ISSN 2786-6661
eISSN 2786-667X

UDC: 616.34-002:616.34-008.314.4]-06:616-008.9]-085:[615.324:579.8-026.81
https://doi.org/10.32345/USMYJ.4(142).2023.55-61

Received: June 26, 2023
Accepted: October 31, 2023

Modification of bile acids metabolism with multi-strain probiotic in patients with diarrhea predominant irritable bowel syndrome: a randomized study

Neverovskyi Artem, Polishchuk Serhii

Department of internal medicine №1, Bogomolets National Medical University, Kyiv, Ukraine.

Adress for correspondence:

Neverovskyi Artem

E-mail: artemneverovskiy@gmail.com

Abstract. *one of the irritable bowel syndrome with diarrhea (IBS-D) mechanisms of development is bile acids (BA) malabsorption (BAM). The promising new therapeutic approach for BAM – probiotic bacteria producing bile salt hydrolase (BSH). The aim of the study was to compare the effect of multi-strain probiotic and cholestyramine combination with cholestyramine monotherapy on modifying the parameters of BA metabolism in IBS-D patients. Materials and methods. The trial was conducted as a randomized, open, parallel study and included 108 patients with IBS-D divided into 2 groups: case group (n=57) that received combination of probiotic (L. rhamnosus, L. plantarum, S. thermophilus, L. acidophilus, B. bifidum, B. longum, B. infantis, S. boulardii) with cholestyramine, and control group (n=51) that received cholestyramine monotherapy during 12 weeks. The total relative activity (RA) of gut bacterial BSH, serum BA (sBA) and fecal BA (fBA) were assessed in all patients. Results: total, primary and secondary sBA and fBA, proportions of primary and secondary fBA were significantly different after 12 weeks within each group comparing to baseline, p<0.05. In case group the proportions of primary and secondary sBA, RA of gut bacterial BSH were significantly different after 12 weeks comparing to baseline, p<0.05. All the parameters of BA metabolism except absolute levels of secondary sBA were significantly different after 12 weeks between the control and case groups, p<0.05. Conclusions: combination of cholestyramine and multi-strain probiotic led to more pronounced alterations of BA metabolism and increasing of gut bacterial BSH-activity comparing to cholestyramine monotherapy. It may explain possible mechanism of action of probiotics in patients with IBS-D and assumed BAM.*

Key words: Bile Acids and Salts, Diarrhea, Irritable Bowel Syndrome, Malabsorption Syndromes, Probiotics

Introduction

Irritable bowel syndrome (IBS) is one of the most prevalent functional gastrointestinal disorders in routine outpatient clinical practice of gastroenterologists and primary care specialists (Sperber et al., 2021). Scientific understanding of IBS development mechanisms and origin has been changing over the decades: from truly «functional» when it has been considered as a disease of exclusion without morphological and another pathophysiological basis to disorder of gut-brain interaction (DGBI) (Drossman, 2016). Current concept of IBS as a variant of DGBI is that different structural and biochemical factors may contribute to the development of IBS: genetic abnormalities, immune dysregulation, low-grade intestinal inflammation, visceral hypersensitivity, altered brain processing, changes of gut microbiota,

ISSN 2786-6661
eISSN 2786-667X

bile acids malabsorption (BAM) etc. (Holtmann et al., 2016). The latter – BAM – deserves special attention because it was shown that up to half patients with diarrhea predominant IBS (IBS-D) and functional diarrhea (FD) have the evidences of BAM and consequently bile acids diarrhea (BAD) (Min et al., 2022; Camilleri, 2015). Moreover, the Rome Foundation considers the BAM as one of the possible mechanisms of IBS-D development (Mearin et al., 2016). But unfortunately, due to absence of specific clinical features in patients with IBS-D the BAM is commonly overlooked leading to inappropriate management (Kinoshita et al., 2021). Guidelines on the management of BAD recommend the bile acid sequestrants (BAS) as the first line treatment for patients with BAD (Sadowski et al., 2020). Also, BAS are recommended by Rome Foundation (Mearin et al., 2016), Japanese Society of Gastroenterology (Fukudo et al., 2021), United European Gastroenterology and European Society for Neurogastroenterology and Motility (Savarino et al., 2022) as therapeutic option for the treatment of diarrhea in patients with functional gastrointestinal disorders including IBS even without confirmed BAM due to limited access to the diagnostic tests and statistically high prevalence of BAM in IBS-D and FD patients. But side effects and poor toleration of BAS limit their clinical application (Farrugia et al., 2020). Therefore, new therapeutic approaches are need to be investigated. One of the promising directions – probiotics capable to produce bile salt hydrolase (BSH) that ferments primary bile acids (BA) to their secondary forms (Min et al., 2022). But despite the current evidences of the possible connection between altered BA metabolism, microbiota and IBS-D, there are limiting data regarding the using probiotic bacteria and their mechanisms of action in patients with IBS-D and suspected BAM (Zhan et al., 2020).

Aim

So, the aim of present study was to evaluate and compare the effect of combination therapy (multi-strain probiotic and cholestyramine) with cholestyramine monotherapy on modifying the parameters of BA metabolism in patients with IBS-D.

Materials and methods

This clinical investigation was performed in accordance to Good Clinical Practice (GCP) requirements, Declaration of Helsinki and Ukrainian legislation. All participants of the present trial have signed the written informed consent. The protocol of investigation was approved by the Bioethical Committee of Bogomolets National Medical University (Kyiv, Ukraine).

Design of the trial was chosen as a randomized, open, parallel study. Participants were men and women, aged 18-44 years, with IBS-D. Inclusion criteria were: both sexes, age 18-45 years, diagnosis of IBS-D according to Rome IV criteria (Mearin et al., 2016), negative fecal occult blood and calprotectin tests, negative celiac serology (IgA and IgA to tissue transglutaminase), for women – negative pregnancy test. Exclusion criteria were age > 45 years, any «alarm» feature (weight loss, signs of hemorrhage, anemia, night symptoms, visible blood in stool, palpable abdominal mass, family anamnesis of colorectal cancer), any organic disease of the intestines, medication history of taking the probiotics, antibiotics, laxatives, BAS less than 3 months before the starting of the study; oncological disorders; acute illness less than 2 months before the starting of the study; pregnancy and lactation.

A total of 108 patients with IBS-D were enrolled to the investigation and completed all the steps of the trial. Participants were divided into the 2 groups: case group (n=57) that received combination of investigational multi-strain probiotic (1 capsule b.i.d.) with cholestyramine (4 g b.i.d.) and control group (n=51) that received cholestyramine monotherapy (4 g b.i.d.). The trial was conducted in 2 phases: 1) screening up to 5 days and 2) treatment with investigational therapeutic regimens during 12 weeks. Each 4 weeks patients visited the research center according to individual schedules. All the patients received lifestyle and diet recommendations according to international guidelines (Vasanr et al., 2021). During the investigations it was prohibited to take probiotics, antibiotic, anti-diarrheal drugs.

Investigational medications:

1) Capsules containing live lyophilized bacteria $1.94*10^9$ CFU (Lactobacillus rhamnosus – $0.5*10^9$ CFU, Lactobacillus plantarum – $0.2*10^9$ CFU, Streptococcus thermophilus – $0.5*10^9$ CFU, Lactobacillus acidophilus – $0.5*10^9$ CFU, Bifidobacterium spp. (Bifidobacterium

ISSN 2786-6661
eISSN 2786-667X

bifidum, Bifidobacterium longum, Bifidobacterium infantis) – 0.24*10^9 CFU); Saccharomyces boulardii – 65 mg; dry extract of chamomile flowers (Matricaria chamomilla L.) – 50 mg; inulin - 200 mg) – «Opefera» manufactured by World Medicine, Romania.

2) Sachets with powder for oral suspension containing cholestyramine resin 4 g («PMS-cholestyramine regular with orange flavor» manufactured by Pharmascience Inc., Canada).

Assessment of total relative activity (RA) of gut bacterial BSH. The fecal samples of patients were collected and then stored at -80 °C. The ultra-performance liquid chromatography – mass spectrometry (UPLC-MS) was used to evaluate the total enzyme activity of gut bacterial BSH as was previously described (Joyce et al., 2014). The RA of gut bacterial BSH was expressed in units of choloylglycine hydrolase/mL (from Clostridium perfringens, EC 3.5.1.24, Sigma-Aldrich).

Assessment of serum BA (sBA). The high-performance liquid chromatography – mass spectrometry (HPLC-MS) of fasting blood samples was used to measure the levels of serum total, primarily (cholic acid (CA) and chenodeoxycholic acid (CDCA)) and secondary (deoxycholic acid (DCA) and lithocholic acid (LCA)) BA as was previously described (Dior et al., 2016). The obtained levels of BA were expressed in nmol/l. Additionally, the levels of primarily and secondary BA were expressed in proportions of total BA.

Assessment of fecal BA (fBA). After the collection the patient`s fecal samples were stored under the anaerobic conditions, at 4 °C and then homogenized during the 18 hours with subsequent storing at -80 °C (Dior et al., 2016). The HPLC-MS was used to measure the levels of fecal total, primarily (CA and CDCA) and secondary (DCA and LCA) BA as was previously described (Dior et al., 2016). The obtained levels of BA were expressed in nmol/g of feces. The levels of primarily and secondary BA were additionally expressed in proportions of total BA.

Statistical analysis. The SPSS software (version 23, IBM Corp., Armonk, NY, USA) was used to analyze the results of present trial. Normality of data distribution of continuous variables was checked by the Shapiro-Wilk test. The data were presented as mean with standard deviation (Mean ± SD) or median with first and third quartiles [Median (Q1-Q3)] depending on normality of distribution. Unpaired t-test or Wilcoxon test was used to check the difference between the means of groups. Paired t-test and Wilcoxon matched pairs test was used to check difference of repeated variables during study time points. Differences between groups were considered significant in $p<0.05$.

Results

The baseline characteristics of the study groups in terms of age, sex ratio and BA metabolism indicators were not different (Table 1).

Modification of BA metabolism indicators after 12 weeks of the trial. The absolute levels of total, primary and secondary sBA and fBA, relative levels of primary and secondary fBA were significantly different after 12 weeks of therapy if compare with baseline values within each trial`s group, $p<0.05$. Additionally, in case group the relative levels of primary and secondary sBA, RA of gut bacterial BSH were also significantly different after 12 weeks of therapy if compare with baseline values, $p<0.05$ (Table 1).

Comparison of study groups with each other shown that after 12 weeks of treatment all the parameters of BA metabolism except absolute levels of secondary sBA were significantly different between the control and case groups, $p<0.05$ (Table 1).

Discussion

Our investigation revealed that both treatment options (cholestyramine monotherapy and combination of cholestyramine with multi-strain probiotic) significantly changed the most parameters of BA metabolism after 12 weeks of therapy. In terms of serum BA, it was found the decreasing of the absolute levels of total, primary and secondary sBA in both groups. While the relative levels of primary sBA were decreased and secondary sBA were increased only in case group received combination treatment. In terms of fecal BA, it was found the increasing of the absolute levels of total and secondary fBA as well as relative levels of secondary fBA in both groups. But absolute and relative levels of primary fBA were decreased in both groups. These results are comparable with the data from literature. Previous investigations also shown that cholestyramine

ISSN 2786-6661
eISSN 2786-667X

Table 1. Characteristics of the study groups at baseline and after 12 weeks of treatment

Indicator		Control group (n=51)*	Case group (n=57)*	Difference, p**
Age, years		30 (23-38)	31 (26-36)	0,978
Sex, women [n(%)]		35 (68,6)	42 (73,7)	0,712
sBA total, nmol/l	Baseline	1,99±0,94	1,86±1,08	0,498
	12 weeks	0,95±0,32#	0,76±0,26#	**0,001**
sBA primary abs, nmol/l	Baseline	0,89 (0,71-1,56)	0,88 (0,61-1,4)	0,496
	12 weeks	0,57±0,25#	0,41±0,2#	**<0,001**
sBA primary %	Baseline	55,6±10,9	58,5±13,3	0,214
	12 weeks	60,4 (45-72)	53,6 (40,5-66,6) #	**0,045**
sBA secondary abs, nmol/l	Baseline	0,73 (0,51-1,24)	0,66 (0,42-0,96)	0,132
	12 weeks	0,34 (0,2-0,52) #	0,35 (0,24-0,42) #	0,603
sBA secondary %	Baseline	44,4±10,9	41,5±13,3	0,214
	12 weeks	39,6 (28,1-55)	46,4 (33,4-59,5) #	**0,045**
fBA total, nmol/g	Baseline	5,78 (5,41-6,24)	5,49 (5,1-6,52)	0,406
	12 weeks	13,3 (11,2-14,82) #	14,7 (12-19) #	**0,005**
fBA primary abs, nmol/g	Baseline	1,27 (1,1-1,45)	1,28 (1,1-1,58)	0,569
	12 weeks	1,02 (0,8-1,42) #	0,73 (0,51-1,07) #	<**0,001**
fBA primary %	Baseline	22,3±4,8	23,1±4,2	0,392
	12 weeks	7,7 (5,8-10,9) #	5 (3,6-7,2) #	<**0,001**
fBA secondary abs, nmol/g	Baseline	4,56±0,71	4,48±0,91	0,639
	12 weeks	12,4 (10,3-13,8) #	14,3 (11,3-17,8) #	**0,001**
fBA secondary %	Baseline	77,7±4,8	77±4,2	0,392
	12 weeks	92,3 (89,1-94,2) #	95 (92,8-96,4) #	<**0,001**
RA of gut bacterial BSH, U/ml	Baseline	0,098 (0,05-0,13)	0,098 (0,048-0,13)	0,691
	12 weeks	0,1 (0,05-0,13)	0,18 (0,13-0,22) #	<**0,001**

** The data were presented as Mean±SD or Median (Q1-Q3) depending on the normality of data distribution;*
*** comparison between control and case groups; #significant difference in comparison with baseline, p<0.05.*

may alter the composition of BA. In patients with primary biliary cholangitis (Li et al., 2021) cholestyramine led to decreasing of total sBA without differences in proportions of primary and secondary sBA, increasing of total and secondary fBA. But in the same time, there were no differences in composition of primary fBA if compare with our trial. In investigation (Vijayvargiya et al., 2020) with applying of another BAS – colesevelam – in patients with BAD it was found the increased level of total fBA and relative level DCA (secondary fBA) after 4 weeks of treatment. But there were no differences in values of primary fBA. The similar trial (Camilleri et al., 2015a) with the applying of colesevelam in patients with IBS-D revealed also increased levels of total fBA and DCA as well as reduction in CA (primary fBA) after 10 days of treatment. So, results of our investigation in terms of cholestyramine impact on BA metabolism parameters are similar with the data from previous trials but with some exceptions that should be studied in next investigations.

Regarding the role of probiotic in modification of BA metabolism, there were found limited and compromising data. Jones et al. (2012) revealed that consumption of L. reuteri led to increased absolute levels of serum unconjugated BA (consist mostly of secondary BA) in healthy participants. In opposite, our trial shown the decreased absolute values of secondary sBA in response to treatment with multi-strain probiotic, but relative levels of these BA were increased. In another trial (Wang et

ISSN 2786-6661
eISSN 2786-667X

al., 2014) 4-week prescribing of L.plantarum was associated with decreased levels of total fBA. But in more early investigation with healthy patients (Zampa et al., 2004) Lactobacilli led to increasing of total fBA. Also, animal studies revealed increased total fBA after L. fermentum (Lye et al., 2017) and L. gasseri (Li et al., 2022) consumption, decreased conjugated fBA (that consist mostly of primary BA) and increased secondary fBA (Li et al., 2022) in response to L. gasseri treatment. However, recent human study (Boonma et al., 2021) with the applying of multi-strain probiotic VSL#3 to IBS patients didn`t find any changes in fecal BA profile, and authors related such results with insufficiently powered trial. So, different probiotic bacteria may alter BA metabolism, but exact effect is not clear. It should be noticed that we didn`t find the investigations studying the impact of probiotics with cholestyramine combination on BA metabolism.

The present study also found the difference in most parameters of BA metabolism between the trial`s groups. It means that additional prescribing of probiotic bacteria may probably enhance the modification of BA metabolism. Such effect may be explained by BSH activity of the investigated probiotic. And our previous investigation with the same probiotic (Polishchuk & Neverovskyi, 2023) revealed it`s high BSH activity. Moreover, in present trial it was found that after 12 weeks of treatment the RA of gut bacterial BSH significantly increased in case group received combination with probiotic if compare with baseline levels and with the group on cholestyramine monotherapy. It should be mentioned, that this trial was the continuation of our previous investigation (Polishchuk & Neverovskyi, 2023) where we found that additional to cholestyramine prescribing of investigated probiotic to patients with IBS-D was more effective in terms of symptomatic relief and treatment efficacy end-points achievement than cholestyramine monotherapy. So, present investigation revealed possible explanation of such effect of additional applying of probiotic bacteria.

Conclusions

In patients with IBS-D combination of cholestyramine and multi-strain probiotic (with L. rhamnosus, L. plantarum, S. thermophilus, L. acidophilus, B. bifidum, B. longum, B. infantis, S. boulardii) led to more pronounced alterations of BA metabolism indicators, including composition of serum and fecal BA as well as increasing of gut bacterial BSH-activity comparing to cholestyramine monotherapy. So, such results may explain possible mechanism of action of probiotic bacteria and their effectiveness in patients with IBS-D and assumed BAM. But obtained results require confirmation in the next investigations.

Financing

None declared.

Conflict if interests

None declared.

Consent to publication

All participants gave the permission for article publication.

ORCID ID and authors contribution

0000-0002-2618-6347 (A, B, C, D, E, F) Artem Neverovsky

0000-0001-6926-9911 (A , B, C, D, E, F) Polishchuk Serhii

A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of article

REFERENCES

Boonma, P., Shapiro, J. M., Hollister, E. B., Badu, S., Wu, Q., Weidler, E. M., Abraham, B. P., Devaraj, S., Luna, R. A., Versalovic, J., Heitkemper, M. M., Savidge, T. C., & Shulman, R. J. (2021). Probiotic VSL#3 Treatment Reduces Colonic Permeability and Abdominal Pain Symptoms in Patients With Irritable Bowel Syndrome. Frontiers in pain research (Lausanne, Switzerland), 2, 691689. https://doi.org/10.3389/fpain.2021.691689.

Camilleri M. (2015). Bile Acid diarrhea: prevalence, pathogenesis, and therapy. Gut and liver, 9(3), 332–339. https://doi.org/10.5009/gnl14397.

Camilleri, M., Acosta, A., Busciglio, I., Boldingh, A., Dyer, R. B., Zinsmeister, A. R., Lueke, A., Gray, A., & Donato, L. J. (2015a). Effect of colesevelam on faecal bile acids and bowel functions in diarrhoea-predominant irritable bowel syndrome. Alimentary pharmacology & therapeutics, 41(5), 438–448. https://doi.org/10.1111/apt.13065.

Dior, M., Delagrèverie, H., Duboc, H., Jouet, P., Coffin, B., Brot, L., Humbert, L., Trugnan, G., Seksik, P., Sokol, H., Rainteau, D., & Sabate, J. M. (2016). Interplay between bile acid metabolism and microbiota in irritable bowel syndrome.

ISSN 2786-6661
eISSN 2786-667X

Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society, 28(9), 1330–1340. https://doi.org/10.1111/nmo.12829.

Drossman D. A. (2016). Functional Gastrointestinal Disorders: History, Pathophysiology, Clinical Features and Rome IV. Gastroenterology, S0016-5085(16)00223-7. Advance online publication. https://doi.org/10.1053/j.gastro.2016.02.032.

Farrugia, A., & Arasaradnam, R. (2020). Bile acid diarrhoea: pathophysiology, diagnosis and management. Frontline gastroenterology, 12(6), 500–507. https://doi.org/10.1136/flgastro-2020-101436.

Fukudo, S., Okumura, T., Inamori, M., Okuyama, Y., Kanazawa, M., Kamiya, T., Sato, K., Shiotani, A., Naito, Y., Fujikawa, Y., Hokari, R., Masaoka, T., Fujimoto, K., Kaneko, H., Torii, A., Matsueda, K., Miwa, H., Enomoto, N., Shimosegawa, T., & Koike, K. (2021). Evidence-based clinical practice guidelines for irritable bowel syndrome 2020. Journal of gastroenterology, 56(3), 193–217. https://doi.org/10.1007/s00535-020-01746-z.

Holtmann, G. J., Ford, A. C., & Talley, N. J. (2016). Pathophysiology of irritable bowel syndrome. The lancet. Gastroenterology & hepatology, 1(2), 133–146. https://doi.org/10.1016/S2468-1253(16)30023-1.

Jones, M. L., Martoni, C. J., & Prakash, S. (2012). Cholesterol lowering and inhibition of sterol absorption by Lactobacillus reuteri NCIMB 30242: a randomized controlled trial. European journal of clinical nutrition, 66(11), 1234–1241. https://doi.org/10.1038/ejcn.2012.126.

Joyce, S. A., MacSharry, J., Casey, P. G., Kinsella, M., Murphy, E. F., Shanahan, F., Hill, C., & Gahan, C. G. (2014). Regulation of host weight gain and lipid metabolism by bacterial bile acid modification in the gut. Proceedings of the National Academy of Sciences of the United States of America, 111(20), 7421–7426. https://doi.org/10.1073/pnas.1323599111.

Li, B., Zhang, J., Chen, Y., Wang, Q., Yan, L., Wang, R., Wei, Y., You, Z., Li, Y., Miao, Q., Xiao, X., Lian, M., Chen, W., Qiu, D., Fang, J., Gershwin, M. E., Tang, R., & Ma, X. (2021). Alterations in microbiota and their metabolites are associated with beneficial effects of bile acid sequestrant on icteric primary biliary Cholangitis. Gut microbes, 13(1), 1946366. https://doi.org/10.1080/19490976.2021.1946366.

Li, X., Xiao, Y., Huang, Y., Song, L., Li, M., & Ren, Z. (2022). Lactobacillus gasseri RW2014 Ameliorates Hyperlipidemia by Modulating Bile Acid Metabolism and Gut Microbiota Composition in Rats. Nutrients, 14(23), 4945. https://doi.org/10.3390/nu14234945.

Lye, H. S., Kato, T., Low, W. Y., Taylor, T. D., Prakash, T., Lew, L. C., Ohno, H., & Liong, M. T. (2017). Lactobacillus fermentum FTDC 8312 combats hypercholesterolemia via alteration of gut microbiota. Journal of biotechnology, 262, 75–83. https://doi.org/10.1016/j.jbiotec.2017.09.007.

Mearin, F., Lacy, B. E., Chang, L., Chey, W. D., Lembo, A. J., Simren, M., & Spiller, R. (2016). Bowel Disorders. Gastroenterology, S0016-5085(16)00222-5. Advance online publication. https://doi.org/10.1053/j.gastro.2016.02.031.

Min, Y. W., Rezaie, A., & Pimentel, M. (2022). Bile Acid and Gut Microbiota in Irritable Bowel Syndrome. Journal of neurogastroenterology and motility, 28(4), 549–561. https://doi.org/10.5056/jnm22129.

Polishchuk, S., & Neverovskyi, A. (2023). Efficacy of bile salt hydrolase synthesizing probiotic bacteria in the treatment of irritable bowel syndrome with diarrhea. GASTROENTEROLOGY, 57(2), 108–114. https://doi.org/10.22141/2308-2097.57.2.2023.540.

Sadowski, D. C., Camilleri, M., Chey, W. D., Leontiadis, G. I., Marshall, J. K., Shaffer, E. A., Tse, F., & Walters, J. R. F. (2020). Canadian Association of Gastroenterology Clinical Practice Guideline on the Management of Bile Acid Diarrhea. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association, 18(1), 24–41.e1. https://doi.org/10.1016/j.cgh.2019.08.062.

Savarino, E., Zingone, F., Barberio, B., Marasco, G., Akyuz, F., Akpinar, H., Barboi, O., Bodini, G., Bor, S., Chiarioni, G., Cristian, G., Corsetti, M., Di Sabatino, A., Dimitriu, A. M., Drug, V., Dumitrascu, D. L., Ford, A. C., Hauser, G., Nakov, R., Patel, N., … Barbara, G. (2022). Functional bowel disorders with diarrhoea: Clinical guidelines of the United European Gastroenterology and European Society for Neurogastroenterology and Motility. United European gastroenterology journal, 10(6), 556–584. https://doi.org/10.1002/ueg2.12259.

Sperber, A. D., Bangdiwala, S. I., Drossman, D. A., Ghoshal, U. C., Simren, M., Tack, J., Whitehead, W. E., Dumitrascu, D. L., Fang, X., Fukudo, S., Kellow, J., Okeke, E., Quigley, E. M. M., Schmulson, M., Whorwell, P., Archampong, T., Adibi, P., Andresen, V., Benninga, M. A., Bonaz, B., … Palsson, O. S. (2021). Worldwide Prevalence and Burden of Functional Gastrointestinal Disorders, Results of Rome Foundation Global Study. Gastroenterology, 160(1), 99–114.e3. https://doi.org/10.1053/j.gastro.2020.04.014.

Vasant, D. H., Paine, P. A., Black, C. J., Houghton, L. A., Everitt, H. A., Corsetti, M., Agrawal, A., Aziz, I., Farmer, A. D., Eugenicos, M. P., Moss-Morris, R., Yiannakou, Y., & Ford, A. C. (2021). British Society of Gastroenterology guidelines on the management of irritable bowel syndrome. Gut, 70(7), 1214–1240. https://doi.org/10.1136/gutjnl-2021-324598.

Vijayvargiya, P., Camilleri, M., Carlson, P., Nair, A., Nord, S. L., Ryks, M., Rhoten, D., Burton, D., Busciglio, I., Lueke, A., Harmsen, W. S., & Donato, L. J. (2020). Effects of Colesevelam on Bowel Symptoms, Biomarkers, and Colonic Mucosal Gene Expression in Patients With Bile Acid Diarrhea in a Randomized Trial. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association, 18(13), 2962–2970.e6. https://doi.org/10.1016/j.cgh.2020.02.027.

ISSN 2786-6661
eISSN 2786-667X

Wang, L., Zhang, J., Guo, Z., Kwok, L., Ma, C., Zhang, W., Lv, Q., Huang, W., & Zhang, H. (2014). Effect of oral consumption of probiotic Lactobacillus planatarum P-8 on fecal microbiota, SIgA, SCFAs, and TBAs of adults of different ages. Nutrition (Burbank, Los Angeles County, Calif.), 30(7-8), 776–83.e1. https://doi.org/10.1016/j.nut.2013.11.018.

Yoshikazu Kinoshita, Tsuyoshi Sanuki, Sachiko Oouchi, Kousaku Kawashima & Shunji Ishihara (2021). Bile Acid Diarrhea: An Etiology of Chronic Diarrhea Easily Overlooked. Shimane J. Med. Sci., 38, 89-97. https://doi.org/10.51010/sjms.38.3_89.

Zampa, A., Silvi, S., Fabiani, R., Morozzi, G., Orpianesi, C., & Cresci, A. (2004). Effects of different digestible carbohydrates on bile acid metabolism and SCFA production by human gut micro-flora grown in an in vitro semi-continuous culture. Anaerobe, 10(1), 19–26. https://doi.org/10.1016/j.anaerobe.2003.12.002.

Zhan, K., Zheng, H., Li, J., Wu, H., Qin, S., Luo, L., & Huang, S. (2020). Gut Microbiota-Bile Acid Crosstalk in Diarrhea-Irritable Bowel Syndrome. BioMed research international, 2020, 3828249. https://doi.org/10.1155/2020/3828249.

Модифікація обміну жовчних кислот при застосуванні мультиштамового пробіотику у пацієнтів із синдромом подразненого кишечника з діареєю: рандомізоване дослідження

Неверовський Артем, Поліщук Сергій

Кафедра внутрішньої медицини №1, Національний медичний університет імені О.О. Богомольця, Київ, Україна

Adress for correspondence:

Neverovskyi Artem

E-mail: artemneverovskiy@gmail.com

Анотація: *одним із механізмів розвитку синдрому подразненого кишечника з діареєю (СПК-Д) є мальабсорбція жовчних кислот (МЖК). Новий перспективний терапевтичний підхід до МЖК – застосування пробіотичних бактерій, що продукують гідролазу солей жовчних солей (ГСЖК). Метою дослідження було порівняти вплив комбінації мультиштамового пробіотику і холестираміну з монотерапією холестираміном на модифікацію показників метаболізму жовчних кислот (ЖК) у пацієнтів із СПК-Д. Матеріали та методи. Дослідження було проведене за дизайном рандомізованого, відкритого, паралельного та включало 108 пацієнтів із СПК-Д, розділених на 2 групи: дослідна група (n=57), де призначалась комбінація пробіотику (на основі L. rhamnosus, L. plantarum, S. thermophilus, L. acidophilus, B. bifidum, B. longum, B. infantis, S. boulardii) та холестираміну та контрольна група (n=51), яка отримувала монотерапію холестираміном протягом 12 тижнів. У всіх пацієнтів оцінювали загальну відносну активність (ВА) кишкової бактеріальної ГСЖК, рівні сироваткових ЖК (сЖК) і фекальних ЖК (фЖК). Результати: абсолютні рівні загальних, первинних та вторинних сЖК та фЖК, відносні рівні первинних та вторинних фЖК значно відрізнялися через 12 тижнів у кожній групі порівняно з вихідними значеннями, p<0,05. У дослідній групі відносні рівні первинних та вторинних сЖК, ВА кишкової бактеріальної ГСЖК значно відрізнялися через 12 тижнів порівняно з вихідними значеннями, p<0,05. Усі показники метаболізму ЖК, окрім абсолютних рівнів вторинних сЖК, достовірно відрізнялися через 12 тижнів між контрольною та дослідною групами, p<0,05. Висновки: комбінація холестираміну та мультиштамового пробіотику призводила до більш виражених змін метаболізму ЖК та підвищення ВА кишкової бактеріальної ГСЖК порівняно з монотерапією холестираміном. Це може пояснити можливий механізм дії пробіотиків у пацієнтів із СПК-Д та ймовірною МЖК.*

Ключові слова: жовчні кислоти та солі, діарея, синдром подразненого кишечника, синдроми мальабсорбції, пробіотики.