

Approach to a Child with Irritable Bowel Syndrome: A Review

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Abstract

Irritable bowel syndrome (IBS) is one of the most common and best studied disorders among the group of functional gastrointestinal disorders. It is a functional bowel disorder in which abdominal pain or discomfort is associated with defecation or a change in bowel habit. Visceral hypersensitivity and increased GIT motility are the main patho-physiological mechanism for developing IBS. IBS present with diarrhoea or constipation or both. Investigations are least needed for diagnosis of IBS rather done to exclude differential diagnosis. Diagnosis of IBS is done on the basis of Rome-III criteria. Proper counseling, dietary management, antispasmodic and antidepressant are the mainstay of treatment. [Journal of National Institute of Neurosciences Bangladesh, 2016;2(1): 34-39]

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Introduction

Irritable bowel syndrome (IBS) has been recognized as one of the most common and best studied disorder among the group of functional gastrointestinal disorders¹. It is a functional bowel disorder in which abdominal pain or discomfort is associated with defecation or a change in bowel habit². Prevalence of IBS in adults is gradually increasing, about 20% in western population³, 6.5–10.1% in Asian countries⁴ and 4% in northern India, showing in recent studies⁵. One study of children in North America found that 14% of high school students and 6% of middle school students have IBS. The study also found that IBS affects boys and girls equally⁶. Through its exact incidence is hard to assess, but it appears that those attending

gastroenterology clinics represent a few person go to the tertiary centre from where the above prevalence data are collected⁷.

Some questions therefore remain to be answered – Is there a significant difference in the incidence of IBS in developing and developed countries? Will the incidence of IBS increase by adoption of a Western lifestyle? Are predisposing factors different in developing and developed countries? Is the increasing stress on young children to achieve or family break-up responsible for IBS symptoms becoming evident at a younger age? The answer is probably ‘yes’ to a certain extent. Infective pathology is considered the trigger for IBS in developing country. According to Rome III criteria¹, for the diagnosis of IBS following requirements are

needed- Criteria must include both of the following:

1. Abdominal discomfort or pain associated with two or more of the following at least 25% of the time: a) Improvement with defecation; b) Onset associated with a change in frequency of stool and c) Onset associated with a change in form (appearance) of stool
2. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the subject's symptoms. Criteria fulfilled at least once per week for at least 2 months prior to diagnosis. Discomfort means an uncomfortable sensation not described as pain.

2.0. Pathophysiology of IBS

Pathophysiology of IBS is multifactorial.

2.1. **Visceral Hypersensitivity:** Increased sensitivity to stimuli is a frequent finding in irritable bowel syndrome patients⁸. Perception in the gastrointestinal tract results from stimulation of various receptors in the gut wall. These receptors transmit signals via afferent neural pathways to the dorsal horn of the spinal cord and ultimately to the brain. Hyper-sensitization of visceral afferent nerves in the gut, triggered by bowel distention or bloating may be the possible explanation for IBS. Hypersensitivity of the intestines to normal sensations may be mediated by the local GI nervous system, by central modulation from the brain, or by some combination of the two⁹. Other factors may contribute to visceral hyperalgesia, such as specific gastrointestinal mediators (serotonin, kinins)¹⁰.

2.2. **Gastrointestinal Motility:** Motor abnormalities of the gastrointestinal tract are detectable in some patients with IBS. Abnormalities include increased frequency and irregularity of luminal contractions, prolonged transit time in constipation-predominant IBS, and an exaggerated motor response to cholecystokinin and meal ingestion in diarrhea-predominant IBS¹¹.

2.3. **Intestinal Inflammation-** Mucosal immune system activation occurs and is characterized by alterations in particular immune cells and markers in some patients with irritable bowel syndrome. Increased numbers of lymphocytes and mast cells are found in the colon and small intestine in patients with IBS^{12,13}. Elevated levels of plasma pro-inflammatory interleukins have been observed in patients with IBS. In addition, peripheral blood mononuclear cells of IBS patients produce higher amounts of tumor necrosis factor than healthy controls

2.4. **Post-Infectious:** Irritable bowel syndrome may occur following infectious enteritis. The increased risk of post-infectious IBS is associated with bacterial, protozoan, helminthes, infections, and viral infections. The cause of bowel symptoms following acute infection is uncertain, although several theories have been

proposed¹⁴:

- Mal-absorption: The development of idiopathic bile acid mal-absorption has been observed following enteric infections, which may be result in diarrhea-predominant IBS.
- Increase in entero-endocrine cells/lymphocytes: An increase in serotonin-containing entero-endocrine cells and T lymphocytes, has been demonstrated following acute *Campylobacter* enteritis.
- Antibiotic use: The use of antibiotics for GI or other infections may be a risk factor for developing functional bowel symptoms.
- Bacterial overgrowth- Small intestinal bacterial overgrowth may be associated with IBS¹⁵.

2.5. Alteration in Fecal Microflora

Changes in the composition of intestinal microflora may be associated with IBS. Patients with diarrhea-predominant IBS would benefit from probiotics, which influence the composition and metabolism of the microflora¹⁶.

2.6. Food Sensitivity

The role of food in the pathophysiology of IBS is not clear. Some patients with IBS report worsening of symptoms after eating and perceive food intolerance to certain foods. Food allergy, carbohydrate mal-absorption, and gluten sensitivity may be involved in IBS.

2.7. Food Allergy

Eliminating specific foods in patients who have elevated IgG titers associated with those food antigens may reduce IBS symptoms¹⁷.

2.8. Carbohydrate Malabsorption

Fermentable oligo-, di-, and monosaccharides and polyols (FODMAPs) enter the distal small bowel and colon where they are fermented, leading to symptoms and increased intestinal permeability and possibly inflammation¹⁸⁻²⁰. Fructose intolerance has been suggested as a possible form of carbohydrate malabsorption contributing to gastrointestinal symptoms such as flatus, pain, bloating, belching and altered bowel habits.

2.9. Genetics

Familial studies suggest a modest contribution of genetics to the development of IBS²¹.

2.10. Psychosocial dysfunction

Psychosocial factors influence the expression of IBS. Anxiety, sleep problems, somatic symptoms are risk factors for IBS.

3.0. Types of IBS: Four subtypes of IBS were recognized:

- 3.1. IBS with constipation (hard or lumpy stools ≥ 25

percent / loose or watery stools <25 percent of bowel movements)

3.2. IBS with diarrhea (loose or water stools \geq 25 percent / hard or lumpy stools <5 percent of bowel movements)

3.3. Mixed IBS (hard or lumpy stools \geq 25 percent / loose or watery stools \geq 25 percent of bowel movements)

3.4. Un-subtyped IBS (insufficient abnormality of stool consistency to meet the above subtypes)

4.0. Clinical features

The clinical features of IBS are lower abdominal cramps, gas and bloating, constipation or diarrhea, may be both, feeling the immediate urgency to have bowel movement when waking up as well as during or after eating, feeling of incomplete emptying even after having defecation, pain relief after defecation, presence of mucus in stools, may have psychological symptoms like anxiety and depression and physical findings are unremarkable.

5.0. Investigations

No investigation is usually needed. Investigations are done to exclude the differential diagnosis. Since many disorders present with symptoms similar to IBS, other causes of abdominal pain should be excluded by Complete blood count, ESR & CRP, Stool for ova, parasites, and blood, Abdominal x-rays, Urinalysis, Serum tTG IgA, MT, CXR, Breath tests for fructose and lactose intolerances, Breath test for small intestine bacterial overgrowth (SIBO), Upper GI endoscopy and Colonoscopy. Routine laboratory studies are normal in IBS.

5.1. Red flags in diagnosing IBS: The red flags in diagnosis of IBS are confirmed weight loss, nocturnal or progressive abdominal pain, unexplained anemia, bleeding per rectum, severe diarrhea and/or vomiting, delayed puberty, unexplained fever and strong family history of inflammatory bowel.

6.0. Treatment of irritable bowel syndrome

Treatments include counseling, dietary management, medication, physical activity and psychotherapy.

6.1. Counseling: The focus of treatment should be on relief of symptoms and addressing the patient's concerns. Patients should be informed of the chronic and benign nature of IBS, and also informed that the diagnosis is not likely to be changed, and that he or she should have a normal life span.

6.2. Dietary Management: A careful dietary history may reveal patterns of symptoms related to specific foods. A number of dietary interventions have been proposed but their efficacy has not been well established²².

6.2.1. Lactose

Lactose free diet should be considered in patients suspected IBS. Exclusion of gas-producing foods, likes-beans, onions, celery, carrots, raisins, bananas, apricots, prunes, brussels sprouts, wheat germ, pretzels, and bagels should be avoided.

6.2.2. Food Allergies

Food allergy may have role in the development of symptom.

6.2.3. Gluten Sensitivity

Gluten sensitivity (without overt celiac disease) has been proposed as a cause of functional bowel disorders.

6.2.4. Carbohydrate Mal-absorption

Fermentable oligo-, di-, and monosaccharides and polyols (FODMAPs) in patients with IBS or IBD enter the distal small bowel and colon where they are fermented, leading to symptoms. Some examples of FODMAPs include: Fructans (found in wheat, onions, and artichokes), Galactans (found in legumes, cabbage, and Brussels' sprouts), Lactose, Fructose, Sorbitol, Xylitol, Mannitol

6.2.5. Fiber

A decrease in fiber intake to 12 g per day (particularly insoluble fiber such as bran) was suggested in a British guideline, because of the potential of fiber to exacerbate symptoms. An increase in the intake of fiber is often recommended. Proposed mechanisms for fiber's beneficial effects include: enhancement of water holding properties of the stool; formation of gels to provide lubrication; bulking of the stool; and binding of agents such as bile. Clinical trials found no convincing evidence that the commonly-used bulking agents were more effective than placebo at relieving global IBS symptoms. Although the efficacy of fiber supplements has not been proven²³, some improvement has been demonstrated in patients with IBS whose primary complaints are abdominal pain and constipation. Dose of fibre is age plus 5 grams of fiber daily.

6.3. Medication

Pharmacologic agents are only an adjunct to treatment in irritable bowel syndrome (IBS). Furthermore, the drug chosen varies depending on the patient's major symptoms; diarrhea-predominant IBS is treated differently from constipation-predominant disease.

6.3.1. Antispasmodic agents: The antispasmodic agents include

6.3.1.1. Directly affect intestinal smooth muscle relaxation eg, mebeverine, pinaverine, peppermint oil.

Mebeverine is licensed in the United Kingdom and is generally well tolerated; and can be used on an as required basis before meals. A systematic review²⁴

which searched medical databases and all relevant literature from 1965 to June 2009 for any placebo-controlled clinical trials of mebeverine, identified 14 relevant papers (8 were randomized trials with 555 patients) and concluded that mebeverine is mostly well tolerated with no significant adverse effects; however, its efficacy in global improvement of IBS was not found to be statistically significant²⁴.

6.3.1.2. Act via their anticholinergic or antimuscarinic properties like Dicyclomine and hyoscyamine, duration on demand basis; Inhibition of GI smooth muscle reduces stimulated colonic motor activity & may be beneficial in patient with postprandial abdominal pain, gas, bloating, and fecal urgency.

6.3.2. Antidepressants

Antidepressants have analgesic properties independent of their mood improving effects and may therefore be beneficial in patients with neuropathic pain. The postulated mechanisms of pain modulation with tricyclic antidepressants (TCA) and possibly serotonin reuptake inhibitors in IBS are facilitation of endogenous endorphin release, blockade of norepinephrine reuptake leading to enhancement of descending inhibitory pain pathways, and blockade of the pain neuro-modulator, serotonin. TCAs, via their anti-cholinergic properties, also slow intestinal transit time, which provide benefit in diarrhea-predominant IBS. Improvement in neuropathic pain with TCAs occurs at lower doses than required for treatment of depression. As a result, if an antidepressant is chosen for the treatment of IBS, low doses should be administered initially and titrated to pain control or tolerance. Because of the delayed onset of action, three to four weeks of therapy should be attempted before considering treatment insufficient and increasing the dose. Examples of antidepressant medications used in patients with IBS include amitriptyline, imipramine, nortriptyline, and desipramine. The initial dose should be adjusted based upon tolerance and response. TCAs should be used cautiously in patients with constipation. Amitriptyline, nortriptyline, and imipramine can be started at a dose of 10 to 25 mg at bedtime and increased every three to four weeks based upon clinical response and tolerance²⁵. Desipramine is used in a similar fashion beginning at 12.5 to 25 mg at bedtime. If the patient is intolerant of one TCA, another may be tried. Paroxetine (10 to 20 mg daily), fluoxetine (20 to 40 mg daily), sertraline (50 to 100 mg daily), or other antidepressant medications can be considered if depression is a cofactor.

6.3.3. Benzodiazepines

Anxiolytic agents are of limited usefulness in IBS because of the risk of drug interactions, habituation, and

rebound withdrawal. Furthermore, benzodiazepines may lower pain thresholds by stimulating gamma aminobutyric acid (GABA) receptors, thereby decreasing brain serotonin. They may, however, be useful for short-term (less than two weeks) reduction of acute situational anxiety that may be contributing to symptoms.

6.3.4. 5-hydroxytryptamine 3 receptor antagonists

5-hydroxytryptamine-3 receptor antagonists such as ondansetron, alosetron and granisetron modulate visceral afferent activity from the gastrointestinal tract and may improve abdominal pain.

6.3.5. 5-hydroxytryptamine 4 receptor agonists

Agonists of 5-hydroxytryptamine-4 receptor stimulate the release of neurotransmitters and increase colonic motility, providing a rationale for their use in constipation predominant IBS. The first of this class of drugs is tegaserod was approved for IBS and constipation but removed from the market due to cardiovascular side-effects.

6.3.6. Lubiprostone

Lubiprostone is a locally acting chloride channel activator that enhances chloride-rich intestinal fluid secretion. Lubiprostone has been approved by the United States Food and Drug Administration for treatment of irritable bowel syndrome with constipation in women 18 years and older. The approved dose is 8 micrograms twice daily for 12 weeks²⁶.

6.3.7. Linaclotide

An agonist of guanylatecyclase, linaclotide is a unique agent which was recently approved by both American and European regulatory agencies for the treatment of IBS-C. Stimulation of guanylatecyclase receptors leads to increased secretion of both guanylin and uroguanylin into the intestinal lumen where they act as a second messenger for both fluid and electrolyte release into the large bowel²⁷. Linaclotide is minimally absorbed and has a strong affinity for the guanylatecyclase receptor.

6.3.8. Other Drugs

Peppermint oil, laxatives-polyethylene glycol, mast cell stabilizer, antibiotics-rifaximin, probiotics, loperamide

6.3.8.1. Mast cell stabilizers

Ketotifen is a mast cell stabilizer that has been studied for the treatment of IBS based upon the theory that mast cell activation contributes to visceral hypersensitivity. In a randomized trial of 60 patients, the use of ketotifen for eight weeks increased the threshold for discomfort with rectal distension in patients who were hypersensitive to rectal balloon distension at baseline, but not in those with normal sensitivity at baseline.

in patients who received ketotifen compared with those who received placebo, the results did not reach statistical significance.

6.3.8.2. Antibiotics

Rifaximin, a nonabsorbable antibiotic, led to symptomatic improvement in global IBS symptoms and bloating. The mechanisms leading to the benefit are unclear but may be due to suppression of gas producing bacteria in the colon. It is reasonable to consider two-week trial of rifaximin²⁸.

6.4. Physical Activity and Psychosocial Therapy

6.4.1. Physical activity

Increased physical activity may help with the symptoms of IBS. Increased physical activity was comprised of 20 to 60 minutes of moderate to vigorous activity three to five days per week.

6.4.2. Psychosocial therapies

Behavioral treatments may be considered for motivated patients who associate symptoms with stressors, although their benefits remain controversial. Hypnosis, biofeedback, and psychotherapy help to reduce anxiety levels, encourage health promoting behavior, increase patient responsibility and involvement in the treatment, and improve pain tolerance.

Conclusion

IBS is a clinical diagnosis of exclusion. The diagnosis is challenging because of the nature and range of associated symptoms and their interpretation amongst parents and pediatricians. A detailed focused history and use of Rome III criteria will be helpful to clarify uncertainties about the diagnosis. Investigations should be kept to the minimum and used for selected cases to exclude other serious pathologies with similar presenting features. For successful management of IBS in children initially enough time should be spent at explaining and reassuring the child and the parents. Therapy needs to be individualized to patient needs. Before initiating therapy it is important to explain the expected benefits and possible side-effects to the family. Multi-disciplinary team approach is needed for management of difficult cases.

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