin, pus, erosion, ulsers)	
	absent	0
	insignificant,	2
	dominated	4
16.	Localization damage	
	distal colitis	1
	left-side colitis	2
	subtotal colitis	3
	total colitis	4
	total colitis with retrograde leitis	5

Figure 1: The dynamics (course of disease) state of patients with ulcer colitis disease in a treatment with salofalk and sulfasalazine.



During the treatment with sulfasalazine - in twos tablets (1, 0) 3- 4 times a day (the 2nd group) the whole sum poins indicator has decreased in 7 days duration has decreased till 10 %. On the 14th day this indicator in the first group has decreased on 71, 2 % in comparison with the 1st day, and in compliance with the second group it has decreased on 24 %. On appraisal of ulcer colitis activity, in each of observable patients of the 1st group has been established that the full clinic- endoscopic phase came to the 28th day in salofalk treatment and was successful among eight observed, and among patients of the 2nd group – just a only in twos patients.

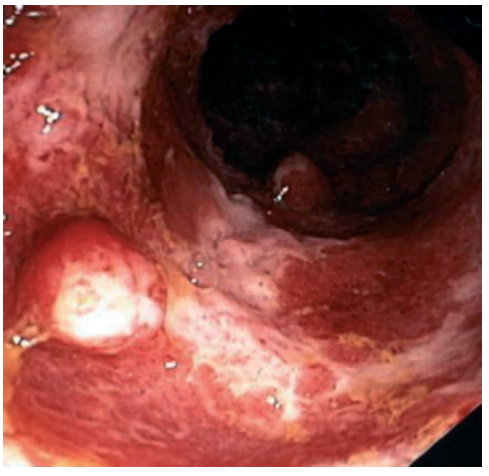
Appointment of salofalk - in twos tablets (0, 5) 3-4 times a day per os, and also 2,0 gr in the form of a rectal enema unitary for a period of seven days, then had transferd the patients to reception 2,0 gr salofalk per os, allowed to achieve substantial improvement patients' clinic-laboratory and endoscopic symptoms with a heavy intensification of ulcer colitis variation, providing full clinic-labaratory remissions achievements of disease at 8 (34 %) patients.

In the Minister of the Uzbek Public Health of the Republican Science Coloproctological Center at 10 patients with the IDI have spent the therapy remicade, 7 of them had NUC and 3 patients had the Crohn's disease. 7 of them were men, and 4- women. The middle age of patients was about 28 years. Average duration of disease lasts for a 1 year. The diagnosis was established to all patients on the basis of clinic laboratory and instrumental methods of the research. Total defeat of a thick gut diagnosed at all diseased.

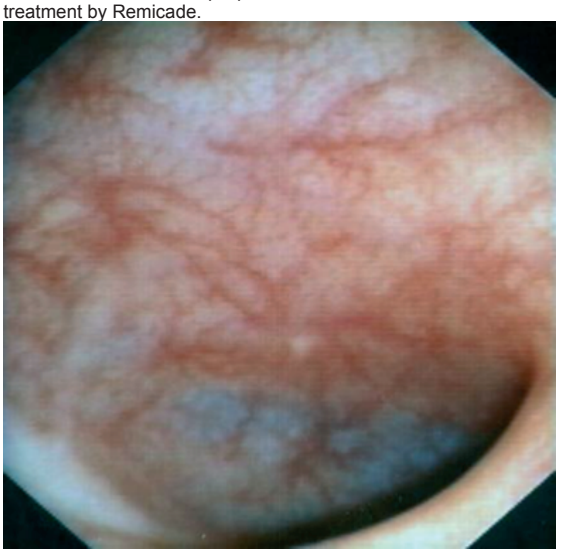
Remicade prescribed due to calculation of weight of a body of 5 mg/kg. The preparation was entered intravenously in the course of 3-5 hours with a speed by initially 0, 5 mlg /a minute and further raised till 2mlg/a minute. Thus each 15 minutes the condition of the patients was estimated, and also measured arterial pressure and puls. All patients had a triple preparation (by 0, 2 and 6 weeks after the first introduction). Throughout the course of infusions at patients were marked slight increase of body temperature, decrease in arterial pressure and headaches, so there were appointmented the analgetics which stopped and decreased in speed of infusion.

Therefore, all patients no longer than on the first week after introduction of remicade had improvement of a course disease which was expressed in defering stool, extinction or reduction of pathological impurity in excrement and subsidence bellyaches.

Picture 1a. The Endoscopic picture of a rectum before 30 weeks of treatment by Remicade.



Picture 1b. The Endoscopic picture of a rectum after 30 weeks of treatment by Remicade.



During colonoscopical inspection, in 12-18 weeks after the first infusion at 80% of the patients had observed disappearance of ulcers and erosion. In terms of 6 months of supervision of relapse of disease was not noted.

CONCLUSION

Summarizing the above-stated, optimum should be confessed the periodicity of introduction of remicade at every 8 week. This position confirms the data of researches, showing that the preparation entered in a dose of 5 mg/kg, persists in an organism in therapeutic concentration during this term, and at a dose of 10 mk/kg – for 12 weeks. In the presence of the serious nidus of an infection (abdominal cavity abscesses, a sepsis, tuberculosis, pneumonia, paraproctitis) because of danger of strengthening of infectious process remicade should not necessary to appoint. It is important to exclude possibility of presence at patients of the latent tuberculosis menacing by an aggravation at appointment of a preparation.

Nowadays, there are considerable quantities of "biological" methods of the treatment developed which are based on influence of various cytokines. All new directions in treatment of the IDI, apparently, are perspective, but while are proved only theoretically and had no practical development. Unique and enough effective and safe method at the IDI and already has clinical acknowledgement is remicade.

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