The Ways of Optimizing Treatment the Patients with Liver Cirrhosis

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We examined 65 patients with liver cirrhosis combined with intestinal dysbiosis, studied the influence of the characteristics of its flow intestinal microbiota and included in the combined treatment of medications of Lactobacillus and Bifidobacterium – «Bifilakt Exta» (LB) and Methylsiliconic acid hydrogel – «Enterosgelum » (MAH).

Inclusion to the complex treatment of the patients suffering from cirrhosis of medications LB and MAH led to a significantly better reduction of subjective and objective symptoms of liver cirrhosis, regimentation indicators of intestinal microbiota and symptoms of hepatic encephalopathy.

Keyword: Liver Cirrhosis, Hepatic Encephalopathy, Intestinal Dysbiosis, Medication of Lactobacillus and Bifidobacterium, Methylsiliconic acid Hydrogel.

1. Introduction
The problem of chronic diffuse liver diseases currently is one of the most important in modern gastroenterology and determined, above all, the severity of prognosis, the complexity of diagnosis and treatment, has general medical and social importance. The liver cirrhosis (LC) with chronic hepatitis are on the 2-4th place leading cause of hospitalization and disability at the age of 20-60 years. In Ukraine for the last 10 years the incidence of cirrhosis increased by 75.6%, the prevalence of cirrhosis - by 59.6%\textsuperscript{\cite{3,5,9,12}}.

The main features of LC is portal hypertension, which leads to hepatosplenomegaly, varicose veins dilation are in esophagus and stomach, hepatic encephalopathy. Prolonged portal hypertension also leads to quantitative and qualitative disturbances of intestinal microbiota. The more severe portal hypertension, the more neurotoxins, passing by the liver, fall into the large blood circulation, causing the hepatic encephalopathy\textsuperscript{\cite{11,12}}. Nowadays, the question of intestinal dysbiosis and it’s contribution to the development and progression of hepatic encephalopathy remains unproved. Literature datas, available to us, are ambiguous and contradictory.

Based on the foregoing, the study of effective approaches to the treatment of liver cirrhosis on the basis of the analyzed pathogenetic contribution to the process as intestinal dysbiosis is the actual problem of modern medical science and practice.

2. The Aim of Research
Improving of the treatment of liver cirrhosis by studying its effect on the flow characteristics and intestinal dysbiosis and inclusion to complex treatment medications LB and MAH.
3. Material and Methods

The study involved 65 patients with LC of different origin and 15 healthy individuals in the control group. Patients were examined in gastroenterological department in Clinical Hospital № 1 in Ivano-Frankivsk. By gender all patients were examined the following way: 15 patients were women (23.1%) and 50 patients - men (76.9%). Ratio of men to women is 4.3:1.

The average age of patients is 47.7 ± 0.82 years, while dominated by patients of working age that emphasizes not only medical but also social value problems of diagnosis and treatment of LC. Duration of disease range from 1 to 10 years (mean duration of 4.38 ± 2.38). In the diagnosis of LC classification using the International Working Group and the World Congress of Gastroenterology in Los Angeles in 1994 and ICD-10. The diagnosis of LC was verified by clinical data (complaints, anamnesis, physical data) and laboratory and instrumental examination in accordance with the order of the Ministry of Health of Ukraine № 271 from 13.06.2005. Diagnosis of viral LC included determination of markers of hepatitis B and C according to the diagnostic of algorithm[13].

Alcohol liver disease was diagnosed based on: daily data on alcohol at a dose of at least 50 g of ethanol conversion over 2-5 years, the results of the questionnaire of the European Gastroenterological Association (SAGE), Clinical and biochemical manifestations of liver disease, detection stigmas of alcohol disease, and typical laboratory datas (anemia, leukopenia, thrombocytopenia, increased aminotransferases)[6].

Hepatic encephalopathy was assessed by several tests: number connection test – Reyton’s test, asterixis - («clapping tremor») and defined constructive apraxia. Reyton’s test showed cognitive impairment. Constructive apraxia was assessed by writing and building a five-pointed star[1,2,7,8,10,14].

Bacteriological examination of feces was performed by conventional microbiological method (M.E. Mykelsaar and others, 1990). Material (5-10 g) were collected from the last portion of feces sterile spoon and placed in a sterile tube. From the moment of capture material and before seeding did not go more than 2 hours. From the material (1 g) was prepared from homogenates of saline expectation 10:1 and then preparing serial dilutions (1:100, 1:1000, 1:10,000, 1:100,000, etc.). 0.1 ml of the appropriate dilutions of the material was planted at various selective culture media (Endo, Saburo, Blaurukka, milk-salt agar, blood agar and other). After incubation cups it was sat down each number of microorganisms in 1 g of the material. It was calculated using the formula:

$$K = \frac{E}{kvn},$$

Where,

- K is the number of bacteria;
- E-amount of this type of colonies in all dilutions used;
- v-volume of slurry deposited in the cup;
- n-degree of dilution.

Results of bacteriological examination were fixed in the analysis and expressed as CFU / g[4].

Distribution of patients per group were used approaches to their treatment. Patients were divided into 2 groups:
- Patients of first group, consisting of 33 people, received basic treatment with the inclusion hepatoprotectors, sorbents, metabolic and infusion therapy, vitamin therapy, if necessary diuretic therapy;
- Patients of second group, consisting of 32 people, on a background of basic therapy received medications LB and MAH.

A control group was formed from 15 healthy individuals.

Statistical analysis of the results of research conducted through programs «Statistica for Windows v. 7.1». Probability differences of quantitative indicators were determined by Student's t-test. The difference between the figures considered statistically significant at p <0.05.

4. Results and Discussion:

After treatment, all patients felt improving of their health, but it was noted that in patients of the second group were shown more rapid elimination fatigue, weakness, abdominal pain, diarrhea, jaundice, hemorrhagic syndromes - for 7-12 days, and in patients of group 1 given symptoms persisted until 15-18 days of treatment.
It analyzes the dynamics of the Reyton’s test during treatment (Table 1). According to Table 1, before treatment the patients in group 2 (basic) performed Reyton’s test on average 91.03 ± 2.4 s, while the patients of group 1 (comparison) did it during 88.24 ± 1.51 s. After treatment in patients in 2nd group the time of doing test was decreased for 35%. This figure is better than that of the comparison group. Also analyzed the dynamics of the degree asterixis during treatment (tab.2).

### Table 1: The dynamics of Reyton’s test during treatment, M ± m

<table>
<thead>
<tr>
<th>Reyton’s test, s</th>
<th>Control group, n=15</th>
<th>The first group, n=33</th>
<th>The second group, (n=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
<td>Before treatment</td>
</tr>
<tr>
<td></td>
<td>28.53±0.34</td>
<td>88.24±1.51</td>
<td>69.42±1.76*</td>
</tr>
</tbody>
</table>

Notes: differences in probability before and after treatment: * - p <0.05; n - number of patients.

### Table 2: The dynamics of Asterixis Degree During Treatment

<table>
<thead>
<tr>
<th>Degree asterixis</th>
<th>The first group, n=33</th>
<th>The second group, (n=32)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>5(15.2%)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>16(48.5%)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>8(24.2%)</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>4(12.1%)</td>
</tr>
</tbody>
</table>

After treatment in 2nd group the number of patients, who didn’t have asterixis increased for 51.3 % and in first group – 15.1%. After a complex treatment, the constructive apraxia was observed in 10 (31.25%) patients of the main group and in 16 (48.5%) patients of comparison group.

Thus, given the foregoing it can be argued that the regression of hepatic encephalopathy is more pronounced in the study group where patients received basic therapy in addition to medications LB and MAH.

After a comprehensive treatment of the species composition of microorganisms that persist in the oral colon, underwent some changes (Table 3).

According to Table 3, after the complex treatment of switching medications LB and MAH in the intervention group significantly increased titers of Bifidobacterium and Lactobacillus (5.34 x108 ± 0.38 x108 cfu / g and 3.32 x107 ± 0.82 x107 CFU / g, respectively), p <0.05. Against the total number of E.coli with normal enzymatic activity (3.02 x106 ± 0.68 x106KUO / g) persisted in the presence of E.coli lactosonegative 1.35 x103 ± 0.21 x103 cfu / g (no more than 10% of E.coli), p <0.05 and complete elimination of hemolytic E.coli. At the same time, the titer of Staphylococcus aureus decreased to 1.31 x104 ± 0.26 x104 cfu / g, p <0.05, but not reaching the level of the control group.

After treatment CNS cultured in the amount of 7.7 x105 ± 1.6 x105 cfu / g to 4.4 x106 ± 0.91 x106 cfu / g before treatment (p <0.05). Title yeast fungi decreased from 5.3 x105 ± 1.3 x105 to 3.75 x104 ± 1.5 x104 cfu / g, p <0.05, but not reaching the level of the control group. Enterococci sown in the amount 2.48 x106 ± 0.4 x106 cfu / g, p <0.05. The treatment promoted elimination of CPE.

Analyzing the dynamics of the intestinal microflora in the comparison group in the application of basic therapy was noted that such treatment is not accompanied dynamics titer of
Bifidobacterium and Lactobacillus, lactosonegative and hemolytic E.coli and CNS (P>0.05). Also in the comparison group significantly increased titers of CPE, Staphylococcus aureus, and yeast-like fungi (p<0.05).

Table 3: The dynamics of intestinal microflora in patients with liver cirrhosis, M±m

<table>
<thead>
<tr>
<th>The indicator, CFU/g</th>
<th>Control group, n=15</th>
<th>The first group, n=33</th>
<th>The second group, n=32</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
<td>Before treatment</td>
</tr>
<tr>
<td>Bifidobacterium</td>
<td>5.67x10^6±0.53</td>
<td>3.23x10^6±1.21</td>
<td>7.71x10^6±3.1x10^5</td>
</tr>
<tr>
<td>Lactobacillus</td>
<td>6.93x10^6±0.47</td>
<td>7.64x10^6±2.96</td>
<td>3.41x10^6±0.81x10^5</td>
</tr>
<tr>
<td>- E.coli:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- with normal enzymatic activity</td>
<td>5.4x10^7±0.43</td>
<td>1.47x10^6±0.66</td>
<td>4.56x10^4±1.21x10^4</td>
</tr>
<tr>
<td>- lactosonegative</td>
<td>3.7x10^5±0.76</td>
<td>4.57x10^5±1.4x10^6</td>
<td>5.64x10^4±0.96x10^4</td>
</tr>
<tr>
<td>- hemolytic</td>
<td>3.7x10^5±0.76</td>
<td>3.73x10^5±0.76</td>
<td>9.95x10^5±3.36x10^2</td>
</tr>
<tr>
<td>Staph. aureus</td>
<td>2.33x10^6±0.31</td>
<td>5.90x10^6±1.43</td>
<td>2.21x10^6±0.74x10^5</td>
</tr>
<tr>
<td>Coagulase negative</td>
<td>3.27x10^6±0.33</td>
<td>3.90x10^6±0.54</td>
<td>9.8x10^6±3.8x10^6</td>
</tr>
<tr>
<td>staphylococci (CNS)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterococci</td>
<td>5.8x10^6±0.39</td>
<td>9.64x10^5±4.07</td>
<td>2.47x10^6±1.08x10^6</td>
</tr>
<tr>
<td>Yeast-like fungi</td>
<td></td>
<td>4.95x10^5±1.8x10^2</td>
<td>2.3x10^6±0.88x10^5</td>
</tr>
<tr>
<td>Conditionally pathogenic enterobacteria (CPE)</td>
<td>there is not</td>
<td>4.15x10^5±1.40</td>
<td>1.64x10^6±0.56</td>
</tr>
</tbody>
</table>

Note: the probability of difference indices before and after treatment * - p<0.05; *n - number of patients.

5. Conclusion:
1. Application of medications LB and MAH on the background of basic therapy resulted in a significant regimentation microbiota in the examined patients manifested an increase in titer of Bifidobacterium and Lactobacillus, E.coli with normal enzymatic activity, a significant decrease in titer lactosonegative elimination of hemolytic E.coli and E.coli and CPE.

2. Inclusion in the complex treatment of the patients suffering from cirrhosis of medications LB and MAH led to a significantly better reduction of subjective and objective signs of cirrhosis, allowed more effectively influence the manifestations of hepatic encephalopathy.

6. References
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