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ORIGINAL RESEARCH

Role Of Ramosetron 5-HT3 Receptor Antagonists In The Treatment Of Irritable Bowel Syndrome (Diarrhea Dominant)

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Abstract

Background: One of the most common functional gastrointestinal illnesses, irritable bowel syndrome (IBS), significantly impairs quality of life. The present study was conducted to assess the role of the 5-HT3 receptor antagonist Ramosetron in the treatment of irritable bowel syndrome.

Materials and Methods: 60 patients with IBS of both genders were divided into three groups of 20 each. Group I (control), Group II (placebo), and Group III (test). Patients were given 5 mg Ramosetron daily for 3 months, and parameters such as duration of IBS, severity of abdominal pain or discomfort (0–4), stool form (appearance, 1–7), stool frequency (bowel movements per day), adverse events, etc. were recorded.

Results: In groups I, II, and III, the mean duration of IBS was 146.2 months, 139.5 months, and 145.1 months, respectively. The severity of abdominal pain or discomfort (0–4) was 3.2, 2.8, and 1.1, and the and the stool form was 5.4, 5.7, and 2.3, respectively. The difference was significant ($P < 0.05$). Relief of overall IBS symptoms at 1 month was 12%, 14%, and 63%; at 2 months, it was 15%, 18%, and 75%; and at 3 months, it was 25%, 29%, and 87% in groups I, II, and III, respectively. The difference was significant ($P < 0.05$). Common adverse events were gastrointestinal disorders in 2, 4, and 1, hard stool in 6, 2, and 0, nasopharyngitis in 3, 1, and 2, infections in 1, 2, and 1, and pyrexia in 4, 3, and 0 patients, respectively.

Conclusion: The outcomes show that Ramosetron medication is safe and effective over the long term for IBS-D patients.

Keywords: Irritable bowel syndrome, Nasopharyngitis, Stool

Introduction

One of the most common functional gastrointestinal illnesses, irritable bowel syndrome (IBS), significantly impairs quality of life (QOL). Visceral hypersensitivity, gut dysmotility, psychological comorbidity, stress vulnerability, low-grade inflammation, increased gut permeability, changes in gut microbiota, genetic factors, and exaggerated brain-gut interaction are among the many potential causes and pathophysiologies of irritable bowel syndrome (IBS).[1,2]

As a result, probiotics, antibiotics, soluble fibres, visceral neuromodulators, mucosal epithelium modifiers, antidepressants, anti-allergic medications, hypnotherapy, and cognitive behavioural therapy are some of the multimodal treatments for IBS. One of the most

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important aspects of the clinical care of IBS is figuring out the best course of action for patients with long-term efficacy.[3]

Serotonin (5-hydroxytryptamine; 5-HT) is a neurotransmitter that is involved in mood, gastrointestinal motility, and visceral perception. It is also probably linked, either directly or indirectly, to the pathophysiology of IBS.[4] The use of 5-HT3 receptor antagonists for IBS with diarrhoea (IBS-D), 5-HT4 receptor agonists for IBS with constipation (IBS-C), and antidepressants for IBS abdominal pain—which is caused by an inhibition of serotonin transport in the presynaptic membrane—all lend credence to this idea. Inhibiting the activation of 5-HT3 receptors on the mucosal processes of intrinsic and extrinsic primary afferent neurons is thought to be how 5-HT3 receptor antagonists in IBS-D function.[5] Abdominal pain and discomfort are inhibited by blocking 5-HT3 receptors on intrinsic sensory neurons, which also decreases the depolarization of extrinsic sensory neurons that relay signals to the brain and attenuates motor and secretory reflex activity.[6]

Aims and objectives

The present study was conducted to assess the role of the 5-HT3 receptor antagonist Ramosetron in the treatment of irritable bowel syndrome.

Materials & Methods

The present prospective study was conducted on 60 male patients with IBS admitted through OPD or IPD. The study was conducted at the Department of Pharmacology. In collaboration with the General Medicine Department, Sri Krishna Medical College & Hospital, Muzaffarpur, Bihar, India. All were informed regarding the study, and their written consent was obtained. The Institutional Ethics Committee gave the study its approval. Data such as name, age, etc. was recorded. The duration of the study was from January 31, 2020, to July 30, 2020.

Inclusion criteria

- Patients are to give written informed consent.
- Patients diagnosed with IBS based on clinician opinion or having met diagnostic Rome I, II, or III criteria; negative investigations were used as a supplement. (3) 5-HT3 receptor antagonists were compared with placebo or conventional therapy.
- Abdominal pain or IBS symptoms: global assessment following therapy.
- Abnormal bowel habits or stool consistency symptoms following therapy
- Patients aged between 18 and 60 years
- Available for follow-up.

Exclusion criteria

- Patients do not give written, informed consent.
- Patients aged < 18 years or > 60 years
- IBS is not distinguished from functional GI disorders.
- There are no 5-HT_3 receptor antagonist treatment groups or combined 5-HT_3 receptor antagonists for a single patient.
- Patients with systemic diseases (renal dysfunction, cardiac problems)
- Patients on other diabetic medications, requiring hospitalisation
- Not available for follow-up.

Patients were divided into three groups of 20 each. Group I (control), group II (placebo), and group III (test) were chosen randomly. Patients were given one tablet (5 mg) of ramosetron daily for 3 months, and parameters such as duration of IBS, severity of abdominal pain or discomfort (0–4), stool form (appearance, 1–7), stool frequency (bowel movements per day), adverse events, etc. were recorded.

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Statistical analysis

The data thus obtained were subjected to statistical analysis by the Statistical Package for Social Sciences (SPSS), and the data was entered using Microsoft Windows Excel. We used frequency (%) and mean ± standard deviation to summarise categorical data. The Student's t test was used to evaluate the statistical differences in mean values of continuous variables between participants and IBS patients. The difference in categorical variable frequencies between the two groups of study participants was compared using the chi-square test.A P value < 0.05 was considered significant.

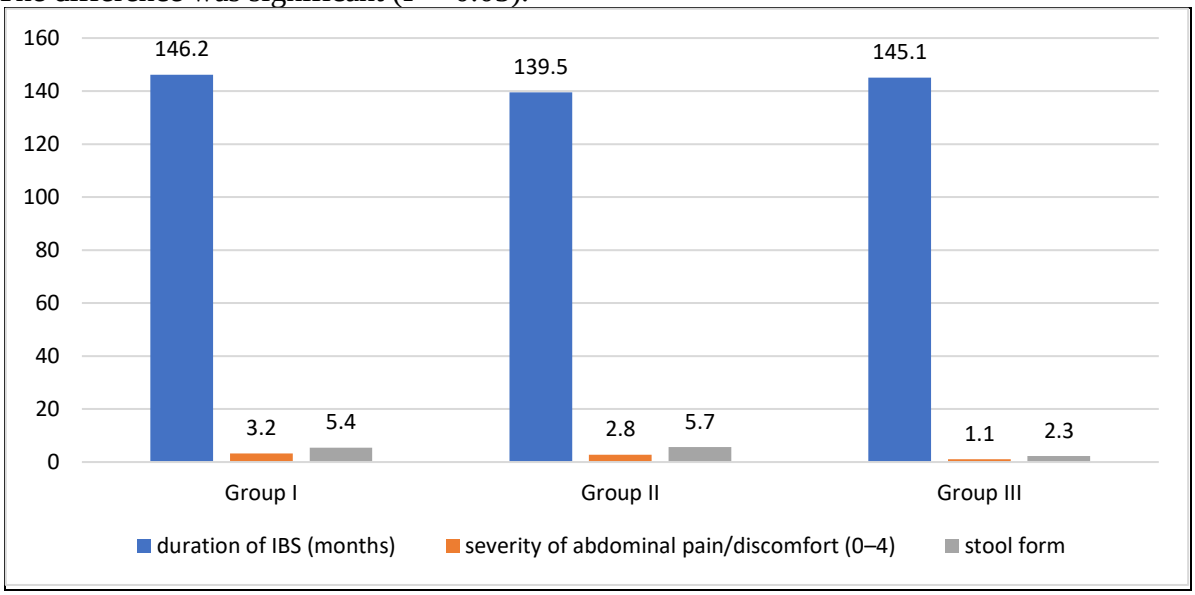
Results

The mean age in group I was 38.36±10.79, in group II was 40.50±10.57, and in group III was 40.95±10.60 years, respectively.

Table 1: Assessment of Demographics and Baseline Characteristics patients

Parameters	Group I	Group II	Group III	P value
duration of IBS (months)	146.2±120.7	139.5±126.5	145.1±125.79	0.98
severity of abdominal pain/discomfort (0–4)	3.2±0.7	2.8±0.6	1.1±0.9	0.05
stool form(appearance)	5.4±0.5	5.7±0.5	2.3±0.4	0.03

Table 1 and graph I show that in groups I, II, and III, the mean duration of IBS was 146.2 months, 139.5 months, and 145.1 months, respectively. The severity of abdominal pain or discomfort (0–4) was 3.2, 2.8, and 1.1, and the stool form was 5.4, 5.7, and 2.3, respectively. The difference was significant (P < 0.05).



Graph I: Assessment of baseline parameters

Table 2: Assessment of relief of overall IBS symptoms

Parameters	Group I	Group II	Group III	P value
1 month	12%	14%	63%	0.04
2 months	15%	18%	75%	0.02
3 months	25%	29%	87%	0.01

Table 2, shows that relief of overall IBS symptoms at 1 month was 12%, 14%, and 63%; at 2 months, it was 15%, 18%, and 75%; and at 3 months, it was 25%, 29%, and 87% in groups I, II, and III, respectively. The difference was significant (P < 0.05).

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Table 3: Adverse events

Adverse events	Group I	Group II	Group III	P value
Gastrointestinal disorders	2	4	1	0.04
Hard stool	6	2	0	
Nasopharyngitis	3	1	2	
Infections	1	2	1	
Pyrexia	4	3	0	

Table 3, shows that common adverse events were gastrointestinal disorders in 2, 4, and 1, hard stool in 6, 2, and 0, nasopharyngitis in 3, 1, and 2, infections in 1, 2, and 1, and pyrexia in 4, 3, and 0 patients, respectively. The difference was significant ($P < 0.05$).

Discussion

Irritable bowel syndrome (IBS) is a highly prevalent functional bowel disorder. Although the pathogenesis of symptoms in IBS is incompletely understood, altered bowel motility, visceral hypersensitivity, mucosal immune activation, increased mucosal permeability, enteric neuromuscular dysfunction, abnormal brain-gut interactions, alteration in the gut microbiome, and psychological disturbance have been hypothesized.[7] Serotonin type 3 (5-HT3) receptor antagonists have been reported to slow colon transit, blunt the gastrocolonic reflex, and reduce rectal sensitivity and postprandial motility.[8] Serotonin (5-HT) is known to play a physiological and pathophysiological role in the regulation of gastrointestinal function. In experimental studies, 5-HT3 receptor antagonists have been reported to slow colon transit, blunt the gastrocolonic reflex, and reduce rectal sensitivity.[9]

We found that in groups I, II, and III, the mean duration of IBS was 146.2 months, 139.5 months, and 145.1 months, respectively. The severity of abdominal pain or discomfort (0–4) was 3.2, 2.8, and 1.1, and the and the stool form was 5.4, 5.7, and 2.3, respectively. Fukudoet al.[10] assessed the long-term safety, tolerability, and outcomes of the use of ramosetron in female patients with IBS-D. Concerning safety, no serious adverse event related to ramosetron, specifically ischemic colitis, was observed in patients with either dose of ramosetron. However, constipation occurred in 19.7% of patients given 2.5 mg and in 10.5% of patients given 5 mg of ramosetron. Ramosetron-treated patients showed high rates of global improvement. Stool consistency, abdominal pain and discomfort, and IBS-QOL were also improved at the last evaluation point.

We observed that relief of overall IBS symptoms at 1 month was 12%, 14%, and 63%; at 2 months, it was 15%, 18%, and 75%; and at 3 months, it was 25%, 29%, and 87% in groups I, II, and III, respectively. Common adverse events were gastrointestinal disorders in 2, 4, and 1, hard stool in 6, 2, and 0, nasopharyngitis in 3, 1, and 2, infections in 1, 2, and 1, and pyrexia in 4, 3, and 0 patients, respectively. In two randomised controlled studies including 957 patients with IBS-D, Min et al.[11] found that ramosetron increased monthly responder rates of patient-reported global assessment of IBS symptom relief compared with placebo. Ramosetron was also as effective as mebeverine in male patients with IBS-D. In a recent randomised controlled trial with 343 male patients with IBS-D, ramosetron proved effective in improving stool consistency, relieving abdominal pain and discomfort, and improving health-related quality of life. Regarding safety, ramosetron is associated with a lower incidence of constipation compared with other 5-HT3 receptor antagonists and has not been associated with ischemic colitis.

Qi et al.[12] analysed the efficacy and safety of ramosetron for irritable bowel syndrome with diarrhoea (IBS-D). Four randomised controlled trials involving 1623 participants were included. Compared with placebo, ramosetron could lead to relief of overall IBS symptoms, relief of abdominal discomfort or pain, improvement in abnormal bowel habits, and improvement in stool consistency. Ramosetron could lead to relief of overall IBS symptoms

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in both male and female patients. The RR for reported adverse events of ramosetron vs. placebo was 1.10 across all studies. No serious adverse events (e.g., ischemic colitis) were reported. The incidences of hard stool and constipation were higher in the ramosetron group compared with the placebo group.

Limitations of the study

The shortcoming of the study is the small sample size and the short duration of the study.

Conclusion

Authors found that the outcomes show that ramosetron medication is safe and effective over the long term for IBS-D patients. The present study concludes that ramosetron is superior to placebo in improving stool consistency with a low incidence of adverse events in male IBS-D patients. Additionally, the data show that ramosetron improves HR-QOL in IBS-D patients. Thus, among the 5-HT3 antagonists that are currently on the market for the treatment of IBS-D, ramosetron is recommended as the most promising drug.

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