Use of enterosorbent Enterosgel in complex therapy of acute viral hepatitis B with concomitant intestinal dysbiosis

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Summary

Enterosorbent Enterosgel in Comprehensive Treatment of Acute Viral Hepatitis B with Concurrent Intestinal Dysbiosis

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In this study, which enrolled 144 patients with acute viral hepatitis B, we investigated the peculiarities of acute viral hepatitides accompanied with dysbiotic disturbances and the possible ways to correct the latter using an enterosorbent Enterosgel, as well as the effects of this medicinal product on immunological markers. It has been established that adding enterosorbent Enterosgel to the comprehensive treatment of such patients contributed to toxidrome suppression, prompt regression of major clinical signs of the disorder, gastrointestinal microbiocenosis normalization and improvement of immunological markers. Enterosgel can be safely used in patients due to its good tolerability profile and absence of adverse effects.

Key words: Key words: viral hepatitis, dysbiosis, comprehensive treatment, Enterosgel

Viral hepatitis is one of the widespread infectious diseases in Ukraine. The pathology often has unfavourable course manifested by immunity disorders. In this disease, essential changes in T-system immunity are determined as well as insufficiency of total T-lymphocyte number, disbalance of immune-regulatory subpopulations and disorders of macrophage functional status.

GIT pathology emerging on the background of viral hepatitis also plays an important role in mechanisms of the disease and its clinical course. It is evident that in the human body two main detoxification organs exist: liver performing the body defense via oxidative reactions as well as GIT microflora that involves hydrolytic restoration processes for these purposes. Disorders of interaction between these systems causes their mutual functional and structural changes as well as in the body as a whole. Reduction in detoxification function of GIT microflora in intesrtinal dysbiosis increases the load of liver enzyme system and in a certain sense stimulates development and accelerates metabolic and structural changes [4, 5].

Intestinal microflora plays and active role in formation of immunobiological body functions. Bacterial modules of bifido- and lactobacteria stimulate synthesis of immunoglobulins, interferons, cytokines, increase the complement number as well as lisocyme activity, maturation of macrophage-histiocyte system, take part in metabolism of cholesterol and bile acids that without any doubts has a great importance in liver pathology [3].

In the conditions of synthesis disorders and disturbances of bile transport there exist some prerequisites for a change of intestinal biocenosis, that stimulates te development of not only opportunistic pathogens, but also of pathogenic microflora. Circulation of such endotoxins of intestinal bacteria in the body is an additional load for liver Kupffer cells induces inflammatory changes which often complicates liver functioning and regeneration, while the viral infection in its turn can cause persistence of pathogenic bacteria in the patient's body [3]. Acute and chronic viral hepatitis is accompanied by expressed pathological shifts in the composition of intestinal microflora and stimulate insufficiency of obligate microorganisms and increase in colon contamination [2, 5–7].

Study objectives. The study objective was to determine course specifics of various types of acute viral hepatitis combined with dysbiotic disorders, possibility of their correction with the help of enterosorbent Enterosgel as well as to study its influence on the immunological values.

Enterosorbent Enterosgel possesses selective detoxification action regarding toxins with small- and medium-sized molecules [8]. Enterosgel acts selectively in relation to microorganisms: it adsorbs only pathogenic bacteria, while normal microflora is not influenced or depressed. Thank to it, use of Enterosgel makes sense in patients with viral hepatitis with concomitnant intestinal dysbiosis [1, 9].

Study materials and methods

The study involved patients with acute viral hepatitis B of moderate severity. 144 patients in the age from 19 till 57 years (the mean age – 42.01±2.59 years). Diagnosis of viral hepatitis B is confirmed by determining HBsAg and AbHBcIgM in the blood serum by IFA (ELISA); in 20 (13,8%) patients, liver puncture biopsy (LPB)was performed.

Study participants were randomized in three groups:

1st group (control) – 24 patients without intestinal microbiocenosis disorders;

2nd group– 120 patients with viral hepatitis B and concomitant intestinal dysbiosis, of them 59 patients received only background therapy;

3rd group (main) – 61 patients receiving, along with background therapy, Enterosgel. The groups were matched in age, gender and severity of the disease course. Enterosgel was administered 15 g three times a day during 15 days.

Clinical efficiency of Enterosgel was determined according to the following values:

- subjective data (weakness, fatigue, loss of appetite, nausea, flatulence, stool disorders, heaviness in the right hypochondrium, itching);

- data of objective study (colour of skin and the mucosa, stomach percussion and palpation, change of urine color);

- laboratory values (complete blood count and urinalysis, total protein, alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, prothrombine index, microbiolod=gical feces studiy);

• immunological values– determination of level of T-lymphocytes by method of combined rosette assay.

Dynamics of clinical and laboratory values in the groups was assessed on days 5-, 10 and 20 from initiation of the treatment. Influence of Enterosgel on immunological values was estimated by immune-stimulating activity rate (ISR) and immune-modulating activity rate (IMR).

ISR was estimated according to the formula:

$$ISR= (T_l2/T_l1) (T_{lb}2/T_{lb}1),$$

Where Tl – level of T-lymphocytes in patients receiving Enterosgel before (1) and after (2) treatment; T_{lb} – level of T-lymphocytes in patients receiving background therapy before (1) and after (2) treatment. In case ISR>1, the sorbent possesses immune-stimulating activity.

IMR was estimated according to the formula:

$$IMR = T_l2-T_l1, TN = T_lN-T_{lb}1,$$

Where T_l1 – percentage of T-lymphocytes before treatment, T_l2 - percentage of T-lymphocytes after treatment, T_lN – mean percentage of T-lymphocytes in healthy patients

Results and their discussion

To determine course specifics of viral hepatitis B with concomitant dysbiosis, presence and development rate of basic clinical symptoms was compared in group 1 and 2 of the patients. While analyzing the duration of objective manifestation of the disease (jaundice and change of urine colour), it was determined that, in comparison with the control group, in patients suffering from viral hepatitis B with intestinal dysbiosis, jaundice duration increased (26.1±1.17 vs 22.5±0.92), and further on, "urine" crisis occurred. During jaundice in patients with viral hepatitis B with dysbiosis, frequency of almost all symptoms increased, though significant were only stool disorders: 47.5±10.8% vs 25.0±8.83% ($t=2.06$, $p<0.05$). Much more frequent, though without significant difference, was flatulence frequency– 66.1±10.2% vs 37.5±9.87% and stomach discomfort– 76.2±9.25% vs 62.5±9.87%, which is connected with intestinal dysbiosis in these patients.

Duration of the disease manifestation is noteworthy in the jaundice period. Among the most persistent symptoms in both groups were: weakness, heaviness in the right hypochondrium and nausea. Hovewer, duration of stomach discomfort (33.3±10.2% vs 12.6±6.74%) and flatulence (14.3±7.62% vs 4.16±4.07%) was more frequent, though without significant difference, in the patients with hepatitis and dysbiosis.

Changes of the colon microbiocenosis in120 patients with acute viral hepatitis B were characterized by disorders of quantitative and qualitative composition of microflora. Compensated dysbiosis was determined in 48 (40%) patients, subcompensated dysbiosis– in 72 (60%) patients.

The most frequent among was anaerobe microflora – E.coli with weak enzymatic properties and E. coli with hemolytic activity. It has been determined that bifidobacteria insufficiency was accompanied both with reduction of E.coli as well as with presence of E.coli with weak enzymatic properties and E. coli with hemolytic activity.

Table 1. Persistence duration of symptoms in the jaundice period in patients with viral hepatitis B

Clinical symptoms	Patient group 2 (n=59)						Patient group 2 (n=61)					
	Day 5		Day 10		Day 20		Day 5		Day 10		Day 20	
	Abs.	%	Abs.	%	Abs.	%	Abs.	%	Abs.	%	Abs.	%
Weakness	33	57	25	43	17	29	32	53	16	26	7	11
Pain while moving or articulating	14	24	8	14	6	10	13	21	7	11	3	5
Itching	11	19	8	14	6	10	10	16	7	11	3	5
Stomach discomfort	39	67	25	43	19	33	62	53	19	32	3	10
Stool disorders	28	48	17	29	8	14	23	37	13	21	3	10
Heaviness in the right hypochondrium	39	67	30	52	17	29	35	58	29	47	3	26
Nausea	33	57	17	29	11	19	26	42	13	21	3	5
Faltulence	30	52	19	33	8	14	26	42	13	21	3	5
Loss of appetite	30	52	11	19	6	10	29	47	10	16	3	5

Table 2. Cell immunity values in patients with viral hepatitis B (M±m)

Group of patients	Lymphocyte population, %			
	T	T-active	T-tr	T-ch
Group 2:				
Before treatment	54,70±2,52	36,89±1,79	44,80±4,00	8,10±1,90
After treatment	55,46±2,58	41,30±1,00	45,50±2,27	8,30±1,33
Group 3:				
Before treatment	53,62±3,19	38,76±3,16	45,61±3,45	7,94±1,51
After treatment	54,53±3,21	40,83±3,57	46,17±3,70	8,50±1,33

In the analysis of clinical signs in patient groups 2 and 3 it has been determined that use of Enterosgel stimulated quicker regress of syptoms in the jaundice period of hepatitis (see Table 1). Among patients of group 3, flatulence persisted until day 5 of the treatment in 42% patients, until day 10– in 21% patients, until 20– in 5% patients; stool disorders persisted in 37%, 21% and 10% patients, respectively. In patients of group 2, duration of these disorders was higher: flatulence persisted until day 5 in 57% patients, until day 10– in 33% patients, until day 20– in 14% patients; stool disorders persisted in 43%, 28% and 14% patients, respectively. That is, dyspeptic disorders persisted until day 20in 1/3 patients of group 2 and in 1/5 patients of group 3.

Absence of any complaints until day 20 from initiation of the treatment was determined in 1/2 patients of group 2 and 1/4 patients of the control group.

In patients of group 3 using taking Enterosgel, faster normalization of total bilirubin dynamics I the blood serum was observed. For example, by day 5 of the treatment, total bilirubin was equal to 255±14.35, by day 10 – 162.3±13.01, by day 20 – 49.5±3.85. In the patients of group 2, this value was 258.0±12.66, 193.5±12.4 and 80.9±3.71, respectively. ALT and AST levels in the groups compared did not differ significantly.

After Enterosgel therapy, most of the patients (51; 83.6%) experienced normalization of intestinal microbiocenosis, unlike patients in the control group, in which positive changes were determined only in 25 (42.3%) patients (significant difference).

Analysis of Enterosgel influence on immune values (except T-cell element of the immunity) showed improvement (though not a significant one) of immune homeostasis in the patients studied (Table 2). For example, in patients of group 3, ISR was 1.00, in group 2 – 0.89. Moreover, the study has determined essential positive dynamics in the level of circulating immune complexes (CIC): reduction to 136±23 in the group 3, to 245±20 in the group 2 ($p<0.05$). Regarding immune-modulating activity, although this value improved after use of Enterosgel, the difference with group 2 (basic treatment group) was also insignificant: IMR in the group 3 was 0.58, in the group 2– 0.50. It is possible that other data on Enterosgel ifluence on immunological values in treatment of this patient category can be also used in an additional study of the status of other immunity elements.

Beside that, use of Enterosgel enterosorbent in patients with acute viral hepatitis B with moderate to heavy course and concomitant intestinal dysbiosis is deasible, while it improves general status of the patients eliminating dyspeptic and intoxication syndromes, accelerates positive dynamics of biochemical values and intestinal microbiosis normalization as well as actively stimulates renewal of immunity homeostasis.

During the treatment, no complications or afverse events of Enterosgel was detected.

Conclusions

1. Course of acute viral hepatitis B with concomitant intestinal dysbiosis is characterized by increase in endogenous intoxication as well as longer duration of dyspeptic disorders that requires additional detoxification methods.

2. Inclusion of enterosorbent Enterosgel in the complex therapy of patients with viral hepatitis B and dysbiosis disorders not only eliminates toxicosis, but also favors fast regression of the main clinical symptoms of the disease and normalization of the intestinal microbiocenosis.

3. Enterosgel actively stimulates improvement of various immunological values in patients with viral hepatitis B and intestinal dysbiosis, but the most expressed effect from use of Enterosgel is a significant reduction in circulating immune complexes.

4. Treatment with Enterosgel is safe for the patients thanks to its high tolerability and absence of side effects.

5. Study results show necessity of inclusion of Enterosgel in the complex therapy of patients with viral hepatitis B with concomitant disbiotic disorders. It allows to improve the results of the treatment and to reduce treatment duration.

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