

Research Article

# Dynamics of Indicators of Psychoemotional Condition in Patients with Chronic Pancreatitis and Atherosclerosis on the Background of Intestinal Dysbiosis Correction

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## Abstract

The article describes and analyzes the psycho-emotional state indicators in patients with chronic alcoholic pancreatitis and atherosclerosis against the complex therapy background with the use of probiotics and melatonin. All patients were performed clinical-laboratory studies: lipid profile study (determination of total blood plasma cholesterol (LC), triglycerides (TG), high-density lipoprotein (HDL) and low-density lipoproteins (LDL), atherogenicity coefficient (CA)); feces research on dysbiosis. The alcoholic etiology of chronic pancreatitis was determined based on anamnestic data and using the AUDIT screening test. The dynamics of psycho-emotional disorders were studied using the HADS questionnaire and the "Emotional Condition Screening" technique. The emotional state screening was used to evaluate the subjects' emotional state to identify critically (subclinical and pathological) abnormalities such as hypomania, somatoform, depressive, anxiety states and the tendency to abuse psychoactive substances. The intestinal dysbiosis degree was evaluated according to the classification of Kuvaeva IB, Ladodo KS. (1991).

The improvement in the colon microflora was observed in all patients who received Mucofalk and melatonin additionally to the complex treatment of chronic pancreatitis and atherosclerosis. Decrease in the subclinical and clinical manifestations of anxiety and depression according to the HADS questionnaire in these patients (subclinical and clinical manifestations of anxiety from 72.1% to 38.7%; subclinical and clinical manifestations of depression from 65.9% to 36.3 %) was observed after the treatment. According to the Emotional Condition Screening technique, there was a decrease in the level of pre-clinical and clinical emotional state disorders (hypomania and somatoform disorders; depressive and anxiety states; tendency to abuse psychoactive substances). At the same time, there was an increase in the frequency of emotional state critical indicators on the background of a decrease in the emotional disorders' frequency in general, which we also regarded as some positive dynamics in such patients.

## Keywords

chronic pancreatitis; atherosclerosis; dysbiosis; treatment

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## Problem statement and analysis of the latest research

For many years, the role of the intestinal microbiota was transferred only to the function of di-

gestion. However, new scientific studies suggest a link between intestinal microbiota dysbiosis and the pathogenesis of extraintestinal disorders. The influence of intestinal dysbiosis on the course of

cardiovascular disease, chronic pancreatitis (CP), metabolic syndrome and obesity has been determined. Key pathogenetic mechanisms leading to the development of the disease include the relationship between the colon microbiota, the products of their metabolism, and the patient's immune system [4, 5, 6].

The involvement of the colon microbiota in lipid metabolism is extremely important. The microflora metabolize cholesterol, which is released into the colon, into coprostanol, and then – into coprostanon. Acetate and propionate formed as a result of fermentation, being absorbed into the blood can affect the synthesis of cholesterol. In particular, it was found that acetate stimulates its synthesis and propionate inhibits it. Dysbiotic disorders and increase of pH in the large intestine contribute to the increase of the activity of enzymes that lead to the synthesis of deoxycholic acid, increase its solubility, absorption and, consequently, increase in blood levels of bile acids, cholesterol and triglycerides [1, 5, 7].

Chronic alcohol consumption is the main cause of CP, which is also accompanied by the development of dysbacteriosis and inflammatory processes in the large intestine [2]. Clinic of CP with concomitant colon dysbiosis is complicated by the increased intestinal dyspepsia syndrome (flatulence, gurgling, abdominal distention, discomfort, feeling of heaviness and abrasion, unstable bowel movement), digestion disorder syndrome (steatorrhea, faulty absorption of fat-soluble vitamins D and K, disorder of water-electrolyte balance), astheno-vegetative syndrome caused by hypo- and avitaminosis, dysproteinemia, intoxication, central nervous system asthenisation [10].

Since recently, many studies have focused on the determination of the role of the intestinal microbiota in regulating the behavior and pathophysiology of some mental disorders, including depression. The colon microflora synthesizes the exact hormone analogues of mammals involved in the mood formation and behavioral responses. Serotonin, as a "hormone of joy", is mainly formed in the intestine [8]. Colon dysbiosis is accompanied by hypovitaminosis of B<sub>1</sub> and B<sub>6</sub>, which are manifested by clinical symptoms of nervous system damage

such as headache, irritability, memory impairment, and drowsiness [9]. Often, depressive disorders are associated with severe chronic conditions such as chronic pancreatitis and atherosclerosis. That is why it is important to study the indicators of psychoemotional state in patients with CP and atherosclerosis [3, 5]. Thus, given the involvement of dysbiosis in the development of disorders of the emotional state, it is important to choose the comprehensive treatment and correction of dysbiosis in patients with CP and atherosclerosis.

**The objective of the research** is to investigate the dynamics of indicators of psycho-emotional state in patients with chronic pancreatitis and atherosclerosis against the background of complex therapy with the use of probiotic and melatonin.

## **1. Materials and Methods**

In our study, there were 84 patients with chronic alcoholic pancreatitis and atherosclerosis who were hospitalized at the Gastroenterology and Endocrinological Departments of the Transcarpathian Regional Clinical Hospital named after Novak A., Uzhgorod, and patients undergoing outpatient treatment. Patients ranged in age from 35 to 76 years, with an average age of  $51.1 \pm 6.0$  years old; there were 59 men (70.24%), 25 women (29.76%). The control group included 20 practically healthy individuals, aged from 36 to 70 years old, with an average age of  $52.4 \pm 3.9$  years old. There were 14 men (70.0%), 6 women (30.0%).

The diagnosis of CP was made in accordance with the Marseille-Roman criteria (1989), supplemented by Ya.S. Zimmerman (1995) and refinements of ICD-10. The alcoholic genesis of the disease was established on the basis of a AUDIT screening test. Dangerous alcohol consumption was set using the AUDIT test rating scale (8 points or more). Dyslipidemic disorders were detected by analyzing lipidogram parameters. Laboratory studies were performed on a ChemWell automatic biochemical analyzer, Awareness Technology INC (USA). The coefficient of atherogenicity (CA) was calculated according to the formula of A.M. Klimova:  $CA = (LC-HDL) / HDL$ ; very low density lipopro-

tein (LDL) – according to the formula  $LDL = TG / 2.2 * 0.45$ , mmol/l; the level of low-density lipoprotein cholesterol (LDL) – according to the formula  $LDL = LC - (LDL + HDL)$ , mmol/l.

Dysbiotic disorders were determined by analyzing the quantitative count of microorganisms grown on agar, Saburo, Endo and 5% blood agar in 1 gram of faeces. In addition, a 5% blood agar plate indicated the presence of hemolytic forms of both intestinal and cocci microflora, a percentage of the total number of colonies that grew, the ratio of intestinal and cocci microflora. The presence of bifidobacteria was determined by the nature of growth on Blaurock medium and Gram stained microscopy. The number of bifidobacteria and lactobacilli in one gram of faeces was determined by the limit dilution at which their growth was observed. The degree of intestinal dysbiosis was evaluated according to the classification of Kuvaeva IB, Ladodo KS. (1991).

The study of the dynamics of the psychoemotional state of the examined patients was conducted by analyzing the results of questioning on the hospital scale of anxiety and depression (Hospital Anxiety And Depression Scale - HADS) and the method of "Screening of emotional state" (SES). According to the SES scale, the emotional state of the studied subjects was evaluated to identify critical (subclinical and pathological) abnormalities: hypomaniacal (H), somatoform (S), depressive (D), anxiety (A) states, and a tendency to abuse psychoactive substances (P).

All studies were performed with the consent of the patients, and their methodology was consistent with the 1975 Declaration of Helsinki and its revision in 1983.

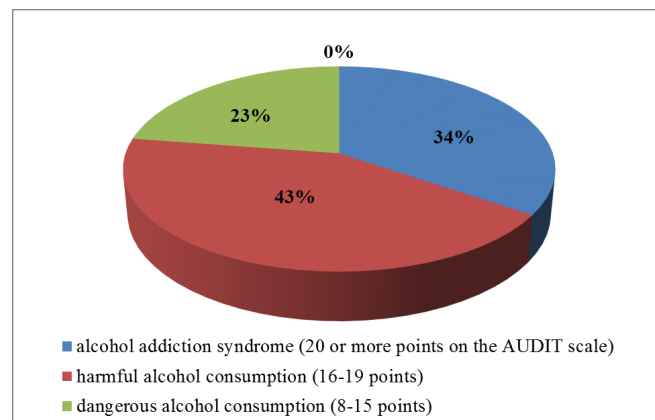
All patients with CP and atherosclerosis were divided into two groups depending on the treatment prescribed. The first group included 40 patients who received treatment in volume: balanced diet, replacement therapy with pancreatic enzymes, selective antispasmodics, proton pump inhibitors, medicine of ursodeoxycholic acid (15 mg per 1 kg of body weight), neurobex (1 caps./day for a month) and neoflorum (2 caps./day, after meals). The second group consisted of 44 patients receiving similar therapy, with the addition of *Plantago Ovata* (Mu-

cofalk), 1 charta dissolved in 150 ml of water, three times a day for one month and the medicine melatonin (3 mg per day 30 minutes before bedtime for one month).

The methodology for conducting all the studies was in accordance with the 1975 Declaration of Helsinki and its revision in 1983. The analysis and processing of the results of the patient examination were performed using the STATISTICA 10.0 computer program (StatSoft Inc, USA) using parametric and non-parametric methods of estimation of the obtained results.

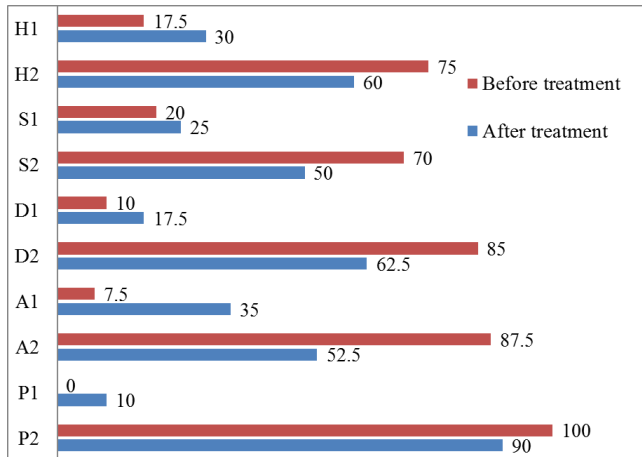
## 2. Results

All patients were diagnosed with alcoholic genesis CP according to the AUDIT scale (Fig. 1). In particular, 29 patients had alcohol dependency syndrome (20 or more points according to the AUDIT scale), 36 patients had alcohol misuse (16-19 points), and 19 patients had hazardous alcohol consumption (8-15 points). Fig. 1 shows the results of the AUDIT survey.

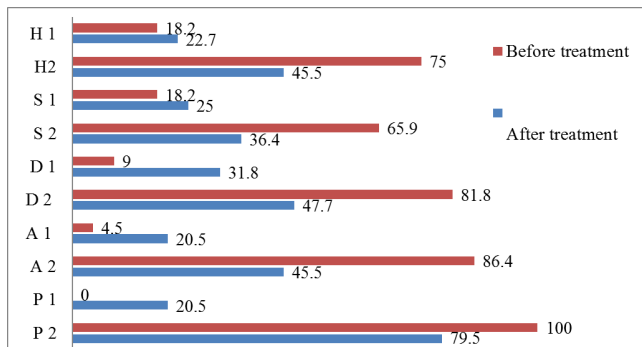


**Figure 1.** Results of questionnaires of patients with CP and atherosclerosis according to the scale of AUDIT.

Laboratory study of feces for dysbiosis was performed in all patients with alcoholic genesis of CP, in combination with atherosclerosis in the dynamics with an interval of 2 months (Table 1). All of the patients examined showed changes in the microbial composition of the colon contents before treatment.



**Figure 2.** Results of questioning according to the SES method in patients of group I before and after the treatment (%).



**Figure 3.** Results of the SES survey in patients of group II before and after the treatment (%).

Notes: 1 – a critical indicator of emotional state; 2 – preclinical and clinical shifts of emotional state

Table 1 shows the results of stool culture for dysbiosis in patients with CP and atherosclerosis, as well as the control group before and after the treatment.

To assess the emotional state, all the patients before and after the treatment were surveyed according to the HADS questionnaire scale (Table 2).

Based on the results of the HADS survey, we showed subclinical (6-9 points) or clinical (10 or more points) anxiety manifestations in 90.0% of patients with CP and atherosclerosis of group I and in 84.1% of patients of group II before the treatment. Subclinical (6-9 points) or clinical (10 or more points) manifestations of depression were reported in 60.0% of patients in group I and 65.9% of patients in group II, respectively. Table 2 shows the

results of the questionnaire on the HADS scale by groups before and after the treatment.

In order to monitor the dynamics of emotional state during therapy, we've performed a questionnaire survey according to the SES method in all patients studied before and after the treatment (Fig. 2, 3).

### 3. Discussion

Intestinal dysbiosis observed in depressed patients is associated with the increased level of Bacteroidetes, Enterobacteriaceae, Alistipes and the decreased level of Firmicutes and Faecalibacterium in the intestine, when compared to healthy subjects [11], triggering local and systemic immune response [12]. Intestinal dysbiosis compromises the intestine-brain communication as well as bacterial translocation triggers the increased level of bacterial endotoxin in the blood. Bacterial endotoxin in turn sustains neuro-inflammatory alterations induced by depression [12].

According to the research results, in all patients there was an improvement in the indicators of the microflora of the colon against the background of complex therapy of patients with CP and atherosclerosis. However, in patients of group II, whose complex therapy included the medicines Mukofalk and melatonin, the positive dynamics was more pronounced, and the quantitative indicators were statistically significant compared to those before treatment.

The scientific literature analysis shows that the developed and adapted methods of emotional states studies do not always satisfy the practitioner needs. There is still a lack of reliable and convenient, easy-to-understand, compact tools that can comprehensively evaluate most of the emotional manifestations' range, such as its intensity, identify diagnostically important links between different disorders, assess the severity of social problems associated with critical changed emotional state. In this case, the SES technique is designed to dynamically assess the emotional state of the subjects in order to identify critical (subclinical and pathological) deviations from its optimal characteristics [13]. Accord-

**Table 1.** Changes in the quantitative and qualitative composition of colon microflora in patients with CP and atherosclerosis and the control group on the background of treatment.

Indicator (Frequency(%)/lg CFU/g)	I group (n=40)		II group (n=44)		Control group (n=20)
	Before treatment	After treatment	Before treatment	After treatment	
Bifidobacterium	80.0 (6.17±0.05)	90.0 (6.99±0.04)	79.5 (6.1±0.02)	100.0* (8.3±0.01)	100.0 (8.81±0.22)
Lactobacillus	87.5 (5.43±0.12)	92.5 (5.88±0.11)	84.1 (5.28±0.15)	97.7* (6.34±0.11)	100.0 (6.79±0.22)
Escherichia	80.0 (5.83±0.2)	87.5 (6.69±0.4)	77.3 (5.92±0.18)	88.6 (7.43±0.13)	100.0 (8.13±0.07)
Enterococcus	45.0 (6.12±0.28)	72.5* (6.91±0.3)	45.5 (6.09±0.27)	95.5* (7.4±0.32)	100.0 (7.42±0.4)
Enterobacter	60.0 (3.27±0.11)	40.0* (2.72±0.08)	59.1 (3.29±0.18)	31.8* (1.76±0.11)	25.0 (1.17±0.05)
Citrobacter	27.5 (2.41±0.03)	40.0* (1.99±0.01)	31.8 (2.4±0.02)	45.5* (1.56±0.03)	45.0 (1.46±0.05)
Staphylococcus	57.5 (4.48±0.22)	45.0 (4.02±0.18)	56.8 (4.51±0.2)	38.6* (3.37±0.2)	35.0 (3.19±0.14)
Klebsiella	55.0 (3.58±0.14)	30.0 (2.86±0.14)	54.5 (3.61±0.21)	25.0* (1.62±0.15)	20.0 (1.03±0.02)
Clostridium	50.0 (5.03±0.05)	27.5* (4.76±0.04)	47.7 (5.16±0.05)	18.2* (4.22±0.03)	15.0 (4.14±0.12)
Proteus	42.5 (2.41±0.04)	22.5* (1.75±0.02)	43.2 (2.38±0.04)	13.6* (1.08±0.01)	10.0 (0.33±0.02)
Candida	30.0 (4.19±0.19)	20.0 (4.03±0.13)	31.8 (4.22±0.12)	11.4* (3.18±0.06)	10.0 (3.19±0.2)

Note: differences between indicators are significant: \* – p < 0.05.

**Table 2.** Results of the HADS survey in patients with CP and atherosclerosis.

Indicator	I group (n=40)		II group (n=44)	
	Before treatment	After treatment	Before treatment	After treatment
Subclinical manifestations of anxiety	47.5 %	40.0 %	47.7 %	18.2* %
Clinical manifestations of anxiety	42.5 %	35.0 %	36.4 %	20.5* %
Subclinical manifestations of depression	35.0 %	30.0 %	40.9 %	22.7* %
Clinical manifestations of depression	25.0 %	22.5 %	25.0 %	13.6* %

Note. \* - statistically significant difference between pre- and post-treatment rates, p < 0.05.

ing to the results of the SES, critical (subclinical and pathological) deviations of psycho-emotional status were revealed in patients with CP and atherosclerosis and their dynamic assessment was performed

depending on the prescribed therapy. It was determined that patients of both groups had hypomanic and somatoform disorders, depressive and anxiety states, and tendency to abuse psychoactive

substances according to the screening before the treatment. After the performed treatment, we've noted a decrease in the level of preclinical and clinical disorders of emotional state in both groups according to all scales of this questionnaire. At the same time, there was an increase in the frequency of detection of critical indicators of emotional state against the background of a decrease in the frequency of emotional disorders in general, which we also regarded as some positive dynamics in such patients. Also, it should be noted that more positive dynamics of indicators of psycho-emotional status were in patients of group II compared with group I.

According to some authors, patients with chronic pancreatitis have been shown to be more anxious and more prone to depression. The combination of pancreatitis and psychological disorders complicates the course and promotes resistance to the prescribed therapy [14]. After the treatment, there was a decrease in the incidence of subclinical and clinical manifestations of anxiety and depression according to the HADS scale in all of our patients. However, more positive and statistically significant changes were observed in patients of group II and were at the level of: subclinical and clinical manifestations of anxiety - in 38.7% of patients; subclinical and clinical manifestations of depression in 36.3% of patients with CP and atherosclerosis who received in addition to the treatment *Plantago Ovata* and melatonin.

The results obtained indicate that patients with alcoholic genesis of CP in combination with atherosclerosis, show significant disturbances of psycho-emotional status against the background of large intestine dysbiosis. Such patients often feel weak, diseased, it is difficult to concentrate, note memory impairment, anxiety/fear, exhaustion, and depression. It is known that depressive states of different severity can affect the effectiveness of treatment and even contribute to the increase in non-specific inflammatory factors [14]. The use of the HADS and SES questionnaires makes it possible to carry out an objective assessment of the psycho-emotional state, to identify existing disorders and, accordingly, to choose the right tactics for the treatment of such patients. Therefore, summarizing the above data,

the positive effect of prescribing of the medicines *Mukofalk* and melatonin in addition to complex therapy for patients with CP and atherosclerosis was determined. These medicines have proved effective, well tolerated by patients and can be used in the complex treatment of dysbiotic disorders in patients with CP and atherosclerosis. This, in turn, was accompanied by a decrease in clinical manifestations of the disease and contributed to the improvement of psycho-emotional indicators in these patients in accordance with the screening of the emotional state and according to the HADS scale.

#### **4. Prospects of Further Researches**

Further study of psycho-emotional disorders in patients with CP and atherosclerosis.

#### **5. Conclusions**

Complex therapy with the use of the medicines *Mucofalk* and melatonin is an effective means of correction of colon dysbiosis in patients with CP and atherosclerosis, as well as effectively influence the indicators of psycho-emotional state according to the questionnaire according to the HADS scale and the results of the emotional condition screening of these patients.

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