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REVIEW ARTICLE

Treatment of irritable bowel syndrome with predominance of constipation

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Abstract

Irritable bowel syndrome with constipation (IBS-C) is a multifactorial and highly prevalent disorder of gut–brain interaction. Its management remains challenging due to symptom variability, overlapping pathophysiological mechanisms, and heterogeneous treatment responses. This review aims to integrate and critically examine current evidence on therapeutic strategies for IBS -C, encompassing clinical trials, meta-analyses, and expert consensus guidelines on dietary, pharmacological, microbiota-targeted, and behavioral interventions. Notable findings highlight that soluble fiber, low-FODMAP diets, and individualized dietary approaches yield meaningful symptom improvement. Pharmacologic therapies, including osmotic laxatives and guanylate cyclase-C agonists (linaclotide, lubiprostone, tenapanor), have shown efficacy in enhancing bowel function and reducing abdominal pain ($p < 0.05$). Prucalopride, selected probiotics, and non-absorbable antibiotics appear beneficial in specific subpopulations. In refractory patients, biofeedback, pelvic floor retraining, and cognitive behavioral therapy provide added value. We emphasize that IBS-C treatment should be individualized and pathophysiology-driven, within a multidisciplinary framework. This review offers a clinically grounded synthesis to support therapeutic decision-making in a complex and heterogeneous patient population.

Keywords: Irritable bowel syndrome. Constipation. Dietary fiber. FODMAP diet. Guanylate cyclase-C agonists. Gut microbiota.

Tratamiento del síndrome de intestino irritable con predominio de estreñimiento

Resumen

El síndrome de intestino irritable con predominio de estreñimiento (SII-E) es una enfermedad multifactorial y uno de los trastornos de la interacción intestino-cerebro más frecuentes en la práctica clínica. Su abordaje representa un reto terapéutico significativo, debido a la variabilidad de los síntomas y la respuesta heterogénea al tratamiento. El propósito de esta revisión es integrar y analizar críticamente la evidencia disponible sobre las estrategias actuales para el manejo del SII-E. Se incluyeron estudios clínicos, metaanálisis y consensos de expertos que evalúan la eficacia de intervenciones dietéticas, agentes farmacológicos, terapias dirigidas a la microbiota intestinal y abordajes no farmacológicos. Entre los principales hallazgos se destaca que la fibra soluble, las dietas bajas en FODMAP y las estrategias de personalización dietética muestran beneficios sintomáticos significativos. Farmacológicamente, los laxantes osmóticos y secretagogos, como linaclotida, lubiprostona y tenapanor, han demostrado mejorar el tránsito intestinal y reducir el dolor abdominal ($p < 0.05$). El uso de prucaloprida, así como de probióticos y antibióticos no absorbibles, resulta prometedor en casos seleccionados. En pacientes refractarios,

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técnicas como la retroalimentación biológica *(biofeedback),* la reeducación del piso pélvico y la terapia cognitivo-conductual han mostrado utilidad clínica. Concluimos que el tratamiento del SII-E debe ser individualizado, secuencial y multidisciplinario, considerando la fisiopatología predominante en cada paciente. La presente revisión aporta un enfoque clínico actualizado y sintetizado para el abordaje integral del SII-E, con potencial para optimizar la toma de decisiones terapéuticas.

Palabras clave: Síndrome de intestino irritable. Estreñimiento. Fibra alimentaria. Dieta FODMAP. Agonistas de la guanilato ciclasa C. Microbiota intestinal.

Introduction

Irritable bowel syndrome with constipation predominance (IBS-C) is one of the most common forms of IBS and the most frequently diagnosed disorder of the brain-gut interaction in clinical practice[1]. It is characterized by the presence of abdominal pain or discomfort accompanied by alterations in bowel habits, especially constipation, and other symptoms such as bloating, a sensation of abdominal swelling, incomplete evacuation, urgency, straining, and tenesmus. The multifactorial nature of this syndrome has posed a significant challenge for the development of effective treatments[2]. The management of IBS-C is primarily focused on relieving symptoms and improving patients' quality of life through a comprehensive approach that may include lifestyle changes, diet, psychotherapy, and individualized treatment.

Dietary approach as a complement to pharmacological treatment

Role of soluble and insoluble fiber in constipation management

Fiber regulates colonic transit in IBS through several mechanisms[3,4]. Bulk-forming agents and fiber supplements (soluble: psyllium, ispaghula; insoluble: bran, corn) are useful across all IBS subtypes, especially IBS-C, as they increase stool bulk and consistency due to their osmotic effect. However, their efficacy remains controversial because of adverse effects such as bloating and flatulence that may occur during therapy.

Systematic reviews and meta-analyses indicate that soluble fiber can relieve IBS symptoms and improve stool frequency and consistency, though results are variable. In one study, soluble fiber showed a relative risk (RR) of persistent symptoms of 0.83 (95% confidence interval [CI], 0.73-0.94), whereas bran did not show significant benefits (RR, 0.90; 95% CI, 0.79-1.03)[5].

A meta-analysis that excluded low-quality studies found no differences between bulk-forming agents and placebo, highlighting that bran, being highly fermentable, may increase abdominal pain and bloating[6]. According to the Mexican Consensus on the management of IBS, soluble fiber has a strong recommendation (A2), while bran has a weak recommendation against (B2), according to the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) system[7]. Low-fermentation soluble fibers, due to their viscosity, may serve as a first-line option in IBS-C management by reducing stool hardness[8].

Personalized diets according to individual tolerance and clinical response

In contemporary IBS-C management, dietary changes represent a first-line therapeutic tool. Traditional recommendations (reducing alcohol, caffeine, fats, and spicy foods, and increasing fluids and fiber), although low-risk, yield variable and often unsustained results[9].

In recent years, dietary approaches have evolved toward more structured, mechanism-based interventions. Among these, the low-FODMAP (Fermentable Oligo-, Di-, Monosaccharides and Polyols) diet has demonstrated superior efficacy in reducing GI symptoms—particularly bloating, flatulence, and abdominal pain—attributable to colonic fermentation and the osmolarity of these compounds in the intestinal lumen[10-12]. This strategy is implemented in 3 sequential phases requiring specialized supervision and a clear educational framework for the patient:

- Restriction: temporary elimination (2-6 weeks) of high-FODMAP foods to evaluate their direct relationship with symptom expression. Clinical response during this phase identifies responders, who then proceed to the next stage[13].
- Reintroduction: through progressive protocols, a specific FODMAP is reintroduced each week in increasing doses, monitoring the presence or absence of symptoms. This approach allows characterization of each patient's individual fermentative sensitivity profile.
- Personalization: based on these data, a dietary pattern is structured that maximizes food variety while minimizing symptom recurrence, avoiding unnecessary restrictions that could affect quality of life or nutritional and microbial integrity[14,15].

Despite its clinical benefits, the low-FODMAP diet has been shown to induce changes in gut microbiota, such as a decrease in bifidobacteria and an increase in certain species like *Clostridium* spp., raising questions about its long-term safety and immunomodulatory impact[16,17].

Wheat has also been identified as a relevant trigger in up to 49% of IBS patients, justifying the exploration of gluten-free diets as an alternative intervention[18,19]. Although preliminary randomized studies show sustained symptomatic improvements in some subgroups, better phenotypic characterization and predictive biomarkers of response are still required[20,21].

Other exclusion strategies, such as eliminating milk, eggs, yeast, and chocolate, have also been explored, showing positive results in patients with documented food sensitivities through specific testing, though their generalized use remains debated[5].

Given their complexity and potential metabolic and psychosocial impact, these interventions should be conducted by professionals trained in clinical nutrition specialized in functional GI disorders. The decision to initiate or discontinue such approaches should be based on objective symptomatic response within a reasonable period (ideally 4-6 weeks), under a structured, patient-centered follow-up scheme[22].

Hydration and physical activity as adjuvants in treatment

Adequate hydration softens stools and promotes intestinal transit, enhancing the effect of fiber. Insufficient fluid intake can harden stools and nullify fiber's benefits[23]. It is recommended to consume between 1.5 and 2.5 liters of water daily, considering individual factors such as age, sex, climate, and physical activity[24].

Regular exercise also improves GI function and reduces stress, relieving IBS-C symptoms. Studies have shown that physical activity (walking, cycling, aerobics, etc.) for 20-60 minutes, 3 to 5 times per week, improves IBS-C symptoms and psychological well-being, increasing quality of life[1].

Laxatives

Osmotic laxatives (polyethylene glycol, lactulose): mechanisms of action and long-term safety

Osmotic laxatives, such as polyethylene glycol and lactulose, act mainly by retaining water in the intestine, softening stools and facilitating elimination.

Polyethylene glycol (PEG) 3350 is a synthetic resin that is not absorbed in the GI tract. It has the capacity to attract and retain water in the intestinal lumen, thereby increasing stool volume and stimulating colonic transit[25]. It is considered safe even for prolonged use, as it is not metabolized and does not significantly alter electrolyte balance.

The level of evidence supporting macrogol 3350 in chronic constipation is high (IA). However, clinical evidence of its use in IBS-C is scarce and comes from a single 4-week clinical trial comparing macrogol 3350 with placebo. The primary endpoint was the increase in weekly bowel movements. Results showed that macrogol increased weekly bowel movements vs placebo (4.40 ± 2.5 vs. 3.11 ± 1.9; $p < 0.0001$). Symptoms such as abdominal pain and bloating were lower, but not statistically significant. The most common adverse events were abdominal pain and diarrhea. Based on these findings, the authors concluded that macrogol 3350 may be used in IBS-C[25].

Lactulose, a synthetic disaccharide, is neither digested nor absorbed in the small intestine, reaching the colon intact, where it is fermented by the microbiota. This fermentation produces organic acids that acidify the medium, increase osmotic pressure, and stimulate colonic motility[26]. Although effective in improving stool frequency, it may cause bloating or gas in some patients due to fermentation, limiting its tolerance in IBS-C[27].

No adequate-quality studies exist on lactulose use in IBS-C.

Stimulant laxatives (bisacodyl, senna): indications and precautions

Stimulant laxatives act directly on the colon, increasing peristaltic activity and stimulating fluid and electrolyte secretion into the intestinal lumen. This group includes diphenylmethane derivatives such as sodium picosulfate and bisacodyl.

Bisacodyl, a diacetic acid derivative, is converted to its active form by intestinal esterases, enabling its laxative effect[28].

Sodium picosulfate is a prodrug requiring colonic bacterial enzymes for activation, yielding the same active metabolite as bisacodyl, thus explaining their similar mechanisms[29].

Anthraquinone-containing laxatives (senna, cascara sagrada, senna leaves) are metabolized into active aglycones, which exert their laxative effect by inducing epithelial cell damage. This alters fluid absorption and secretion, increases motility, and facilitates evacuation[30].

Although stimulant laxatives may provide temporary relief of constipation in chronic constipation and IBS-C, there is no strong evidence supporting their regular use in these patients. Caution is needed given their well-known adverse effects, including allergic reactions, fluid-electrolyte imbalance, and *melanosis coli*. Most patients develop tolerance, requiring progressive dose increases. Importantly, there is no evidence that chronic use causes megacolon or colorectal cancer[31].

Prokinetics

Prucalopride

Prucalopride is a selective 5-HT_4 receptor agonist that activates afferent neuronal signaling, enhancing intestinal motility[32]. It was approved in Europe for the treatment of chronic constipation in women when laxatives provide inadequate relief[33]. Prucalopride is safe and not associated with cardiovascular adverse effects. In follow-up analyses of 3 pivotal trials, where patients who had responded after 12 weeks continued treatment for up to 18 months, 40-50% no longer required laxatives. The most common adverse effects were GI (diarrhea, nausea, abdominal pain) and headache. In clinical practice, prucalopride is often used in functional constipation, and its efficacy profile in improving pain, bloating, and digestive discomfort suggests a potential benefit in IBS-C as well[33]. However, to date, no specific clinical trials support its formal use in this subgroup.

Secretagogues

Lubiprostone

Lubiprostone, a prostaglandin E1 derivative, activates type-2 chloride channels in epithelial cells, promoting chloride secretion into the intestinal lumen[34]. Sodium and water follow paracellularly, increasing stool water content and improving transit without altering serum sodium or potassium[35]. In the registration trial by Johanson et al.[33], lubiprostone at 24 μg twice daily for 4 weeks increased spontaneous bowel movements during the first week vs placebo (5.69 vs 3.46; p = 0.0001). Reported adverse events such as nausea, vomiting, and diarrhea were common (incidence rate, 2-75%), but serious adverse effects requiring discontinuation were under 5%[36]. The mechanism behind lubiprostone-induced nausea and vomiting remains unknown.

Linaclotide and plecanatide

Linaclotide and plecanatide induce intestinal fluid secretion via cyclic guanosine monophosphate (cGMP) upregulation and activation of the cystic fibrosis transmembrane regulator (CFTR). Linaclotide, at a dose of 145 μg daily, has been shown to achieve > 3 complete spontaneous bowel movements per week[37]. It also improves stool consistency, straining, and other constipation-associated symptoms, as well as quality of life.

Plecanatide, in addition, has antinociceptive effects[38]. A phase III multicenter trial evaluated plecanatide (3 or 6 mg daily) vs placebo for 12 weeks in 1394 constipated patients. Results showed better response in plecanatide groups (21% for 3 mg; 19.5% for 6 mg) vs 10.2% with placebo (p = 0.001)[39]. Of these 2 drugs, only linaclotide is currently available in Mexico.

Tenapanor

Tenapanor is a minimally absorbed small-molecule inhibitor of sodium/hydrogen exchanger isoform 3, acting in the small intestine and colon. It promotes luminal water retention and improves transit[40,41]. It also reduces colonic permeability and relieves abdominal pain in IBS-C. It was approved by the FDA after phase III trials (T3MPO-1 and T3MPO-2) demonstrated it safety and efficacy profile, with significant benefits over placebo in symptoms such as abdominal pain and stool frequency. The most common adverse effect was diarrhea, generally mild and transient[42]. The T3MPO-3 study evaluated long-term safety, confirming that tenapanor remains safe and well-tolerated during prolonged treatment (≥ 52 weeks), with a low rate of serious adverse events. Collectively, the T3MPO studies support tenapanor as a safe and effective therapeutic option for IBS-C, thanks to its novel mechanism of action[43].

Therapies targeting the gut microbiota

Probiotics and prebiotics: evidence of their utility in IBS-C

Probiotics are live microorganisms which, when consumed in adequate amounts, may provide health benefits to the host. Prebiotics, in turn, are nondigestible dietary substances that selectively stimulate the growth or activity of beneficial intestinal bacteria.

Although the quality of evidence is variable, some clinical studies have shown benefits of specific probiotic strains in IBS-C. For example, *Bifidobacterium lactis* DN-173 010 has been shown to improve intestinal

transit and alleviate symptoms such as bloating and abdominal pain. Other strains such as *Lactobacillus paracasei* NCC2461 and *Escherichia coli* Nissle 1917 have demonstrated reduced visceral hypersensitivity, while *Bifidobacterium infantis* 35624 has been associated with favorable modulation of intestinal inflammatory profiles.

Controlled clinical trials of probiotic combinations have shown modest but statistically significant improvement in global IBS symptoms compared with placebo. However, benefits are highly strain-dependent, and studies show great heterogeneity in design, duration, and outcome criteria.

For instance, one trial with *B. infantis* 35624 demonstrated symptomatic improvement at a specific dose (1×10^8 CFU), while another trial with *Saccharomyces cerevisiae* I-3856 did not show global benefits over placebo, though improvements were observed in IBS-C patients specifically. This highlights the importance of considering both strain and patient subtype[44].

Non-absorbable antibiotics

Small intestinal bacterial overgrowth (SIBO) and IBS share overlapping symptoms, which can complicate differentiation. Studies show that approximately 45% of patients diagnosed with IBS have concomitant SIBO based on breath tests[45].

Treatment of SIBO in IBS patients often includes non-absorbable antibiotics such as rifaximin and neomycin. Rifaximin has been shown to reduce IBS symptoms, particularly in non-constipation subtypes. In two multicenter studies, 41% of rifaximin-treated patients reported adequate symptom relief, compared with 31% in the placebo group[46].

In methane-predominant SIBO, usually associated with constipation, the combination of rifaximin and neomycin has proven more effective. One study found this combination eradicated methane in over 80% of cases, with corresponding clinical improvement[47].

General recommendations and the availability of therapeutic classes are summarized in table 1.

Impact of gut dysbiosis on chronic constipation

Gut dysbiosis, an imbalance in the composition and function of the intestinal microbiota, has been associated with multiple GI disorders, including chronic constipation. Research indicates that individuals with chronic constipation often present with lower levels of beneficial bacteria such as lactobacilli and bifidobacteria, and higher levels of organisms such as methanogenic archaea—particularly *Methanobrevibacter smithii*. This archaeon is associated with methane production, which may slow intestinal transit and contribute to constipation. It has also been proposed that dysbiosis can affect chronic constipation through several mechanisms, such as modulation of the serotonin transporter (SERT). Dysbiosis may induce SERT upregulation, reducing intestinal serotonin availability and thereby impairing motility. Another mechanism involves intestinal permeability: microbiota alterations may compromise barrier integrity and facilitate inflammatory processes that impair colonic motor function[48].

Management of refractory cases

Multidisciplinary approach in non-responders to conventional therapy

Cognitive-behavioral therapy, dynamic psychotherapy, hypnotherapy, and various relaxation methods help patients manage and reduce abdominal pain and discomfort, making them promising alternatives for IBS-C treatment. Psychological care can also assist in stress management and in identifying triggers. Mental health disorders such as depression, anxiety, and somatization frequently coexist with IBS-C; thus, both antidepressant therapy and psychological interventions can be beneficial[49].

Cognitive-behavioral therapy is an effective brain-directed intervention that provides patients with tools to develop information-processing skills and modify maladaptive behaviors. Other techniques include problem-solving, coping strategies, exposure therapy, and relaxation methods using breathing techniques[50]. Benefits extend beyond central nervous system effects, also including analgesic action, modulation of visceral hypersensitivity, and improvement of GI motility.

Biofeedback and pelvic floor retraining techniques in pelvic floor dysfunction

The pelvic floor is a key anatomical structure that supports pelvic organs and ensures their proper function. Pelvic floor dysfunction increases the risk of disorders such as urinary and fecal incontinence. Biofeedback is an effective intervention that strengthens and relaxes pelvic floor muscles. It is considered the therapy of choice for both short- and long-term management of constipation with dyssynergic defecation, present in up

Table 1. Recommendations, indications, and availability of drugs used in Mexico for the management of irritable bowel syndrome with constipation predominance

Therapeutic class	Recommendation or indication	Availability
Osmotic laxatives		
Polyethylene glycol	Recommended for IBS-C management, as it improves stool frequency and consistency No effect on pain	Widely available, marketed by several pharmaceutical companies
Lactulose	Not recommended because it may worsen symptoms such as bloating	Widely available, marketed by several pharmaceutical companies
Stimulant laxatives		
Bisacodyl	May be used occasionally as symptomatic treatment of constipation in IBS-C Promote intestinal motility and evacuation	Widely available, marketed by several pharmaceutical companies
Senna glycosides	May be used as occasional symptomatic treatment in IBS-C patients who do not adequately respond to dietary changes, increased soluble fiber, or first-line treatments such as secretagogues Increase motility and facilitate evacuation	Widely available, marketed by several pharmaceutical companies
Prokinetics		
Prucalopride	Although approved for chronic constipation, it may be used in IBS-C patients as there is evidence of improvement in pain, abdominal discomfort, and subjective bloating	Exclusive, marketed by a single pharmaceutical company
Secretagogues		
Linaclotide	Recommended for IBS-C management Improve stool consistency and frequency, abdominal pain, and bloating Can be used as first-line therapy	Exclusive, marketed by a single pharmaceutical company
Lubiprostone	Its use is recommended for the management of IBS-C It improves stool consistency and frequency, as well a abdominal pain	Currently not available
Non-absorbable antibiotics		
Rifaximin alpha	Recommended for IBS-D and IBS-M management Improves symptoms such as bloating, nausea, and urgency May be used as first-line therapy and repeated if no improvement; if unresponsive after the first course, repeat use is not recommended	Exclusive, marketed by a single pharmaceutical company Although other forms of rifaximin are marketed by several pharmaceutical companies, they are not the alpha polymorph
Probiotics	Recommended as adjuvant therapy for global symptom and abdominal pain management May improve bloating and flatulence	Only 2 strains have sufficient evidence; each is marketed exclusively by a single pharmaceutical company

IBS-D: irritable bowel syndrome with diarrhea predominance; IBS-C: irritable bowel syndrome with constipation predominance; IBS-M: mixed irritable bowel syndrome.

to 40% of cases[33]. The number of sessions varies, but most centers include the following steps in their protocol: patient education on the appropriate force for defecation; training to improve abdominal push strength; training to relax the pelvic floor muscles; and simulated defecation practice using the balloon expulsion test. Therapy is conducted in 5-6 training sessions lasting 30-60 minutes at 2-week intervals. Other methods, such as hypopressive exercises, involve postural and respiratory techniques that reduce pressure in three compartments: thoracic, abdominal, and perineal[51]. It has been hypothesized that complete exhalation followed by apnea blocks the glottis and expands the thoracic cavity in such a way that the diaphragm is stretched, causing involuntary activation of the deep trunk muscles. This maneuver, combined with postural techniques, aims to induce activation of tonic (type I) muscle fibers, which should enhance the synergistic activation of all postural muscles, including the deep trunk muscles[52]. Moreover, these therapies have a positive impact on the patient's emotional and social well-being, improving quality of life.

Indications for advanced studies and specialist referral

There are certain indications for performing advanced studies, such as lack of response to conventional treatment with persistent symptoms despite pharmacological

therapy and dietary modifications; alarm features such as unintentional weight loss, overt GI bleeding (hematochezia, melena), or the presence of iron-deficiency anemia; diagnostic uncertainty or atypical signs such as persistent constipation or diarrhea, severe or progressive abdominal bloating, suspected pelvic floor dysfunction, or gastrointestinal motility disorders[53].

Some recommended advanced studies include colonoscopy—indicated in cases with alarm signs, in patients older than 50 years without prior screening, or with a family history of colorectal cancer; serological testing for celiac disease (anti-tissue transglutaminase IgA) in patients with intermittent diarrhea or atypical symptoms; anorectal manometry and balloon expulsion test in suspected dyssynergic defecation, pelvic floor dysfunction, or refractory constipation not responding to standard medical therapy; and colonic transit studies with radiopaque markers or scintigraphy to evaluate transit time in refractory constipation[54].

The management of IBS requires a multidisciplinary approach due to its complex nature, which involves gastrointestinal, dietary, and psychological factors. Collaboration and timely referral among specialists improve symptom control and patients' quality of life, while allowing for more effective and personalized treatment.

Conclusions

There are various therapeutic options for IBS-C, all aimed at the same goal: achieving effective symptom control and improving the quality of life of those affected. Nevertheless, it is important to recognize that treatment response varies among patients, making it essential to individualize each therapeutic approach according to the specific characteristics and needs of each case. It must also be emphasized that this process should always be carried out under specialist supervision, thereby ensuring safe, effective, and personalized management of the disease.

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Conflicts of interest

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Ethical considerations

Protection of humans and animals. The authors declare that no experiments on humans or animals were conducted for this research.

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