Drotaverine in IBS: Evaluating its Effectiveness

Reviewed by:

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Functional Gastrointestinal Disorders and IBS

Functional gastrointestinal disorders (FGID) are one of the commonest gastrointestinal disorders worldwide. It's characterized by abdominal symptoms including abdominal pain, bloating, diarrhea and constipation, without any evidence of an underlying structural or organic abnormality. There is now a growing realization that they are primarily a result of alteration in the brain-gut axis, a bidirectional communication pathway between the gut and central nervous system. Large scale multinational studies have reported that the prevalence of FGID stands at 40% worldwide, with a higher prevalence in women than in men. Functional gastrointestinal disorders incur significant healthcare costs, significantly affect the quality of life and are frequently associated with psychological symptoms such as anxiety and depression

Irritable bowel syndrome (IBS) is a common FGID characterized by chronic abdominal pain along with changes in bowel habits, including alterations in stool form and/or frequency.[2] More specifically, patients with IBS present with abdominal pain or discomfort, alteration of bowel habits such as constipation, diarrhea, or both; often with co existing with other symptoms such as abdominal distension and/or bloating, and abdominal discomfort following food intake (Figure 1).[3] It is a commonly seen gastrointestinal (GI) disorder in primary practice, and is also the most common GI disorder encountered by gastroenterologists in their day-to-day practice. About 40-60% of these patients with IBS also have associated symptoms of depression or anxiety. Additionally, IBS exerts considerable burden on the family of the affected as well

Figure 1: Commonly reported symptoms in IBS[3]

as the healthcare system as a whole and significantly affect quality-of-life of these patients.[2]

IBS in India – Key highlights

In India, IBS is a commonly diagnosed GI disorder. Its reported prevalence varies from 0.4% to 4.2% in different studies from the country As opposed to the Western literature that report IBS to be a more commonly seen disorder in females, in the Indian population IBS is as important problem in males as in females. In Indian patients, symptoms of IBS often overlap with those of other FGIDs, rendering its diagnosis challenging.

Diagnosis of IBS is primarily based on symptom criteria and the exclusion of organic cases. Several criteria have been used for diagnosis of IBS, including the Manning, Rome, and Asian criteria. Rome IV is among the most acceptable criteria for diagnosis of IBS worldwide; diagnosis of IBS based on this criteria requires recurrent abdominal pain, on average, at least 1 day per week in the last 3 months; with 2 or more of the following criteria: abdominal pain is related to defecation, change in frequency of stool, and/or with change in form or appearance of stool (Table 1). However, a recently published Indian consensus statement on IBS in adults emphasized that ROME III criteria may be preferred over the ROME IV criteria in the Indian population due to its higher sensitivity for diagnosing IBS compared to ROME IV criteria; and non-inclusion of abdominal bloating and discomfort in ROME IV criteria (though included in ROME III criteria) which are frequently seen symptoms in Indian patients with IBS.[4]

Table 1: ROME III and ROME IV criteria for diagnosis of IBS[4]

ROME III CRITERIA	ROME IV CRITERIA
❖ Abdomen pain/discomfort of at least 3 months with onset at least 6 months previously; duration at least 3 days per month, plus ❖ At least 2 listed symptoms with duration • Improvement of pain/discomfort with defecation • Onset associated with change in the form of stool • Onset associated with change in stool frequency	❖ Recurrent abdominal pain, on average, at least 1 day per week in the last 3 months; discomfort as a defining symptom removed, plus ❖ Any 2 or more listed symptoms associated with duration • Pain related to defecation (may decrease or increase) • Change in the form of stool • Change in the frequency of stool

Need to Address Abdominal Pain in IBS on Priority

Abdominal pain or discomfort is among the most common and bothersome symptoms of IBS.[5] In fact, abdominal pain is considered a cardinal symptom in patients of IBS.[6] It is a common reason for patients seeking medical opinion and is also a common underlying cause for impairment of quality-of-life in patients with IBS, therefore needs to be addressed on priority.[5] Abdominal pain/discomfort is frequent symptom of IBS in Indian population. High prevalence of abdominal pain or discomfort was one of the observations of a prospective multicentre Indian study that attempted symptom profiling of Indian population with IBS. The study evaluated 2785 subjects with complaints of chronic lower GI symptoms with no alarm feature and no organic cause. Abdominal pain or discomfort was noted among the most common symptoms (70%; Figure 2); other reported symptoms in these patients including incomplete evacuation (77%); abdominal fullness (70%); subjective feeling of constipation (53%) or diarrhea (47%), mucus with stools (54%), straining at stools (46%), epigastric pain (49%) and milk intolerance (32%).[7]

Another point worth noting is that abdominal pain in IBS patients is frequently co-associated with diarrhea and/or constipation. It has been suggested that when treating IBS, primarily targeting alteration of bowel habits (constipation or diarrhea) in the management can leave abdominal pain unaddressed which as previously discussed is one of the predominant cause of negative impact on quality-of-life; this treatment strategy is therefore conceivably not ideal in IBS patients. Abdominal pain should be symptomatically addressed as other symptoms to improve the distressing effect of the disorder on patients' daily life.[5,6] Since the primary cause of abdominal pain in IBS is attributed to smooth muscle spasm of the GI tract, there appears to be a sound rational for prescribing antispasmodics as the mainstay for abdominal pain management. [5]

Figure 2: Prevalence of abdominal pain or discomfort in Indian population with lower GI symptoms, no alarm features and no underlying organic cause[7]

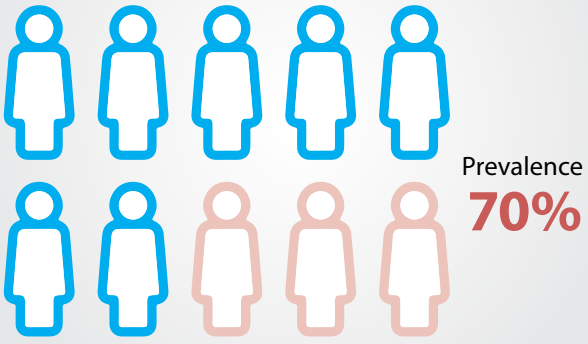
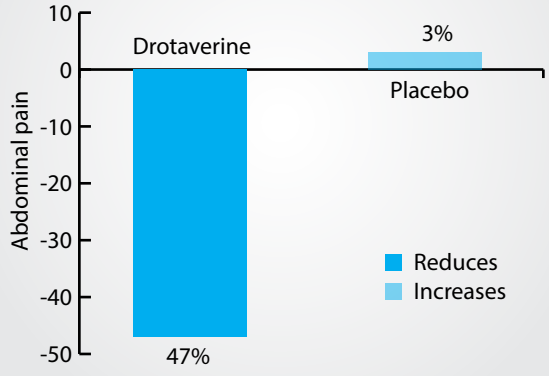


Figure 3: Effect of treatment with drotaverine (80 mg thrice-daily) vs placebo on abdominal pain in patients with IBS and constipation[8]



Drotaverine: A Rational Treatment Approach for Abdominal Pain in IBS

Drotaverine is an antispasmodic drug with relaxant effect on smooth muscles of the GI tract. Importantly, it is devoid of the troublesome anticholinergic adverse effects which many other antispasmodics such as dicyclomine and hyoscyamine are commonly associated with.[5] Its smooth muscle relaxing effect appear to be mediated by changes in intracellular calcium distribution and inhibitory effect on phosphodiesterase. Efficacy of drotaverine on abdominal pain symptoms in IBS patients has been reported in some studies.[8-11]

One study that included 62 patients with IBS and constipation and compared treatment with drotaverine (80 mg thrice-daily) vs placebo showed significant reduction in abdominal pain by 47% with drotaverine while in placebo group it increased by 3% (Figure 3).[8] Similar results were seen in another study that evaluated 70 patients of IBS and randomized them to drotaverine (80 mg thrice-daily) vs placebo over a4-week treatment period followed by a 4-week follow-up period. Drotaverine treatment was associated with reduction in abdominal pain frequency in 31.4% patients after 2 weeks and in 71.4% patients after 4 weeks. In comparison, pain frequency reduced in 5.7% and 31.4% patients at 2 and 4 weeks respectively in the placebogroup ($p<0.001$). Additionally, drotaverine treatment also lead to significantly greater reduction in pain severity scores compared to placebo in IBS patients after 4 weeks of treatment (71.4% vs 31.4%, respectively; $p<0.001$).9A prospective, multicenter study showed that drotaverine treatment may be effective across the spectrum of all IBS subtypes. In this study a total of 217 patients with IBS were treated with oral drotaverine 80 mg thrice-daily for 2 weeks. Overall drotaverine was seen effective, with an efficacy rate of 77.9%. There was significant reduction in average weekly score of abdominal pain compared to pre-treatment after 2 weeks of treatment. Treatment was deemed safe, with no incidence of serious adverse effects associated with drotaverine treatment.[10]

Most studies have compared drotaverine to placebo in IBS patients. Recently an Indian study compared drotaverine to mebeverine, another antispasmodic, in IBS patients. The study randomized patients of IBS to either drotaverineat 80 mg dose or mebeverine at 135 mg dose thrice-daily given for a total period of 4 weeks. Drotaverine was significantly better in reducing abdominal pain severity, with a 74% reduction in pain severity by the end of the study on drotaverine compared to 46.1% reduction with mebeverine. Drotaverine was also superior to mebeverine in significantly improving other outcome measures in the study including pain frequency, straining on stool, and achievement of complete spontaneous smooth bowel movement.[11]

Conclusion

Irritable bowel syndrome (IBS) is one of the common GI disorders seen in both primary care and in gastroenterologist practice. Abdominal pain is a cardinal symptom of IBS with a considerable negative effect on the quality-of-life of the affected patients. Drotaverine is an antispasmodic smooth muscle relaxant, with some studies documenting its efficacy in managing troublesome symptoms of abdominal pain and/or discomfort in patients with IBS. It is devoid of the anticholinergic adverse effects unlike some of the other antispasmodics. Its efficacy in improving severity and/or frequency of abdominal pain has been shown in clinical studies evaluating IBS patients. A study also showed better reduction in pain severity and frequency and in achievement of complete spontaneous bowel movement in IBS patients with drotaverine compared to mebeverine. Drotaverine is an antispasmodic worth considering for management abdominal pain control in IBS.

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