ORIGINAL ARTICLE

CONTENTS

Effectiveness of rifaximin and probiotics for the correction of intestinal permeability in patients with metabolic-associated fatty liver disease in combination with type 2 diabetes mellitus

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ABSTRACT

Aim: To investigate the effectiveness of rifaximin and probiotics for the correction of intestinal permeability in patients with metabolic-associated fatty liver disease (MAFLD) in combination with type 2 diabetes mellitus.

Materials and Methods: The prospective interventional randomized investigation included 68 patients with MAFLD in combination with type 2 diabetes, who were examined and divided into the 2 groups of treatment.

Results: The serum levels of interleukin (IL) - 6, IL-10 and zonulin, indicators of liver functional activity, liver attenuation coefficient between treatment group vs. control group after 2 weeks, 1 month, 3 and 6 months of therapy were significant differed. The serum levels of IL-6 and zonulin significantly decreasing and increasing of IL-10 in the treatment group after 2 weeks, 1, 3 and 6 months of combined therapy. When comparing of stool short-chain fatty acids concentration between treatment group vs. control group after 2 weeks, 1 month, 3 and 6 months of therapy the levels of acetic, butyric and propionic acids significantly differences and increase in their levels were established.

Conclusions: The results of the study in dynamics during 6 months show that the additional appointment of rifaximin, multispecies probiotic and prebiotic to metformin in patients with MAFLD and type 2 diabetes led to the elimination of subclinical inflammation, modulation of the permeability of the intestinal barrier and lowering increased intestinal permeability, as well as to the lower serum activity of liver aminotransferases and decrease the stage of steatosis.

KEY WORDS: inulin, multispecies probiotic, pectin, rifaximin, short-chain fatty acids, zonulin

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INTRODUCTION

Metabolic-associated fatty liver disease (MAFLD) is the most common multisystem chronic liver disease worldwide, which is closely related to obesity, insulin resistance, type 2 diabetes, and atherogenic dyslipidemia, and includes a wide spectrum of diseases from hepatic steatosis to steatohepatitis (NASH), fibrosis and cirrhosis of the liver, and may progress to hepatocellular carcinoma [1]. MAFLD and type 2 diabetes are pathophysiologically interconnected by insulin resistance and lipotoxicity. In recent years, there has been a growing interest in the intestinal-liver axis, the dysfunction of which leads to intestinal dysbiosis, bacterial overgrowth syndrome, and increased intestinal permeability [2].

The results of experimental and clinical studies revealed an increase in the number of gram-negative bacteria of the Bacteroidetes type compared to the number of gram-positive bacteria of the Firmicutes type in patients with MAFLD and type 2 diabetes [3]. Violation of intestinal bacterial homeostasis and changes in the content and distribution of bacteria in the intestine and their metabolic functions in patients with MAFLD and type 2 diabetes lead to increased permeability of the intestinal barrier, bacterial translocation and endotoxemia, which is a trigger for increased synthesis of zonulin, a protein that is one of the regulators of intestinal permeability [4]. Bacterial components of intestinal microbiota are ligands of Toll-like receptors. Intestinal dysbiosis and impaired intestinal barrier permeability contribute to increased hepatic expression of Toll-like receptors (TLRs) (TLR2, TLR4, TLR5, and TLR9) that recognize lipopolysaccharide (LPS), peptidoglycan, flagellin, and bacterial DNA [5]. This leads to the stimulation of Toll- and Nod-like receptors, which trigger a cascade of signaling reactions and the stimulation of excessive production of pro-inflammatory cytokines and chemokines by Kupffer cells, which initiate the process of chronic subclinical inflammation, which leads to inflammatory-destructive changes in the liver with subsequent progression to fibrosis [6].

The modulation of the intestinal microbiota with the help of antibiotics, probiotics, and prebiotics is a mod-

ern promising therapeutic direction for the correction of intestinal dysbiosis and impaired intestinal barrier permeability.

AIM

The aim of the study was to investigate the effectiveness of rifaximin and probiotics for the correction of intestinal permeability in patients with MAFLD in combination with type 2 diabetes mellitus.

MATERIALS AND METHODS

The study was conducted at Bogomolets National Medical University, Department of Internal Medicine № 1 (Kyiv, Ukraine) in accordance with Ukrainian laws, requirements of Good Clinical Practice and ethical principles of the Declaration of Helsinki. Written informed consent for participation in the investigation was obtained from all participants before the trial began. The protocol was approved by the Bioethical Committee of Bogomolets National Medical University (Ref. № 150/18.10.2021). The prospective interventional randomized investigation included 68 patients with MAFLD in combination with type 2 diabetes mellitus, who were examined and divided into the 2 groups of treatment. The control group included 34 patients with MAFLD in combination with type 2 diabetes, who were prescribed metformin monotherapy 500 mg 2 times a day. The treatment group - 34 patients with MAFLD in combination with type 2 diabetes, who were prescribed combined therapy - in addition to metformin, rifaximin 1200 mg/day was prescribed, i.e. in a dose of 200 mg 2 tablets 3 times a day for 14 days, multispecies probiotic containing live lyophilized bacteria (Lactobacillus, Bifidobacterium, Saccharomyces boulardii) 1 capsule 2 times a day and prebiotic containing lyophilized concentrates of Jerusalem artichoke (inulin) and apples (pectin) 1 sachet 2 times a day for 6 months.

Investigational drugs:

1. Metformin 500 mg prolonged-release tablets.
2. Rifaximin 200 mg tablets.
3. Capsules containing live lyophilized bacteria 10.0×10^9 CFU (Lactobacillus acidophilus — 2.0×10^9 CFU, Lactobacillus rhamnosus — 1.5×10^9 CFU, Lactobacillus plantarum — 1.5×10^9 CFU, Lactobacillus reuteri — 1.0×10^9 CFU, Lactobacillus casei — 1.0×10^9 CFU, Bifidobacterium bifidum 1.0×10^9 CFU, Saccharomyces boulardii — 2.0×10^9 CFU).
4. Powder 6 g per sachet containing lyophilized concentrates of Jerusalem artichoke (inulin) and apples (pectin).

The inclusion criteria were men and women aged 25-78 years, patients with MAFLD in combination with type 2 diabetes, whose diagnosis was established by determining the degree of steatosis based on the results of ultrasound steatometry performed on the scale of ultrasound attenuation (coefficient of ultrasound attenuation ≥2.2 dB/cm) and diagnostic criteria disorders of carbohydrate metabolism: 1) HbA1c > 6.5%; 2) fasting plasma glucose (FPG) test ≥ 7.0 mmol/l; 3) 2-hour plasma glucose during 75-g *oral glucose tolerance test* (*OGTT*) ≥ 11.0 mmol/l. The exclusion criteria included viral hepatitis, alcoholic liver disease, autoimmune hepatitis, drug-induced liver damage, Wilson-Konovalov disease, type 1 diabetes, decompensated type 2 diabetes, cancer, pregnancy, refusal to participate in the study.

For the diagnosis of MAFLD in patients, ultrasound steatometry was performed using the Ultrasign soneus P7 device with a 1–6 MHz convex sensor to determine the degree of liver steatosis according to the ultrasound attenuation coefficient scale proposed by M. Sasso et al. Type 2 diabetes mellitus (DM) was diagnosed according to the 2023 American Diabetes Association guidelines [7].

The general clinical examination included collection of complaints, history of illness and life, physical examination. During the physical examination of the patient, anthropometric indicators were measured, including height, body weight, body mass index (BMI) according to the Quetelet formula. Blood samples were collected to evaluate indicators of liver functional activity (alanine aminotransferase (ALT), aspartate aminotransferase (AST)). Analyses were performed using a biochemistry analyzer Cobas 6000 with appropriate reagent kits (Roche Diagnostics, Switzerland). The content of serum zonulin was determined by ELISA using test systems IDK Zonulin ELISA, KR5601 (Immunodiagnostic AG, Germany). The concentration of Human Interleukin 6 (IL-6) and 10 (IL-10) in serum was determined by the ELISA method using the Human Interleukin 6 and 10 ELISA Kit test systems (Elabscience, USA). The content of short-chain fatty acids in feces was determined by gas chromatography with mass spectrometry in Gas Chromatograph Perkin Elmer Clarus 680 GC (manufacturer USA).

The primary outcome measures were the changes in serum levels of interleukins (IL-6, IL-10), zonulin and evaluation of stool short-chain fatty acids (SCFAs) concentration after therapy. Secondary outcomes were the evaluation of indicators of liver functional activity (alanine aminotransferase (ALT), aspartate aminotransferase (AST)) and ultrasound attenuation coefficient after therapy.

Table 1. Baseline clinical-diagnostic characteristics of the treatment and control group participants

Parameter	Control group* (n=34)	Treatment group* (n=34)	P**
Sex (female/male) n (%)	20 (59%) / 14 (41%)	18 (53%) / 16 (47%)	0.169
Age, years	58.6 ± 2.9	59.8 ± 3.4	0.178
BMI, kg/m2	31.6 (28.8 – 35)	31.7 (29.3 – 34.6)	0.993
ALT, U/L	57.6 ± 1.1	57.8 ± 1.1	0.851
AST, U/L	49.9 ± 0.8	50.4 ± 0.9	0.566
Serum zonulin, ng/ml	69.6 ± 1.7	68.2 ± 1.5	0.292
IL-6, pg/ml	8.5 ± 0.3	8.6 ± 0.3	0.614
IL-10, pg/ml	3.6 ± 0.1	3.7 ± 0.1	0.723
Butyric acid, μmol/g	24,5 (16,9 – 25)	24,6 (17,2 – 25,7)	0.451
Acetic acid, μmol/g	74,6 (60,3 – 82,1)	74,7 (61,1 – 82,3)	0.654
Propionic acid, μmol/g	23,2 (21,1 – 26,3)	23,3 (21,4 – 26,6)	0.897
LAC, dB/cm	2.93 ± 0.04	2.94 ± 0.03	0,835

BMI: Body mass index; ALT: alanine aminotransferase; AST: aspartate aminotransferase; Interleukin 6: IL-6; Interleukin 10: IL-10; LAC : Liver attenuation coefficient

* Normally and non-normally distributed data were presented as mean ± standard deviation (SD) and median (Q1-Q3), respectively.

** For normal and non-normal distribution, t-test and Wilcoxon two-sample test were used, respectively.

Table 2. Comparison of indicators of liver functional activity between treatment group *vs*. control group throughout the study

Parameter	Time-Point	Control group* (n=34)	Treatment group* (n=34)	P**
ALT, U/L	Baseline	57.6 ± 1.1	57.8 ± 1.1	0.851
	After 2 weeks of therapy	57.5 ± 1.1	55.6 ± 1.1	0.023
	After 1 month of therapy	56.4 ± 1.2	54.3 ± 1.2	0.159
	After 3 months of therapy	53.1 ± 1.3	51.4 ± 1.3	0.014
	After 6 months of therapy	49.6 ± 1.2	47.5 ± 1.2	0,016
	P#	<0.001	<0.001	
AST, U/L	Baseline	49.9 ± 0.8	50.4 ± 0.9	0.566
	After 2 weeks of therapy	49.7 ± 0.9	47.4 ± 0.8	0.025
	After 1 month of therapy	48.2 ± 0.6	45.1 ± 0.7	0,031
	After 3 months of therapy	46.6 ± 0.5	43.2 ± 0.6	0.018
	After 6 months of therapy	44.7 ± 0.9	40.1 ± 0.8	0.022
	P#	<0.001	<0.001	

ALT: alanine aminotransferase; AST: aspartate aminotransferase

* Normally and non-normally distributed data were presented as mean ± standard deviation (SD) and median (Q1-Q3), respectively.

** For normal and non-normal distribution, t-test and Wilcoxon two-sample test were used, respectively.

For normally and non-normally distributed data, one-way repeated measures ANOVA and the Friedman test were used, respectively.

The GraphPad Prism Version 9.5.1.733 program was used for statistical processing of the obtained results. When checking the distribution of the obtained data for normality, the Shapiro-Wilk test was used. In the case of a normal distribution, quantitative variables were described by the arithmetic mean value with a standard deviation (Mean±SD), if different from the normal distribution, by the median with the first and third quartiles (Median (Q1-Q3)). In the case of a normal distribution of the data, the unpaired Student's t-test was used to check the probability of the difference between the mean values, and in the case of a non-normal distribution, the Wilcoxon test was used.

In the case of a normal distribution, using one-way repeated measures analysis of variance (ANOVA) with a preliminary implementation of the Mockley test of sphericity, or in the case of a non-normal distribution, the Friedman test was used to analyze the difference between the values at different time points of the study. In case of repeated measurements, the probability of difference between three or more mean values in the case of a nor-

Table 3. Comparison of serum levels of interleukins (IL-6, IL-10) and zonulin between treatment group *vs*. control group throughout the study

Parameter	Time-Point	Control group* (n=34)	Treatment group* (n=34)	P**
Serum zonulin, ng/ml	Baseline	69.6 ± 1.7	68.2 ± 1.5	0.292
	After 2 weeks of therapy	69.2 ± 1.2	35.2 ± 1.5	<0.001
	After 1 month of therapy	67.9 ± 1.5	30.3 ± 1.2	<0.001
	After 3 month of therapy	62.8 ± 1.4	19.7 ± 1.1	<0.001
	After 6 month of therapy	58.5 ± 1.0	10.1 ± 1.6	<0.001
	P#	<0.001	<0.001	
IL-6, pg/ml	Baseline	8.5 ± 0.3	8.6 ± 0.3	0.614
	After 2 weeks of therapy	8.4 ± 0.1	6.2 ± 0.1	<0.001
	After 1 month of therapy	8.2 ± 0.2	5.7 ± 0.2	<0.001
	After 3 month of therapy	7.9 ± 0.1	4.6 ± 0.1	<0.001
	After 6 month of therapy	7.6 ± 0.2	3.5 ± 0.2	<0.001
	P#	<0.001	<0.001	
IL-10, pg/ml	Baseline	3.6 (2.9 – 5.0)	3.7 (4.7 – 7.6)	0.723
	After 2 weeks of therapy	3.7 (2.8 – 5.1)	5.8 (4.9 – 7.8)	<0.001
	After 1 month of therapy	4.0 (2.7 – 5.2)	6.2 (5.0 – 8.5)	<0.001
	After 3 month of therapy	4.3 (3.2 – 5.2)	7.1 (6.0 – 8.6)	<0.001
	After 6 month of therapy	4.5 (3.2 – 5.4)	8.2 (7.1 – 9.7)	<0.001
	P#	<0.001	<0.001	

* Normally and non-normally distributed data were presented as mean ± standard deviation (SD) and median (Q1-Q3), respectively.

** For normal and non-normal distribution, t-test and Wilcoxon two-sample test were used, respectively.

For normally and non-normally distributed data, one-way repeated measures ANOVA and the Friedman test were used, respectively,

mal distribution was checked by the repeated measures ANOVA method, in the case of a non-normal distribution - by the Friedman test. The difference between the study groups was considered statistically significant at $P < 0.05$.

RESULTS

The baseline clinical-diagnostic characteristics of the treatment and control group participants are shown in Table 1. There were no statistically significant differences between the treatment and control groups at baseline. In patients of the control and treatment groups were established to increase of hepatic aminotransferases, serum zonulin and IL-6. Increased levels of serum IL-6 and zonulin indicate chronic subclinical inflammation and increased intestinal permeability in patients with MAFLD and type 2 diabetes. The results of steatometry established severe stage of steatosis (S3). The concentration of short-chain fatty acids in feces were reduced.

In the treatment group was significant decrease of ALT, AST activity in serum between baseline and after 2 weeks, 1, 3 and 6 months of therapy and significant differences between after 2 weeks, 1, 3 and 6 months of therapy. In the control group was significant decrease of liver enzymes in serum between baseline and after 3 and 6 months of therapy, but not between baseline and after 2 weeks and significant differences between after 2 weeks, 1, 3 and 6 months of therapy (Table 2).

When comparing of indicators of liver functional activity between treatment group vs. control group after 2 weeks,1 month, 3 and 6 months of therapy the levels of ALT and AST significant differences and decrease in their levels was established. The comparison of liver aminotransferases between the groups showed that ALT and AST levels were significantly lower in the treatment group after 2 weeks, 1, 3 and 6 months of combined therapy (Table 2).

In the treatment group was significantly lower serum levels of IL-6, zonulin and increase concentration of IL-10 between baseline and after 2 weeks, 1, 3 and 6 months of therapy and significantly differences between after 2 weeks, 1, 3 and 6 months of therapy. In the control group was significantly decrease of serum levels of IL-6, zonulin and increase concentration of IL-10 between baseline and after 1, 3 and 6 months of therapy, but not between baseline and after 2 weeks and significantly differed between after 2 weeks, 1, 3 and 6 months of therapy (Table 3).

The serum levels of interleukins (IL-6, IL-10) and zonulin between treatment group vs. control group after 2 weeks, 1 month, 3 and 6 months of therapy were significantly differed. The serum levels of IL-6 and zonulin were significantly decreasing and increasing of IL-10 in the treatment group after 2 weeks, 1, 3 and 6 months of combined therapy (Table 3).

Table 4. Comparison of stool SCFAs concentration profiles between treatment group *vs*. control group throughout the study

Parameter	Time-Point	Control group* (n=34)	Treatment group* (n=34)	P**
Acetic acid, μmol/g	Baseline	74,6 (60,3 – 82,1)	74,7 (61,1 – 82,3)	0.654
	After 2 weeks of therapy	74,8 (61.0 – 82,7)	80,8 (69,2 – 86,9)	0.002
	After 1 month of therapy	76,2 (62.0 – 83,1)	85,3 (75,4 – 92)	0.011
	After 3 month of therapy	79,4 (69,1 – 80,2)	93,1 (83,6 – 93,8)	0.033
	After 6 month of therapy	81,3 (80,7 – 82,9)	98,6 (95,4 – 100,2)	0.004
	P#	<0.001	<0.001	
Butyric acid, μmol/g	Baseline	24,5 (16,9 – 25)	24,6 (17,2 – 25,7)	0.451
	After 2 weeks of therapy	24,7 (17,6 – 25,3)	30,9 (21,5 – 33,6)	0.003
	After 1 month of therapy	26,3 (18,2 – 27,8)	33,7 (23,9 – 38,2)	0.024
	After 3 month of therapy	29,1 (19,6 – 30,2)	38,5 (25,9 – 39,3)	0.016
	After 6 month of therapy	33,2 (20,5 – 34,1)	41,8 (26,7 – 42,6)	0.001
	P#	<0.001	<0.001	
Propionic acid, μmol/g	Baseline	23,2 (21,1 – 26,3)	23,3 (21,4 – 26,6)	0.897
	After 2 weeks of therapy	23,5 (22,5 – 27,8)	29,5 (24.0 – 30,1)	0.013
	After 1 month of therapy	25,7 (23,6 – 28)	30,7 (26,1 – 31,5)	0.011
	After 3 month of therapy	28,2 (25,7 – 29,3)	35,6 (30,4 – 36,8)	0.003
	After 6 month of therapy	29,1 (27,7 – 30,1)	39,2 (35,5 – 40,9)	0.017
	P#	<0.001	<0.001	

* Normally and non-normally distributed data were presented as mean ± standard deviation (SD) and median (Q1-Q3), respectively.
** For normal and non-normal distribution, t-test and Wilcoxon two-sample test were used, respectively.
# For normally and non-normally distributed data, one-way repeated measures ANOVA and the Friedman test were used, respectively·

Table 5. Comparison of liver attenuation coefficient between treatment group *vs*. control group throughout the study

Parameter	Time-Point	Control group* (n=34)	Treatment* group (n=34)	P**
LAC, dB/cm	Baseline	2.93 (2.86 – 2.96)	2.94 (2.85 – 2.98)	0.835
	After 2 weeks of therapy	2.93 (2.86 – 2.96)	2.92 (2.84 – 2.97)	0.663
	After 1 month of therapy	2.93 (2.86 – 2.96)	2.91 (2.82 – 2.96)	0.607
	After 3 month of therapy	2.92 (2.85 – 2.94)	2.89 (2.80 – 2.94)	<0.001
	After 6 month of therapy	2.91 (2.83 – 2.92)	2.87 (2.79 – 2.91)	<0.001
	P#	>0.05	<0.001	

* Normally and non-normally distributed data were presented as mean ± standard deviation (SD) and median (Q1-Q3), respectively.
** For normal and non-normal distribution, t-test and Wilcoxon two-sample test were used, respectively.
# For normally and non-normally distributed data, one-way repeated measures ANOVA and the Friedman test were used, respectively.

In the treatment group was significantly increase of stool SCFAs concentration between baseline and after 2 weeks, 1, 3 and 6 months of therapy and significantly differences between after 2 weeks, 1, 3 and 6 months of therapy. In the control group was significantly increase levels of acetic, butyric and propionic acids between baseline and after 1, 3 and 6 months of therapy, but not between baseline and after 2 weeks and significantly differed between after 2 weeks, 1, 3 and 6 months of therapy (Table 4).

When comparing of stool SCFAs concentration between treatment group vs. control group after 2 weeks, 1 month, 3 and 6 months of therapy the levels of acetic, butyric and propionic acids significantly differences and increase in their levels were established. The comparison of stool SCFAs concentration between the groups showed that levels of acetic, butyric and propionic acids were significantly increase in the treatment group after 2 weeks, 1, 3 and 6 months of combined therapy (Table 4).

In the treatment group was significantly decrease of liver attenuation coefficient between baseline and after 2 weeks, 1, 3 and 6 months of therapy and significantly differences between after 2 weeks, 1, 3 and 6 months of therapy. In the control group was no statistically significant differences of liver attenuation

coefficient between baseline and after 2 weeks, 1, 3 and 6 months of therapy (Table 5).

When comparing of liver attenuation coefficient between treatment group vs. control group after 2 weeks, 1 month, 3 and 6 months of therapy the LAC significantly differences and decrease were established. The comparison of liver attenuation coefficient between the groups showed that liver attenuation coefficient were significantly decrease in the treatment group after 2 weeks, 1, 3 and 6 months of combined therapy (Table 5).

DISCUSSION

Numerous studies indicate that modulation of the intestinal microbiota with rifaximin and probiotic bacteria, yeast (Lactobacillus, Bifidobacterium, Saccharomyces boulardii) and prebiotics provides lowering permeability of the intestinal barrier and promotes its integrity, reduces bacterial translocation and endotoxemia [8]. It was established that rifaximin with probiotics and prebiotics leads to decrease in the level of endotoxin, liver transaminases, indicators of carbohydrate and lipid profile, pro-inflammatory cytokines (IL-6), and decrease in the stage of liver steatosis [9]. According to scientific data, rifaximin has a wide spectrum of antimicrobial action against gram-negative and gram-positive aerobic and anaerobic bacteria, has eubiotic properties and increases the relative amount of Lactobacillus and Bifidobacterium in the intestine. Rifaximin directly upregulates the expression of tight junction proteins, mainly zonula occludin-1 (ZO-1), thus lowering intestinal permeability [10].

Probiotics contain live bacteria that have the potential to strengthen the intestinal barrier layer as well as modulate the immune system. Lactobacillus and Bifidobacterium produce short-chain fatty acids in the colon by bacterial anaerobic fermentation of indigestible polysaccharides and have anti-inflammatory, immunomodulatory, antioxidant, antibacterial properties. The minimum necessary dose suitable to ensure a therapeutic effect should ranges between 8 and 9 log colony forming units (cfu)/mL [11].

SCFAs consist of butyric, propionic and acetic acids, which are an energy substrate for intestinal epithelial cells and regulate the condition of the intestinal barrier and affect the immunity of the intestinal mucosa [12].

Prebiotics are indigestible fermented compounds that induce the growth and activity of some genera of microorganisms in the colon, generally Lactobacillus and Bifidobacterium. Due to their chemical structure, prebiotics are not absorbed in the small intestine, but are fermented and used in the colon by endogenous bacteria as metabolic substrates, including short-chain fatty acids (SCFAs) [13]. The occurrence of prebiotics may inhibit pathogen adhesion, modulate lipid metabolism. Inulin and pectin are two of the most used prebiotics. Inulin is one of the best known prebiotic oligosaccharides with recognized specific and different functional attributes, such as modulation of the gut microbiota, prevention of adhesion and colonization by pathogens, stimulation of anti-inflammatory effects, reduction of food intake, modulation of bowel movements, regulation of alterations in lipid and glucose metabolism. Pectins are complex polysaccharides that exhibit bifidogenic and generally prebiotic properties on different strains of probiotic microorganisms [14].

As a result of our 6-months of treatment, dynamic changes in the level of interleukin 6 and 10, serum zonulin, short-chain fatty acids in feces and liver aminotransferases were noted in patients of both groups.

Already after the 2nd week of treatment, in patients, who received combined therapy were detected decrease level of serum zonulin and IL-6 and reached their reference values, as well as an increase in the concentration of serum IL-10 and short-chain fatty acids (acetic, butyric and propionic acids) in feces. This indicates an anti-inflammatory reaction in the intestinal mucosa, elimination of subclinical inflammation and reduced increased intestinal permeability, as well as restoration of the intestinal microbiota and stabilization of the intestinal barrier function.

In our study, in patients with MAFLD in combination with type 2 diabetes, who were prescribed combined therapy were showed significant lower serum activity of liver aminotransferases and decrease stage of steatosis from severe (S3) to moderate (S2), indicating reduced fatty infiltration in the liver compared to the control group after 6 months of treatment.

CONCLUSIONS

The results of the study in dynamics during 6 months show that the additional appointment of rifaximin, multispecies probiotic containing live lyophilized bacteria (Lactobacillus, Bifidobacterium, Saccharomyces boulardii) and prebiotic containing lyophilized concentrates of Jerusalem artichoke (inulin) and apples (pectin) to metformin in patients with MAFLD and type 2 diabetes led to the elimination of subclinical inflammation, modulation of the permeability of the intestinal barrier and lowering increased intestinal permeability. It was established that the prescribed combined therapy for the treatment of patients with MAFLD and type 2 diabetes contributed lower serum activity of liver aminotransferases and decrease the stage of steatosis from severe (S3) to moderate (S2), which indicates decrease in fatty infiltration in the liver.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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