URBAN, Wojciech, KORNELIA KARAMUS, RAFAŁ WOJCIECH REJMAK, JAN BIŁOGRAS, MARTYNA BOROWSKA - ŁYGAN, KONRAD STRUŻEK and JAKUB TOMASZEWSKI. A literature review on non-pharmacological treatments for irritable bowel syndrome (IBS). Journal of Education, Health and Sport. 2025;80:59395. eISSN 2391-8306. <u>https://doi.org/10.12775/JEHS.2025.80.59395</u> <u>https://apcz.umk.pl/JEHS/article/view/59395</u>

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).

Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu). © The Authors 2025;

This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland

Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike.

(http://creativecommons.org/licenses/by-nc-sa/4.0/) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.

The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 12.03.2025. Revised: 21.03.2025. Accepted:02.04.2025. Published: 28.04.2025.

A literature review on non-pharmacological treatments for irritable bowel syndrome (IBS)

Authors

Wojciech Urban

Wojewódzki Szpital Specjalistyczny im. Stefana Kardynała Wyszyńskiego SPZOZ w Lublinie <u>wojtekurban17@gmail.com</u> Orcid ID: <u>https://orcid.org/0009-0009-1565-0595</u>

Kornelia Karamus

Uniwersytecki Szpital Kliniczny nr 4 w Lublinie <u>kornelia.karamus@interia.pl</u> Orcid ID: https://orcid.org/0000-0001-7453-1427

Rafał Wojciech Rejmak

Uniwersytecki Szpital Kliniczny nr 4 w Lublinie <u>rrejmak@gmail.com</u> Orcid ID: https://orcid.org/0009-0002-9422-8550

Jan Bilogras

1 Wojskowy Szpital Kliniczny z Polikliniką SPZOZ w Lublinie janbilogras@gmail.com Orcid ID: <u>https://orcid.org/0009-0002-6038-9217</u>

Martyna Borowska-Łygan

Mazowiecki Szpital Specjalistyczny w Radomiu borowskamartyna123@gmail.com Orcid ID: https://orcid.org/0009-0001-9402-7444

Konrad Strużek

Wojewódzki Szpital Specjalistyczny im. Stefana Kardynała Wyszyńskiego SPZOZ w Lublinie <u>konradstruzek@gmail.com</u> Orcid ID: <u>https://orcid.org/0009-0000-3146-5132</u>

Jakub Tomaszewski

Uniwersytecki Szpital Kliniczny nr 4 w Lublinie jakub.t.tomaszewski@gmail.com Orcid ID: https://orcid.org/0009-0009-9384-4643

ABSTRACT

Introduction

Irritable bowel syndrome (IBS) is a prevalent condition involving the gut-brain interaction where individuals commonly experience recurring abdominal pain, changes in bowel movements, and frequently bloating.

Aim of the study

The aim of this study was to review literature studies on IBS and non-pharmacological methods for treating this condition.

Method

Data for the article were retrieved by using Pub Med setting the time descriptor to 2019-2024. **Conclusions**

Treating irritable bowel syndrome (IBS) continues to be challenging, as each patient needs a tailored approach. Once the correct IBS subtype is diagnosed, treatment should target the primary symptoms, such as bloating or diarrhea. Non-pharmacological treatment plays a initial, crucial and rapidly developing role in IBS therapy.

Keywords: Irritable bowel syndrome, non-pharmacological treatment, dietary, brain-gut axis, FODMAP

INTRODUCTION

Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disease of unknown origin. IBS is a common condition affecting from 10 to 20% of the general population, with a slightly higher incidence in women [1]. Its main symptoms are abdominal pain and alteration of bowel habits, both diarrhea and constipation. Based on the primary pattern of bowel habit changes, The Rome IV criteria categories IBS into four types : IBS with constipation (IBS-C), IBS with diarrhea

(IBS-D), IBS with a mixed pattern of constipation and diarrhea (IBS-M), and unclassified IBS [2]. This clinical review will focus on the pathophysiology and latest non-pharmacological ways to treat IBS.

PATHOGENESIS OF IBS

The development of IBS is influenced by both host and environmental factors, but the exact mechanisms are still not fully understood. Irritable bowel syndrome (IBS) is classified as braingut disorders, among other functional gastrointestinal conditions [3]. The brain-gut axis allows emotions to influence the gastrointestinal functions such as motility or barrier integrity. Conversely, gastrointestinal stimuli can also affect mental processes [4]. Researches have shown that IBS sufferers have increased secretion of dopamine and serotonin [5]. Regarding intestinal microbiota, their role in pathogenesis of IBS is uncertain, even though they are probably involved in barrier function alteration and mucosal inflammation [6,7]. Several studies tried to characterize the gut microbiota in IBS patients but the results remain unclear. Probably such factors as diet and geographic location have a big part in gut microbiota composition [6 - 9]. Environmental factors including stress, infections, diet and food intolerance play a big role in IBS pathophysiology. Importance of psychological impact in IBS is certain, as conditions such as depression and anxiety are often linked to IBS syndromes [8,10].

DIAGNOSIS

IBS is diagnosed by ruling out other potential organic causes. Considering that so many different factors may lead to this disorder, treatment of IBS is multidisciplinary, complex and tough including both pharmacological and non-pharmacological therapies. Person - centered approach to the patient is crucial [8].

BASIC DIETARY RECOMMENDATIONS

Most important non-pharmacological ways of treating IBS are physical exercises, stress reduction and appropriate diet. According to the publication of the British Gastroenterological Society [11] and updated guidelines from the American College of Gastroenterology dietary advise should be considered as first line treatment. The National Institute for Health and Care Excellence offers several dietary recommendations for IBS patients, including regular meal patterns, avoiding large meals, consuming nearly two liters of liquid daily, reducing alcohol and fizzy drinks and limiting fat, caffeine, alcohol, carbonated beverages and gas-producing foods [12].

FODMAP DIET

Diet low in FODMAP (which limits fermentable oligosaccharides, disaccharides, monosaccharides, polyols and LFD) is currently considered the most effective dietary approach for IBS patients [13]. FODMAP trigger IBS symptoms by influencing the gut-brain axis [14]. The American College of Gastroenterology recommends implanting diet low in FODMAP in three stages. First phase is a strict diet lasting no more than from four to six weeks. During the second stage we gradually reintroduce the FODMAP food. The last step is personalized approach based on the results of the previous phase [15].

The short-term effectiveness and safety of LFD, when compared to a Western or conventional diet, in alleviating symptoms in IBS patients are well-established [16]. Of course, healthy well balanced diet should form the foundation of nutrition.

FOOD INTOLERANCE

There are no conclusive results in terms of using gluten-free diet in IBS treatment. Concededly some benefits of gluten-free diet were observed in a few studies but it is probably because of low FODMAP components [17]. The role of lactose intolerance is also not certain. However some studies show that decreased amount of lactose intake can help with some of IBS syndromes [18].

FIBERS

When it comes to fiber intake, the type of fiber, daily consumption, and IBS subtype are crucial factors [19]. For example insoluble fibers (such as those found in wheat, corn) have no positive impact on treating IBS syndromes and can even worsen the symptoms and cause such side effects as constipation, bloating or pain [20-24]. Soluble fibers on the other hand are much more beneficial for IBS sufferers. The best in IBS therapy among all other soluble fibers are viscous low fermentable fibers like ispaghula and psyllium. They reduce such syndromes as bloating, abdominal distention and flatulence [23-26]. The American Academy of Nutrition and Dietetics suggests the daily intake of the psyllium of 25 g for women and 38 g for men. Such recommendations are advisable not only for IBS suffering patients but also for the healthy ones [27]. Bulking polymers are a good alternative for soluble fibers in IBS treatment. They improve stool consistency by absorbing water [28]. Linseeds are other type of food that have positive impact on IBS suffering patients. The daily intake of them are two tablespoons taken with fluids [29].

PROBIOTICS, FECAL MICROBIOTA TRANSPLANTATION

Probiotics are live nonpathogenic microorganisms (bacterias, yeasts) that administered can have beneficial effect on hosts health mainly over digestive system. To achieve the desired results of probiotics use, appropriate dose of them is required [30]. IBS patients have a different gut microbiota than healthy individuals, and this understanding helps guide treatment strategies [31]. Healthy people's microbiome is more varied then IBS suffering patients. Many different factors like genetics, smoking, diet, depression and past surgeries affects bacterial composition [32]. Scientific researches showed that IBS suffering individuals have low amount of some bacterias especially Lactobacillus sp. and Bifidobacterium sp [32]. Therefore, products containing these bacteria, as well as Saccharomyces species, significantly reduce IBS symptoms by modulating metabolism and reducing low-grade inflammation [33]. Changes in intestinal microbiota is promising new treatment option in IBS therapy. The fact that there are not many data about using certain species of bacteria, duration of the treatment or side effects of probiotics therapy is a big disadvantage [34,35]. Despite these limitations, probiotics are still regarded as a strong recommendation for managing IBS [36,19]. The newest guidelines on the use of probiotics recommend taking them for a period of 12 weeks and discounting if there is no improvement [11].

Fecal microbiota transplantation (FMT) is an emerging treatment for IBS sufferers. This method is currently approved only for resistance Clostridium difficile infection [42]. The effectiveness in the treatment of IBS is contradictory. In an RTC involving 90 patients with IBS-D or IBS-M, FMT administered to 55 patients via colonoscopy demonstrated significant clinical effectiveness compared to placebo [43]. However, another RTC, which included 52 IBS patients who received either active FMT or placebo capsules for 12 months, did not reveal any beneficial effect in favor of FMT [44]. Considering the results of above mentioned results, further research is necessary to explore the use of FMT in the treatment of IBS.

COMPLEMENTARY MEDICINE METHODS

Considering the fact that IBS syndromes are strictly related to psychosocial factors, alternative and complementary medicine has found a role in the treatment of this disorder. Hypnotherapy, relaxation and cognitive - behavior therapy could be helpful for IBS sufferers. However the use of this methods is restricted due to high costs, lengthy treatment duration and limited acceptance by both patients and clinicians [8, 37]. Traditional Chinese Medicine (TCM) treatments such as acupuncture and moxibustion are another approaches for managing IBS disease. Although they are still considered as complementary methods, recent studies have shown their significant potential. The mechanisms through which they may work include regulating the enteric nervous system, enhancing gastrointestinal motility, reducing visceral hypersensitivity, balancing intestinal microbiota, and modulating the immune system to help alleviate IBS symptoms [38]. Finally Chinese herbal treatments were shown to be effective in symptom control but with no statistical difference then pharmacological therapy based on antispasmodics. However this methods have a lot more side effects including skin rash and elevated level of liver enzymes then the conventional methods [39].

PHYSICAL ACTIVITY

Systematic physical activity is beneficial to overall body functioning and lowers chronic diseases such as heart disorders, diabetes or cancers. Beyond its physical benefits, regular exercises enhance mental condition improving cognitive functions like thinking and learning. It also reduces anxiety and depression. The World Health Organization recommends that adults participate in moderate - intensity aerobic exercise for at least 150-300 minutes per week, or at least at 75-150 minutes of vigorous aerobic exercise weekly, or combination of both of them. Additionally adults should perform muscle-strengthening exercises at least two times a week to achieve more health benefits [40]. The National Institute for Health and Care Excellence reminds the importance of educating IBS sufferers about physical activity for the prevention and treatment for IBS syndromes. IBS patients should receive specific advises about physical activity like yoga, walking, cycling or swimming seems to be the best option for IBS sufferers. Such recommendations are specifically important to patients who have led relatively sedentary lifestyle before [41].

SUMMARY

Irritable bowel syndrome (IBS) is a common, idiopathic disease that poses a challenge both in terms of diagnosis and treatment. Diagnosing IBS involves ruling out other organic conditions by thoroughly reviewing the medical history, conducting a physical examination, and performing specific diagnostic tests. The treatment of IBS is also challenging. Two treatment paths are possible: pharmacological and non-pharmacological. As for non-pharmacological one, appropriate, well balanced diet with regular meal patterns and an avoidance of large meals seems to be the most important. LFD diet has promising results in the latest studies in terms on alleviating IBS syndromes. However, long-term use of low FODMAP diet requires further research. Additional studies are also required to investigate the effect of gluten and lactose in IBS syndromes. The benefits of soluble fiber intake are well-established, especially ispaghula and psyllium. Probiotics, prebiotics and symbiotic are common utilized therapeutic option. Complementary medicine methods like hypnotherapy, cognitive behavioral therapy is increasingly used in IBS treatment. The use of Traditional Chinese Medicine (TCM) and fecal microbiota transplantation (FMT) treatments are promising but additional research is needed. The key role of regular physical activity in IBS therapy is undoubted.

DISCLOSURE

Conceptualization: Wojciech Urban and Konrad Strużek Methodology: Wojciech Urban, Jakub Tomaszewski and Kornelia Karamus Software: Jan Biłogras and Martyna Borowska-Łygan Check: Wojciech Urban and Konrad Strużek Formal analysis: Martyna Borowska-Łygan and Kornelia Karamus Investigation: Konrad Strużek Resources: Wojciech Urban and Rafał Wojciech Rejmak Data curation: Jan Biłogras and Jakub Tomaszewski Writing - rough preparation: Wojciech Urban and Konrad Strużek Writing - review and editing: Konrad Strużek and Jan Biłogras Visualization: Martyna Borowska-Łygan; Supervision: Wojciech Urban Project administration; Jan Biłogras and Rafał Rejmak Receiving funding, Not applicable

All authors have read and agreed with the published version of the manuscript.

Funding Statement:

This Research received no external funding.

Institutional Review Board Statement:

Not applicable

Informed Consent Statement:

Not applicable.

Data Availability Statement:

Not applicable.

Conflicts of Interests:

The authors declare no conflict of interest.

REFERENCES

- [1] Lovell RM, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. Clin Gastroenterol Hepatol. 2012; 10: 712-721.e4.
- [2] Mearin F, Lacy BE, Chang L, et al. Bowel disorders. Gastroenterology. 2016; S0016-5085(16)00222-5
- [3] Fagoonee, S, Pellicano, R. Does the microbiota play a pivotal role in the pathogenesis of irritable bowel syndrome? J Clin Med. 2019; 8: 1808.
- [4] Drossman DA. Functional gastrointestinal disorders: history, pathophysiology, clinical features and Rome IV. Gastroenterology. 2016; 150: 1262-1279.
- [5] Chojnacki C, Błońska A, Kaczka A, et al. Evaluation of serotonin and dopamine secretion and metabolism in patients with irritable bowel syndrome. Pol Arch Intern Med. 2018; 128: 711-713.
- [6] Mei L, Zhou J, Su Y, et al. Gut microbiota composition and functional prediction in diarrheapredominant irritable bowel syndrome. BMC Gastroenterol. 2021; 21: 105.
- [7] Polster A, Öhman L, Tap J, et al. A novel stepwise integrative analysis pipeline reveals distinct microbiota-host interactions and link to symptoms in irritable bowel syndrome. Sci Rep. 2021; 11: 5521
- [8] Adriani A, Ribaldone DG, Astegiano M, et al. Irritable bowel syndrome: the clinical approach. Panminerva Med. 2018; 60: 213-222.
- [9] Tap J, Störsrud S, Le Nevé B, et al. Diet and gut microbiome interactions of relevance for symptoms in irritable bowel syndrome
- [10] Ford AC, Sperber AD, Corsetti M, Camilleri M. Irritable bowel syndrome. Lancet. 2020; 396: 1675-1688.
- [11] Vasant DH, Paine PA, Black CJ, et al. British Society of Gastroenterology guidelines on the management of irritable bowel syndrome. Gut. 2021; 70: 1214-1240.
- [12] Irritable bowel syndrome in adults: diagnosis and management. London, United Kingdom: National Institute for Health and Care Excellence; 2017.
- [13] Black CJ, Staudacher HM, Ford AC. Efficacy of a low FODMAP diet in irritable bowel syndrome: systematic review and network meta-analysis. Gut. 2022; 71:1117-1126
- [14] Wu J, Masuy I, Biesiekierski JR, Fitzke HE, Parikh C, Schofield L, Shaikh H, Bhagwanani A, Aziz Q, Taylor SA, Tack J, Van Oudenhove L. Gut-brain axis dysfunction underlies FODMAPinduced symptom generation in irritable bowel syndrome. Aliment Pharmacol Ther. 2022;55:670-682.
- [15] Chey WD, Hashash JG, Manning L, Chang L. AGA Clinical Practice Update on the Role of Diet in Irritable Bowel Syndrome: Expert Review. Gastroenterology. 2022;162:1737-1745.e5.

- [16] Schumann D, Klose P, Lauche R, Dobos G, Langhorst J, Cramer H. Low fermentable, oligo-, di-, mono-saccharides and polyol diet in the treatment of irritable bowel syndrome: A systematic review and meta-analysis. Nutrition. 2018;45:24-31.
- [17] Surdea-Blaga T, Cozma-Petrut A, Dumitrașcu DL. Dietary interventions and irritable bowel syndrome what really works?. Curr Opin Gastroenterol. 2021;37(2):152–157
- [18] Adriani A, Saracco GM, Pellicano R. Irritable bowel syndrome and lactose intolerance: a challenging overlap. Minerva Gastroenterol. 2021; 67: 67-68.
- [19] Dumitrascu DL, Baban A, Bancila I, Barboi O, et al. Romanian Guidelines for Nonpharmacological Therapy of IBS. J Gastrointestin Liver Dis. 2021;30(2):291–306. doi: 10.15403/jgld-3581.
- [20] El-Salhy M, Hatlebakk JG, Hausken T. Diet in Irritable Bowel Syndrome (IBS): Interaction with Gut Microbiota and Gut Hormones. Nutrients. 2019;11(8):1824. doi: 10.3390/nu11081824. [21] Ford AC, Lacy BE, Talley NJ. Irritable Bowel Syndrome. N Engl J Med. 2017;376:2566–2578. doi: 10.1056/NEJMra1607547
- [22] Nagarajan N, Morden A, Bischof D, King EA, et al. The role of fiber supplementation in the treatment of irritable bowel syndrome: a systematic review and meta-analysis. Eur J Gastroenterol Hepatol. 2015;27:1002–1010. doi: 10.1097/MEG.00000000000425
- [23] Moayyedi P, Quigley EM, Lacy BE, Lembo AJ, et al. The effect of fiber supplementation on irritable bowel syndrome: a systematic review and meta-analysis. Am J Gastroenterol. 2014;109(9):1367–1374. doi: 10.1038/ajg.2014.195.
- [24] McRorie JW. Evidence-Based Approach to Fiber Supplements and Clinically Meaningful Health Benefits, Part 1: What to Look for and How to Recommend an Effective Fiber Therapy. Nutr Today. 2015;50:82–89. doi: 10.1097/NT.00000000000082
- [25] Moayyedi P, Andrews CN, MacQueen G, Korownyk C, et al. Canadian Association of Gastroenterology Clinical Practice Guideline for the Management of Irritable Bowel Syndrome (IBS). J Can Assoc Gastroenterol. 2019 Apr;2(1):6–29. doi: 10.1093/jcag/gwy071
- [26] Bijkerk CJ, de Wit NJ, Muris JW, Whorwell PJ, et al. Soluble or insoluble fibre in irritable bowel syndrome in primary care?Randomised placebo controlled trial. BMJ. 2009;339:b3154. doi: 10.1136/bmj.b3154.
- [27] Muir J. An Overview of Fiber and Fiber Supplements for Irritable Bowel Syndrome. Gastroenterol Hepatol (N Y) 2019;15:387–389.
- [28] Toskes PP, Connery KL, Ritchey TW. Calcium polycarbophil compared with placebo in irritable bowel syndrome. Aliment Pharmacol Ther. 1993;7(1):87–92. doi: 10.1111/ j.1365-2036.1993.tb00074.x.
- [29] McKenzie YA, Bowyer RK, Leach H, Gulia P, et al. British Dietetic Association systematic review and evidence-based practice guidelines for the dietary management of irritable bowel syndrome in adults (2016 update). J Hum Nutr Diet. 2016 Oct;29(5):549– 75. doi: 10.1111/jhn.12385.
- [30] Hill C, Guarner F, Reid G, Gibson GR, et al. Expert consensus document. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. Nat Rev Gastroenterol Hepatol. 2014 Aug;11(8):506–14. doi: 10.1038/nrgastro.2014.66.

- [31] Distrutti E, Monaldi L, Ricci P, Fiorucci S. Gut microbiota role in irritable bowel syndrome: New therapeutic strategies. World J Gastroenterol. 2016;22(7):2219–2241. doi: 10.3748/ wjg.v22.i7.2219.
- [32] Thursby E, Juge N. Introduction to the human gut microbiota. Biochem J. 2017 May 16;474(11):1823–1836. doi: 10.1042/BCJ20160510.
- [33] Rodiño-Janeiro BK, Vicario M, Alonso-Cotoner C, Pascua-García R, Santos J. A Review of Microbiota and Irritable Bowel Syndrome: Future in Therapies. Adv Ther. 2018;35(3):289–310. doi: 10.1007/s12325-018-0673-5
- [34] McKenzie YA, Thompson J, Gulia P, Lomer MC, (IBS Dietetic Guideline Review Group on behalf of Gastroenterology Specialist Group of the British Dietetic Association) British Dietetic Association systematic review of systematic reviews and evidence-based practice guidelines for the use of probiotics in the management of irritable bowel syndrome in adults (2016 update). J Hum Nutr Diet. 2016;29(5):576–592. doi: 10.1111/jhn.12386
- [35] Ford AC, Harris LA, Lacy BE, Quigley EMM, Moayyedi P. Systematic review with metaanalysis: the efficacy of prebiotics, probiotics, synbiotics and antibiotics in irritable bowel syndrome. Aliment Pharmacol Ther. 2018 Nov;48(10):1044–1060. doi: 10.1111/apt.15001.
- [36] Fukudo S, Okumura T, Inamori M, Okuyama Y, et al. Evidence-based clinical practice guidelines for irritable bowel syndrome 2020. J Gastroenterol. 2021;56(3):193–217. doi: 10.1007/s00535-020-01746-z
- [37] Saha L. Irritable bowel syndrome: pathogenesis, diagnosis, treatment, and evidence-based medicine. World J Gastroenterol. 2014; 20: 6759-6773.
- [38] Chen GR, Xie XF, Peng C. Treatment of Irritable Bowel Syndrome by Chinese Medicine: A Review. Chin J Integr Med. 2023;29:377-384
- [39] Chen M, Qin D, Huang SL, et al. Chinese herbal medicine versus antispasmodics in the treatment of irritable bowel syndrome: a network meta-analysis. Neurogastroenterol Motil. 2021 Mar 4.
- [40] WHO Guideline. Physical Activity. Updated 5 October 2022.
- [41] NICE. Irritable Bowel Syndrome in Adults: Diagnosis and Management; NICE Clinical Guidelines, No. 61; National Institute for Health and Care Excellence (NICE): London, UK, 2017.
- [42] Jiang ZD, Ajami NJ, Petrosino JF, et al. Randomised clinical trial: faecal microbiota transplantation for recurrent Clostridium difficile infection – fresh, or frozen, or lyophilised microbiota from a small pool of healthy donors delivered by colonoscopy. Aliment Pharmacol Ther. 2017; 45: 899-908.
- [43] Johnsen PH, Hilpüsch F, Cavanagh JP, et al. Faecal microbiota transplantation versus placebo for moderate-to-severe irritable bowel syndrome: a double-blind, randomised, placebo-controlled, parallel-group, single-centre trial. Lancet Gastroenterol Hepatol. 2018; 3: 17-24.
- [44] Halkjær SI, Christensen AH, Lo BZS, et al. Faecal microbiota transplantation alters gut microbiota in patients with irritable bowel syndrome: results from a randomised, double-blind placebo-controlled study. Gut. 2018; 67: 2107-2115.