SUMMARY: ROLE OF ENTERAL SORPTION IN THE LIPID-LOWERING THERAPY IN PATIENTS WITH NONALCOHOLIC STEATOHEPATITIS ACCOMPANIED BY ISCHEMIC HEART DISEASE AND TYPE II DIABETES

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Summary

Research in primary and secondary prevention of atherosclerosis has shown that statin therapy can significantly reduce total and cardiovascular mortality.⁶,⁸,⁹

A number of patients could not take statins for a long time because of parenchyma liver damage and hepatocellular necrosis. In the treatment with the other groups of products in these patients fail to achieve a reduction in levels cholesterol and low density lipoproteins (LDL) to target values.

In most patients with coronary artery disease (CAD) and diabetes type II mellitus (DM), there is a chronic diffuse liver disease - nonalcoholic steatohepatitis (NASH).

Characteristic features of NASH include increased activity of liver enzymes and morphological changes in the liver biopsy samples, similar to those in alcoholic hepatitis. In 20-81% of NASH cases hyperlipidemia was also observed.¹⁻³,⁵,⁷

Given that patients with NASH require an extremely careful approach to the treatment with statins, it is a challenging necessity to develop the methods to reduce cholesterol absorption from the intestine.

Cholesterol pool is maintained in the body plasma and tissues at the expense of cholesterol synthesis in the liver, adrenal cortex, intestine, genital organs, and also adsorption of cholesterol from the intestine (Food and biliary cholesterol).¹⁰

Approximately 30-40% of cholesterol from the food is adsorbed in the intestine.

One of the ways to reduce cholesterol penetration from the intestine into the blood is the use of intestinal sorption.

Adsorbent Enterosgel is effective for medium-weight toxic metabolites in the intestinal contents, including cholesterol, bilirubin, urea, etc., and therefore it is recommended to explore its effect on the lipid metabolism in patients with NASH.
Objectives

The objective of the study was to evaluate the efficiency of Enterosgel for the intestines in connection with standard antianginal, antihypertensive and hypoglycemic therapy in NASH patients with coronary artery disease and type II diabetes.

Materials and Methods

The authors have followed 40 patients with coronary heart disease, type II diabetes and grade 2 hypertension. During the study, the patients were divided into two groups.

The first (experimental) group consisted from 25 patients. The average age of patients was 54.3 ± 5.7 years, BMI - 30.7 ± 7.3 kg/m². Duration of CHD with type 2 diabetes was 10.0 ± 7.1 years. Functional angina (class II-III) was detected in 72.7%, class IV - in 27.2% of patients. In all the patients, stable hyperglycemia was present.

The second (control) group consisted from 15 patients matched in terms of age, gender, the disease nature, condition of cardiac hemodynamics, physical stress tolerance and hyperglycemia severity in patients of the first group. 14 patients in group 1 and 11 patients in the second group were diagnosed with NASH.

Absorbent Enterosgel was administered to the patients in the first group twice daily in a dose of 15 g for one month on the background of standard antianginal, hypoglycemic and antihypertensive therapy. Patients in the second group received only standard antianginal and hypoglycemic therapy. In neither group the patients received lipid-lowering agents.

On admission of the patients to the clinic and one month after initiation of the treatment parameters of lipid metabolism, glucose and glycated hemoglobin (HbA1c), transaminases (ALT, AST) and alkaline phosphatase were determined for all the patients. The activity of systemic inflammation was determined by the levels of C-reactive protein (CRP) in the blood plasma.

Analyses were performed on the unit Cormay Plus using kits produced by Cormay (Poland). The results were statistically analyzed using differential methods and Student-t-test.

Results

In the 1st group of patients receiving Enterosgel, positive dynamics of plasma lipid metabolism parameters was detected: the content reliably decreased VLDL and total cholesterol, while HDL increased; systemic inflammation activity (CRP) significantly reduced, as well as triglyceride blood level (Table 1). Atherogeneity index decreased.

In the control group, a significant change in biochemical markers was experienced due to standard therapy.

It was demonstrated that the use of Enterosgel has a positive effect on the functional state of the liver: ALT, AST and alkaline phosphatase activity significantly decreased. When using Enterosgel, no side effects or adverse reactions were observed.

<table>
<thead>
<tr>
<th>Value</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
</table>

Table 1

Biochemical values in patients with non-alcoholic steatohepatitis, heart disease and type II diabetes mellitus
<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=25)</th>
<th>Group 2 (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol, mmol/l</td>
<td>8,05 ± 1,15</td>
<td>6,45 ± 1,18*</td>
</tr>
<tr>
<td>Triglycerides, mmol/l</td>
<td>2,82 ± 0,18</td>
<td>1,95 ± 0,17*</td>
</tr>
<tr>
<td>Low-density lipoproteins, mmol/l</td>
<td>4,99 ± 1,14</td>
<td>3,54 ± 1,02*</td>
</tr>
<tr>
<td>Very low-density lipoproteins, mmol/l</td>
<td>0,91 ± 0,08</td>
<td>0,71 ± 0,04*</td>
</tr>
<tr>
<td>High-density lipoproteins, mmol/l</td>
<td>1,21 ± 0,06</td>
<td>1,89 ± 0,07*</td>
</tr>
<tr>
<td>Atherogenicity index</td>
<td>4,8 ± 1,05</td>
<td>4,21 ± 0,91*</td>
</tr>
<tr>
<td>C-reactive protein, mg/ml</td>
<td>8,66 ± 1,45</td>
<td>7,12 ± 0,74*</td>
</tr>
<tr>
<td>Glucose, mmol/l</td>
<td>9,78 ± 1,65</td>
<td>8,01 ± 1,89*</td>
</tr>
<tr>
<td>Glycated hemoglobin, umol/g Hb</td>
<td>7,56 ± 2,24</td>
<td>6,21 ± 1,98*</td>
</tr>
<tr>
<td>ALT, IU/l</td>
<td>74,11 ± 5,78</td>
<td>38,84 ± 3,11*</td>
</tr>
<tr>
<td>AST, IU/l</td>
<td>34,45 ± 2,12</td>
<td>29,89 ± 2,15*</td>
</tr>
<tr>
<td>Alkaline phosphatase, IU/l</td>
<td>98,56 ± 6,16</td>
<td>81,15 ± 5,62*</td>
</tr>
</tbody>
</table>

Note.: * - differences of the values are statistically significant (p <0.05 to 0.01)

**Conclusions**

1. The presence of NASH, which occurs in 62.5% of patients with coronary heart disease and type II diabetes, requires reassessment of complex lipid-lowering therapy used in the studied patient groups due to the frequent concomitant liver pathology.

2. Use of Enterosgel in the complex treatment of NASH patients on the background of CHD and type II DM is an effective and safe method of hyperlipidemia correction.

3. Enterosgel helps to eliminate syndrome of lipid distress (lipid distress syndrome-), including diabetic dislipidemia, reduce the activity of systemic inflammation and atherogenic potential of blood plasma.

4. Enterosgel helps to improve the functional state of the liver.

5. Based on the data obtained, absorbent Enterosgel can be considered as an effective means in preventing the progression of the atherosclerotic process in patients with NASH and concomitant coronary artery disease and type II DM.

**Keywords**: adsorbent, hyperlipidemia, lipoproteins, non-alcoholic steatohepatitis, coronary artery disease, diabetes mellitus, sorption, cholesterol, Enterosgel.

**Reference**


6. Heart Protection Study Collaborative Group. MRC / BHF Heart Protection Study of Lowering cholesterol with simvastatin in 20,536 high-risk Individuals and randomized placebocontrolled trial. Lancet. 2002; 360: 7 to 22


