International Journal of Current Science Research and Review
ISSN: 2581-8341
Volume 07 Issue 06 June 2024
DOI: 10.47191/ijcsrr/V7-i6-29, Impact Factor: 7.943
IJCSRR @ 2024
www.ijcsrr.org

Recent Advances in the Treatment of Irritable Bowel Syndrome: Addressing Diarrhea, Constipation, and Abdominal Pain

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ABSTRACT: Irritable bowel syndrome (IBS) is a prevalent gastrointestinal disorder characterized by abdominal pain, bloating, and changes in bowel habits. This paper aim was to provide an overview of recent advancements in the treatment of IBS, focusing on the management of its main symptoms: diarrhea, constipation, and abdominal pain.
For individuals with IBS-D, various therapeutic options are available, including rifaximin, peripheral opioid agonists, mixed opioid agonists/antagonists, bile acid sequestrants, and serotonin 5-HT3 receptor antagonists. Rifaximin, a nonabsorbable antibiotic, has demonstrated significant effectiveness in reducing IBS symptoms, such as bloating and loose stools, with good tolerability and safety. Also the repeated use of rifaximin for managing recurrent IBS symptoms. In IBS-C patients, bulking agents, osmotic laxatives, and prokinetic agents like lubiprostone have shown efficacy in improving constipation and overall symptoms. Linaclotide, a drug that increases intestinal chloride secretion, has demonstrated significant improvement in bowel movements and abdominal pain in IBS-C patients. However, it may cause diarrhea in some individuals. IBS-M, characterized by alternating constipation and diarrhea, poses a challenge in terms of specific drug treatments. A comprehensive assessment of potential underlying causes and careful history taking is crucial for effective management. Abdominal pain is a common symptom in IBS, regardless of subtype. Antispasmodic drugs, peppermint oil, and trimebutine have shown effectiveness in reducing pain and improving symptoms. Antidepressants, such as tricyclic antidepressants and selective serotonin reuptake inhibitors, may offer relief by modulating pain pathways and influencing gastrointestinal motility. Benzodiazepines, particularly dextofisopam, have shown potential in improving stool consistency but require further evaluation.
In conclusion, recent advancements in the treatment of IBS have provided a range of therapeutic options targeting its main symptoms. However, further research is needed to develop tailored treatments for specific IBS subtypes and to explore the efficacy of potential alternatives, including benzodiazepines. Improved management of IBS symptoms can significantly enhance the quality of life for affected individuals.

KEYWORDS: Constipation, Diarrhea, Irritable bowel syndrome, Treatment

INTRODUCTION

Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder characterized by abdominal pain, bloating, and changes in bowel habits. It affects a significant portion of the population worldwide and can have a profound impact on the quality of life of those affected. Over the years, there have been significant advances in the pharmacological treatment of IBS, aiming to alleviate symptoms and improve patients' overall well-being (Adriani et al., 2018; Bonetto et al., 2021).

bowel syndrome (IBS) is a highly prevalent functional disorder that reduces patients' quality of life. It is characterized by chronic abdominal pain/discomfort associated with disordered defecation (constipation, diarrhea, or mixed/alternating symptoms). Symptoms should persist for at least 6 months, with abdominal pain/discomfort occurring at least 3 days per month for 3 months. Additional criteria include improvement with defecation, onset associated with changes in stool frequency or form, and the absence of any other underlying disease that could explain the symptoms. Bloating and abdominal distention are common in IBS patients, indicating sensitivity to normal levels of intestinal gas (Longstreth et al., 2006; Longstreth et al., 2003).

Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal disorder, affecting 9% to 16% of the general population, with a slightly higher incidence in women. It is characterized by abdominal pain associated with changes in stool frequency or form, in the absence of organic disease. IBS is divided into four subgroups based on predominant bowel habits: IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), IBS with a mixed pattern (IBS-M), and unclassified IBS. These subgroups are determined by stool appearance on abnormal bowel movement days, assessed using the Bristol Stool Form scale (Adriani et al., 2018; Lovell & Ford, 2012).

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The objective of this paper was to explore and discuss the recent advances in the treatment of irritable bowel syndrome (IBS) according to the three main symptoms of IBS: diarrhea, constipation, and abdominal pain.

Irritable bowel syndrome with diarrhea

A range of therapeutic options are available for the treatment of irritable bowel syndrome with diarrhea (IBS-D), including antibiotics such as rifaximin, peripheral opioid agonists, mixed opioid agonists/antagonists, bile acid sequestrants, and antagonists that target serotonin 5-HT3 receptors.

The nonabsorbable rifamycin, Rifaximin, has exhibited substantial effectiveness in reducing overall symptoms of irritable bowel syndrome (IBS), such as bloating and loose or watery stools, following a two-week treatment regimen. Importantly, Rifaximin has demonstrated favorable tolerability, with adverse events comparable to those observed with placebo. Furthermore, studies have provided evidence supporting the safety and efficacy of repeated treatments with Rifaximin for managing recurrent IBS symptoms (Frissora & Schiller, 2023; Lembo et al., 2016; Pimentel et al., 2011).

Irritable bowel syndrome with constipation

Bulking agents and osmotic laxatives are commonly employed as first-line therapies for irritable bowel syndrome with constipation (IBS-C) (Saha, 2014). Supplementation of soluble fiber with psyllium and ispaghula has demonstrated improvement in overall symptoms for IBS-C patients, while insoluble fiber like wheat bran has not shown efficacy in symptom relief and, in fact, may exacerbate flatulence and abdominal pain (Adriani et al., 2018). Polyethylene glycol, an osmotic laxative, has exhibited superior efficacy for constipation improvement compared to placebo, with good tolerability, although it did not demonstrate the same effect for relieving abdominal pain (Chapman, Stanghellini, Geraint, & Halphen, 2013). Prokinetic agents acting as agonists of serotonin receptors 5-HT4 enhance gastrointestinal motility. However, the use of cisapride and tegaserod is limited due to the risk of adverse cardiac events. Prucalopride, a highly selective 5-HT4 receptor agonist, has not been evaluated in IBS patients but has shown effectiveness in chronic idiopathic constipation, serving as a viable therapeutic option when laxatives fail (Camilleri, Kerstens, Rykx, & Vandeplassche, 2008; Tack et al., 2012). Lubiprostone, a prostaglandin derivative that activates type 2 chloride channels, stimulates intestinal fluid secretion (Ford, Sperber, Corsetti, & Camilleri, 2020), and has demonstrated significant efficacy in improving constipation and global IBS symptoms, with a modest effect on abdominal pain and a favorable safety profile (Drossman et al., 2009). Linaclotide, which increases intestinal chloride secretion through the cystic fibrosis transmembrane regulator, acting on guanylate cyclase-C, has shown significant improvement in bowel movements and abdominal pain in phase 3 trials, albeit with diarrhea reported by nearly 20% of patients (Rao et al., 2012). Additionally, a recent systematic review and network meta-analysis revealed that linaclotide was the most effective licensed drug for relieving abdominal bloating, a troublesome symptom frequently experienced by IBS-C patients (Nelson et al., 2021).

Irritable bowel syndrome with a mixed pattern of constipation and diarrhea

Irritable bowel syndrome (IBS) with a mixed pattern of constipation and diarrhea poses a diagnostic and therapeutic challenge, as there is a lack of specific drug studies targeting this particular IBS subtype. Additionally, the mixed bowel pattern may arise from an underlying disease or as a consequence of medical interventions. Therefore, a comprehensive history-taking process, including an assessment of prescribed medications, over-the-counter drugs, and supplements, is imperative to identify potential causes of alternating bowel habits. Most individuals with IBS-M frequently experience phases characterized by a decreased frequency of bowel movements and the presence of small, hard stools, followed by periods of multiple stools of varying consistency. In certain instances, this can be attributed to the gradual accumulation of stool during constipation phases, eventually leading to subsequent bowel purging (Chey, Kurlander, & Eswaran, 2015).

Pharmacotherapy for abdominal pain

Abdominal pain frequently accompanies irritable bowel syndrome with diarrhea (IBS-D), constipation (IBS-C), or a mixed pattern (IBS-M), and it is associated with visceral hypersensitivity, abnormal contractility of the gastrointestinal muscular layer, and gut distension.

Antispasmodic drugs exert their effect by reducing gastrointestinal contractility through either an anticholinergic mechanism, as seen with dicyclomine, or calcium channel blocking, as observed with otilonium and mebeverine (Adriani et al., 2018). The efficacy of these drugs in improving symptoms of irritable bowel syndrome (IBS), either as monotherapy or in combination with simethicone,

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has been assessed in several trials. Although the methodologies of these studies vary, a meta-analysis has demonstrated that antispasmodic agents are superior to placebo in the treatment of IBS, with good tolerability. Peppermint oil, functioning as an antispasmodic through calcium channel blocking, has also shown superiority over placebo in relieving symptoms of IBS and abdominal pain. Trimebutine, a peripheral agonist of μ, k, and δ opioid receptors, modulates the release of gastrointestinal peptides such as motilin, vasoactive intestinal peptide, gastrin, and glucagon. It accelerates gastric emptying, modulates gut contractility, and has been found to reduce reflexes induced by gut distension in animal models. In patients with IBS and other functional gastrointestinal disorders, trimebutine has been demonstrated to be more effective than placebo in the treatment of both acute and chronic abdominal pain (Delvaux & Wingate, 1997; Martínez-Vázquez et al., 2012).

In cases of chronic abdominal pain, antidepressants can offer a favorable response due to their ability to enhance endogenous endorphin release, promote the activation of descending inhibitory pain pathways through norepinephrine antagonism, and regulate the neuromodulating effect of serotonin. Additionally, central-acting agents have demonstrated therapeutic effects that are unrelated to mood improvement, as they can influence gastrointestinal motility. The choice of the most suitable antidepressant should be guided by the predominant pattern of irritable bowel syndrome (IBS): tricyclic antidepressants are typically preferred for IBS cases with diarrhea, while selective serotonin reuptake inhibitors may be beneficial for constipation-predominant IBS due to their prokinetic effect (Gorard, Libby, & Farthing, 1995; Saha, 2014). However, it is important to note that, similar to psychological treatments, the use of antidepressants may be limited by social stigma and poor patient acceptance.

Benzodiazepines, due to their modulating effect on the autonomic nervous system, dorsal vagal nuclei, and enteric nervous system, have the potential to be involved in the treatment of irritable bowel syndrome (IBS), particularly in the management of visceral pain. However, limited studies have analyzed their efficacy in this context. In patients with IBS-D or IBS-M, dextofisopam has been shown to improve stool consistency in both men and women. However, while stool frequency was reduced only in women, no significant effects on bloating, partial defecation, or scores on the Hospital Anxiety and Depression Scale were observed (Leventer et al., 2008; Salari & Abdollahi, 2011). As a result, further evaluation is necessary to assess the potential clinical benefit of both dextofisopam and other benzodiazepines in patients with IBS.

CONCLUSION

Irritable bowel syndrome (IBS) is a common disorder that significantly affects public health and patients' quality of life. Diagnosis involves excluding organic disease through medical history, physical examination, and diagnostic tests. Treatment is challenging and requires a personalized approach focused on the main symptom. For IBS-D, pharmacological options include antibiotics, peripheral opioid agonists, bile acid sequestrants, mixed opioid agonists/antagonists, and serotonin 5-HT3 receptor antagonists. In constipation-predominant IBS, first-line therapy includes bulking agents and osmotic laxatives, with additional options like prokinetics, lubiprostone, and linaclotide. Managing acute or chronic pain is also challenging, with antispasmodics and trimebutine effective for acute pain, while central-acting agents like antidepressants may be preferred for chronic pain. Dietary modifications, increased physical activity, and FODMAP restriction are encouraged.

Funding: No funding was received.

REFERENCES

1. Adriani, A., Ribaldone, D. G., Astegiano, M., Durazzo, M., Saracco, G. M., & Pellicano, R. (2018). Irritable bowel syndrome: the clinical approach. *Panminerva Medica*, *60*(4), 213-222.
2. Bonetto, S., Fagoonee, S., Battaglia, E., Grassini, M., Saracco, G. M., & Pellicano, R. (2021). Recent advances in the treatment of irritable bowel syndrome. *Pol Arch Intern Med*, *131*(7-8), 709-715. doi:10.20452/pamw.16067
3. Camilleri, M., Kerstens, R., Rykx, A., & Vandeplassche, L. (2008). A placebo-controlled trial of prucalopride for severe chronic constipation. *New england journal of medicine*, *358*(22), 2344-2354.
4. Chapman, R., Stanghellini, V., Geraint, M., & Halphen, M. (2013). Randomized clinical trial: macrogol/PEG 3350 plus electrolytes for treatment of patients with constipation associated with irritable bowel syndrome. *Official journal of the American College of Gastroenterology| ACG*, *108*(9), 1508-1515.
5. Chey, W. D., Kurlander, J., & Eswaran, S. (2015). Irritable bowel syndrome: a clinical review. *Jama*, *313*(9), 949-958.

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6. Delvaux, M., & Wingate, D. (1997). Trimebutine: mechanism of action, effects on gastrointestinal function and clinical results. *Journal of international medical research, 25*(5), 225-246.
7. Drossman, D., Chey, W. D., Johanson, J., Fass, R., Scott, C., Panas, R., & Ueno, R. (2009). Clinical trial: lubiprostone in patients with constipation-associated irritable bowel syndrome–results of two randomized, placebo-controlled studies. *Alimentary pharmacology & therapeutics, 29*(3), 329-341.
8. Ford, A. C., Sperber, A. D., Corsetti, M., & Camilleri, M. (2020). Functional gastrointestinal disorders 2 irritable bowel syndrome. *Lancet, 396*(10263), 1675-1688.
9. Frissora, C. L., & Schiller, L. R. (2023). Getting the BS out of Irritable Bowel Syndrome with Diarrhea (IBS-D): Let's Make a Diagnosis. *Current Gastroenterology Reports*, 1-10.
10. Gorard, D., Libby, G., & Farthing, M. (1995). Effect of a tricyclic antidepressant on small intestinal motility in health and diarrhea-predominant irritable bowel syndrome. *Digestive diseases and sciences, 40*, 86-95.
11. Lembo, A., Pimentel, M., Rao, S. S., Schoenfeld, P., Cash, B., Weinstock, L. B., . . . Forbes, W. P. (2016). Repeat treatment with rifaximin is safe and effective in patients with diarrhea-predominant irritable bowel syndrome. *Gastroenterology, 151*(6), 1113-1121.
12. Leventer, S., Raudibaugh, K., Frissora, C., Kassem, N., Keogh, J., Phillips, J., & Mangel, A. (2008). Clinical trial: dextofisopam in the treatment of patients with diarrhoea-predominant or alternating irritable bowel syndrome. *Alimentary pharmacology & therapeutics, 27*(2), 197-206.
13. Longstreth, G. F., Thompson, W. G., Chey, W. D., Houghton, L. A., Mearin, F., & Spiller, R. C. (2006). Functional bowel disorders. *Gastroenterology, 130*(5), 1480-1491.
14. Longstreth, G. F., Wilson, A., Knight, K., Wong, J., Chiou, C.-F., Barghout, V., . . . Ofman, J. J. (2003). Irritable bowel syndrome, health care use, and costs: a US managed care perspective. *The American journal of gastroenterology, 98*(3), 600-607.
15. Lovell, R. M., & Ford, A. C. (2012). Global prevalence of and risk factors for irritable bowel syndrome: a meta-analysis. *Clinical gastroenterology and hepatology, 10*(7), 712-721. e714.
16. Martínez-Vázquez, M., Vázquez-Elizondo, G., González-González, J., Gutiérrez-Udave, R., Maldonado-Garza, H., & Bosques-Padilla, F. (2012). Effect of antispasmodic agents, alone or in combination, in the treatment of Irritable Bowel Syndrome: systematic review and meta-analysis. *Revista de Gastroenterologia de Mexico, 77*(2), 82-90.
17. Nelson, A. D., Black, C. J., Houghton, L. A., Lugo-Fagundo, N. S., Lacy, B. E., & Ford, A. C. (2021). Systematic review and network meta-analysis: efficacy of licensed drugs for abdominal bloating in irritable bowel syndrome with constipation. *Alimentary pharmacology & therapeutics, 54*(2), 98-108.
18. Pimentel, M., Lembo, A., Chey, W. D., Zakko, S., Ringel, Y., Yu, J., . . . Forbes, W. P. (2011). Rifaximin therapy for patients with irritable bowel syndrome without constipation. *New england journal of medicine, 364*(1), 22-32.
19. Rao, S., Lembo, A. J., Shiff, S. J., Lavins, B. J., Currie, M. G., Jia, X. D., . . . Eng, P. (2012). A 12-week, randomized, controlled trial with a 4-week randomized withdrawal period to evaluate the efficacy and safety of linaclotide in irritable bowel syndrome with constipation. *The American journal of gastroenterology, 107*(11), 1714.
20. Saha, L. (2014). Irritable bowel syndrome: pathogenesis, diagnosis, treatment, and evidence-based medicine. *World Journal of Gastroenterology: WJG, 20*(22), 6759.
21. Salari, P., & Abdollahi, M. (2011). Systematic review of modulators of benzodiazepine receptors in irritable bowel syndrome: is there hope? *World Journal of Gastroenterology: WJG, 17*(38), 4251.
22. Tack, J., Camilleri, M., Chang, L., Chey, W. D., Galligan, J., Lacy, B., . . . De Maeyer, J. (2012). Systematic review: cardiovascular safety profile of 5-HT 4 agonists developed for gastrointestinal disorders. *Alimentary pharmacology & therapeutics, 35*(7), 745-767.