Efficacy of Rifaximin in Irritable Bowel Syndrome - Diarrhoea

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Abstract:
AbstractBackground Few therapeutic options are available for irritable bowel syndrome (IBS). It has been proposed that alterations in the gut microbiota may play a role in the pathophysiology of IBS, and that modulation of the microbiota may have therapeutic utility in the treatment of IBS. Rifaximin is a nonsystemic antibiotic found to have efficacy in IBS Diarrhoea. AimTo determine the efficacy of Rifaximin in patients with IBS Diarrhoea. Methodology89 participants who met ROME-III criteria for IBS were included. 49 patients received 400mg of rifaximin thrice daily and 40 received placebo for 14 days. Patients were followed up one week after starting therapy, then one week later after completing therapy, next followup 1 month later and last visit 3 months after completion of therapy. During each visit, patients were enquired about symptoms such as improvement in frequency and consistency of stools, abdominal pain and bloating. Results Patients who were treated with rifaximin had adequate relief of IBS symptoms when compared to placebo group. Rifaximin provided better relief of abdomen bloat (78.72 vs 40.0), improvement in stool frequency (72.34 vs 47.5), and improvement in stool consistency (72.34 vs 47.5) than placebo. But the relief of abdominal pain is better with placebo (72.5 vs 44.68) than rifaximin. Rifaximin is well tolerated without any undue side effects. Conclusion In patients with diarrhea predominant IBS, rifaximin provided adequate relief of their symptoms without any undue side effects. Keyword: Key Words Irritable Bowel Syndrome, Diarrhoea, Rifaximin

Introduction:
Irritable Bowel Syndrome (IBS) is defined as the presence of recurrent abdominal pain in association with altered bowel habits in the absence of an organic pathology. Although IBS is a common disorder associated with significant negative impact on quality of life, therapeutic options are limited, especially in patients with IBS–D. The pathogenesis of IBS is not completely understood. Several studies have
investigated the role of altered gut microflora in IBS and have proved the association between IBS and SIBO. Several clinical trials have established the beneficial effect of antibiotics aimed at altering gut microbiota thereby improving IBS symptoms. Rifaximin, a non-systemic antibiotic, is an emerging drug which has shown efficacy in the treatment of diarrhea predominant IBS. The aim of the present study is to evaluate the efficacy of rifaximin in patients suffering from IBS-D.

**Methodology:**

This is a prospective case control study. The study is conducted at the Department of Digestive Health and Diseases from June 2012 to May 2013. Eligible patients who were diagnosed as IBS according to ROME III diagnostic criteria for IBS were included in the study. All those included patients had symptoms of chronic diarrhea, abdominal bloating and recurrent abdominal pain at the time of screening and randomization. Exclusion criteria includes constipation – predominant IBS, a history of inflammatory Bowel Disease, HIV, patients who were on alosetron, tegaserod, lubiprostone, antidiarrhoeals, antispasmodics, probiotics, narcotics, patients who had taken antibiotics within the previous 1 month, or rifaximin within 2 months before entering the study. All patients provided written informed consent before the initiation of the study.

**Study design:**

All eligible patients who were included in the study were randomly assigned either to rifaximin or placebo. Patients who were included in the rifaximin group were given rifaximin 400mg thrice daily for 2 weeks, and those who were included in the placebo group received placebo for 2 weeks.

After completing the 14-day study treatment period, patients were evaluated for 3 months. Study visits were conducted on days 1, 7, 14 and by the end of 1 month and 3 months. During each visit, patients were assessed for drug compliance and the improvement in symptoms such as abdominal pain, abdominal bloating, stool frequency, and stool consistency. All patients were assessed for any adverse effects of the drug.

**Results:**

89 participants who met ROME-III criteria for IBS were included. 49 patients received 400mg of rifaximin thrice daily and 40 participants received placebo for 14 days. In the rifaximin group, 1 patient discontinued drugs and another patient was lost for follow up. Both the patients were excluded from the study (fig 1).

Study Flow Chart

Total number of cases - 87. Males - 36 (41.37%). Females - 51 (58.62%). Age ranged from 20–50 years.
Gender Distribution
In rifaximin group, 21 (44.68%) pts had improvement of abd pain, 34 (72.34%) had improvement in stool frequency, 34 (72.34%) had improvement in consistency of stools, 37 (78.72%) had improvement in abdomen bloat after 2 weeks of rifaximin therapy (Fig: 3).
In the placebo group, 29 (72.5%) pts had improvement of abd pain, 19 (47.5%) had improvement in stool frequency, 19 (47.5%) had improvement in consistency of stools, 16 (40.0%) had improvement in abd bloat after 2 weeks of placebo (Fig: 3).

Comparison Of Symptom Response
Rifaximin provided better relief of abdomen bloat (78.72% vs 40.0%), improvement in stool frequency (72.34% vs 47.5%), and improvement in stool consistency (72.34% vs 47.5%) than placebo. But the relief of abdominal pain was better with placebo (72.5% vs 44.68%) than rifaximin. Rifaximin was well tolerated without any serious side effects. The beneficial effect of rifaximin was sustained throughout the study period even after completion of the 2 weeks treatment duration whereas patients in the placebo group reported recurrence of symptoms after stopping the drug.

Discussion
IBS, the most common functional gastrointestinal disorder is characterised by recurrent abdominal pain along with altered bowel habits in the absence of organic disease. The symptom burden may be severe, leading to a reduced quality of life. The diagnosis of IBS is currently based on the ROME III criteria: recurrent abdominal pain or discomfort at least 3 days per month associated with 2 or more of the following: improvement with defecation; onset associated with a change in frequency of stool and onset associated with a change in form of stool. IBS can be either diarrhoea predominant or constipation predominant. Diarrhoea predominant IBS (IBS-D) affects about one-third of patients with IBS, which is observed in about 12% of people across five continents. Management of IBS has been unsuccessful partly because of our poor understanding of its pathophysiology. There is growing evidence that overgrowth of bacteria in small intestine may play a role in the pathophysiology of IBS. Studies have shown that about 65-84% of patients with IBS presents with SIBO. It is more common in patients with IBS and predominant bloat and diarrhea. Based on the existing epidemiological and pathophysiological link between SIBO and IBS, it has been postulated that...
administration of antimicrobials could be helpful for eliminating symptoms of IBS.\(^2\)\(^-\)\(^5\) However, antimicrobials used should possess several characteristics such as 1) activity against implicated pathogens. 2) favourable pharmacokinetics in the gut lumen; 3) lack of absorption in the systemic circulation. 4) lack of toxicity and 5) lack of induction of antimicrobial resistance. Rifaximin is one such drug that fulfils all the above features. It is a orally administered antimicrobial with limited systemic absorption and considerable potency against bacteria implicated in SIBO.\(^2\)\(^-\)\(^5\) A double – blind randomized prospective trial had compared the efficacy of Rifaximin with that of placebo on the global symptom improvement of IBS.\(^6\)\(^,\)\(^7\)

**Results:**

demonstrated a significant improvement of global symptoms of rifaximin treated patients compared with placebo treated patients. The major benefit of rifaximin treatment was shown in patients with bloating. The beneficial effect of rifaximin was maintained for 10 weeks after stopping therapy.\(^6\)\(^,\)\(^7\)\(^,\)\(^8\)\(^,\)\(^9\) Our study also showed similar results demonstrating greater improvement in patients presenting with abdominal bloat. Similarly our study also showed a sustained improvement of symptoms lasting for several weeks even after stopping therapy.\(^6\)\(^,\)\(^7\)\(^,\)\(^8\)\(^,\)\(^9\)\(^,\)\(^10\)

Available retrospective datas have provided a comparison of efficacy between rifaximin, neomycin, and beta lactums in the management of patients with IBS and SIBO. Results have shown that 69% of patients administered with rifaximin reported clinical improvement compared with 38% of neomycin and 44% of beta lactum treated patients.\(^11\)

One study has shown limited risk for acquisition of resistant isolates after treatment with rifaximin. Rifaximin has also been shown to present favourable pharmacokinetics in the gut lumen. Systemic absorption is lower than 0.4% and it has not been implicated for the induction of clostridium difficile colitis.\(^12\) In our study, rifaximin was well tolerated, with no undue side effects. Most of the previous studies have shown that rifaximin is safe, without any reported adverse effects.\(^10\)\(^,\)\(^11\)\(^,\)\(^12\)

**CONCLUSION:**
The nonabsorbable antibiotic rifaximin had been proven to be a novel treatment option for IBS-D. The benefit of this treatment modality is the short duration of treatment regimen, accompanied by the sustained benefit that extends well beyond the treatment period. The lack of reported systemic side effects with rifaximin is another major advantage. These factors make rifaximin an important strategy in the treatment of IBS predominant diarrhea.

**References:**


4. Kassinen et al. The fecal microbiota of IBS patients differs differently from that of healthy subjects. Gastroenterology 2007;133:24-33

6. Pimentel et al. Rifaximin therapy for patients with IBS without constipation. NEJM 2011;364:22-32


