



A PROSPECTIVE OBSERVATIONAL STUDY ON USAGE OF RIFAXIMIN FOR TREATING GUT MICROBIOTA IN GASTROINTESTINAL AND LIVER DISORDERS.

Gastroenterology

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ABSTRACT

Background : Rifaximin is an antibiotic that selectively targets gastrointestinal tract, with a wide range of antimicrobial activity, minimal drug interactions, excellent safety profile, and negligible impact on the intestinal microbiome. **Aim Of The Study :** To assess the indications, symptomatic score, dosage and duration of rifaximin in GI and liver disorders. **Methods:** Patients participated in this study for a period of six months. Data was collected from 200 Patients including both sexes, who were administered rifaximin for gastrointestinal and liver disorders. Disease severity before and after rifaximin administration was calculated using evaluation of GI symptom questionnaire. **Results:** In this study men 133 (66.5%) were more prevalent than women 67(33.5%). The dose of rifaximin varied between 200 mg TID to 550mg BD based on the present prescription pattern. Higher dose was used for hepatic encephalopathy in liver disease, low dose like 200mg TID was used for travellers (infective) diarrhea. The mean improvement for symptomatic score from the baseline has a significance level of 0.0001. **Conclusion:** Rifaximin therapy in patients with Gastrointestinal and liver disorders has shown to be improved by using questionnaire for evaluation of symptom score. Patients who received rifaximin reported significantly greater mean improvement in symptomatic scores for optimal results, appropriate dosing for the proper indication is important to improve outcomes and prevention of resistance. Appropriate therapy with rifaximin improved the quality of life in subjects requiring the medication.

KEYWORDS

Gastrointestinal disorders, Gut microbiota, Antimicrobial activity.

INTRODUCTION:

Rifaximin was endorsed in the United States in 2004, although its utilization began in 1987 when it was first approved in Italy.³ This oral antibacterial drug, chemically referred to as 4-deoxy-4'-methylpyrido [1',2'-1,2] imidazo-[5,4-c]-rifamycin SV, is a semi-synthetic, non-systemic, and non-absorbable medication with an extensive range of activity.¹ Exhibiting both in vitro bactericidal and bacteriostatic effects, it shows broad-spectrum activity against both gram-positive and gram-negative aerobic and anaerobic bacteria.³ Rifaximin, as a rifamycin antimicrobial agent and an analog of rifampin, attaches itself to the bacterial DNA-dependant RNA polymerase β -subunit and prevents RNA production. The addition of a pyridoimidazole ring into the rifampin structure renders rifaximin mostly water-insoluble and poorly absorbable. Intraluminal and fecal drug concentrations are notably higher, surpassing the minimal inhibitory concentration values observed in vitro against a diverse array of pathogenic organisms.³ Clinicians favour this medication for therapeutic purposes, as it has virtually no significant contraindications or known toxicity. Moreover, its distinctive characteristics, such as a wide-ranging antimicrobial effect, elevated fecal concentrations, an outstanding safety record, minimal interactions with other drugs, and minimal impact on the intestinal microbiome, along with low systemic absorption, position it as an optimal choice for patients dealing with various gastrointestinal disorders.^{1,3} Rifaximin reaches high concentrations within the gastrointestinal lumen, allowing it to effectively treat various gastrointestinal diseases without causing systemic effects.¹ The incidence of bacterial mutation and drug resistance to rifaximin in extra-intestinal bacteria is very low because the drug primarily acts within the intestine. Long-term usage of rifaximin can cause resistant bacterial mutations in the gastrointestinal system.¹ While rifaximin did not alter the overall structure of the gut microbiota, it induces an increase in concentration of Bifidobacterium, Atopobium and Faecalibacterium prausnitzii.¹ Patients treated with rifaximin may develop adverse drug reactions, including nausea, gastrointestinal upset, fatigue, peripheral edema, dizziness, and muscle spasms. In addition, long-term use has been associated with bacterial superinfections.¹ Rifaximin is administered orally and is typically available in 200 mg, 400 mg, 500mg, 550 mg tablets. The minimal absorption of rifaximin in the gastrointestinal tract increases its fecal concentrations of the drug and reduces its systemic toxicity. Studies involving radio-

labeled rifaximin have shown that less than 0.4% of the drug is detectable in the blood and urine, with undetectable levels in the bile and breast milk, and 97% of the drug is excreted unchanged in the stool after oral administration.¹ Drug interactions with rifaximin are rare due to its virtually nonabsorbable nature. Due to minimal systemic absorption, no dosage adjustments are required in cases of hepatic dysfunction, including liver failure and hepatic encephalopathy.¹

METHODS:

The study was conducted in the Gastroenterology department of Yashoda Hospital, Secunderabad, Telangana, a multi-specialty hospital, which caters to the services of people from all over the country. Patients who were undergoing regular follow-ups for gastrointestinal and liver disease were included in the study. The purpose of the study is to evaluate the usage of rifaximin in treating the gut microbiota in gastrointestinal and liver diseases. Prior to the study, all patients were informed about the study and procured their consent. Questionnaire for evaluation of symptom score were assessed regarding the patient's disease symptoms score before and after treatment with rifaximin. This observational cohort study included both male and female inpatients and outpatients over 18 years of age with specific gastrointestinal and liver diseases and were prescribed rifaximin as part of their treatment plan. Patients who were below 18 years of age, pregnant and breastfeeding women, individual with known allergies or hypersensitivity to rifaximin, patients taking other antibiotics and those who had undergone recent GI surgeries were excluded. The institutional review board at Yashoda Hospital granted permission to conduct the study.

A comprehensive data collection form was designed to capture demographic details of subjects (name, age, sex, etc.), past medical history, present medication history, allergies, diagnostic tests, haematology and other biochemical investigations, indications, drugs prescribed, social history, personal history, comorbidities, dosage and treatment duration of rifaximin for GI and liver disease, and other necessary information. A total of 200 patients who satisfied the pre-determined criteria were included in the study and the requisite data were collected. This study evaluated the impact of rifaximin on pre and post treatment, various indications for which it is proposed,

dosages and duration of treatment usually used in clinical practice. The assessment of symptoms utilized the Research gate Evaluation of Gastrointestinal Symptoms questionnaire at baseline and 1-month post-treatment, where each item was rated on a 6-point scale (0- None, 6- Worst).²³ A high mean score was found in this study among 200 patients with gastrointestinal disorders.

RESULTS :

Table I : Distribution Based On Gender

GENDER	FREQUENCY	PERCENTAGE
MALE	133	66.5%
FEMALE	67	33.5%

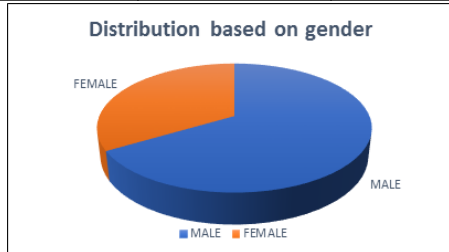


Figure 1: Gender wise distribution

Table II: Distribution Based On Age

Age	Frequency	Percentage
18-40	62	31%
41-60	88	44%
61-80	47	23.5%
81-100	3	1.5%

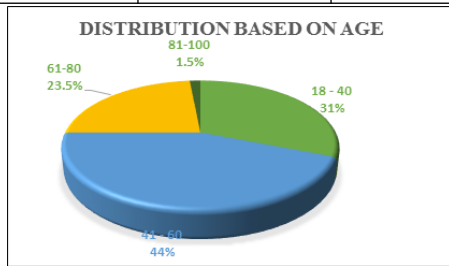


Fig 2: Age wise distribution

Table III: Distribution Based On Different Indications Of Gastrointestinal And Liver Disorders In Rifaximin Therapy

Indications	Number (n)	Percent age	p-value
Chronic liver disease	69	34.5	
Inflammatory bowel disease	25	12.5	
Small intestinal bacterial overgrowth	22	11.0	
Irritable bowel syndrome	33	16.5	
Diverticular disease	3	1.5	0.0001
Clostridium difficile infection	1	0.5	
Travelers/diarrhoea	33	16.5	
Subacute intestinal obstruction	5	2.5	
Spontaneous bacterial peritonitis	9	4.5	

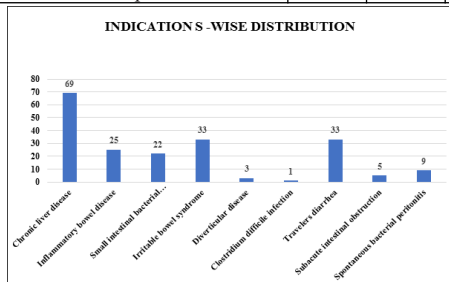


Figure 3: Indication wise distribution as per rifaximin therapy.

Table IV: Evaluation Of Symptoms Mean Improvement Score Before And After Rifaximin Treatment

Symptomatic score	Mean
Score before treatment	15.21

Score after treatment	5.60
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Table V : Paired T-test Values For Evaluation Of Symptoms Mean Improvement Score Before And After Rifaximin Treatment

Paired Differences	t		P-Value
	Lower	Upper	
Score before Treatment -Score after	9.231	9.995	49.581 0.0001

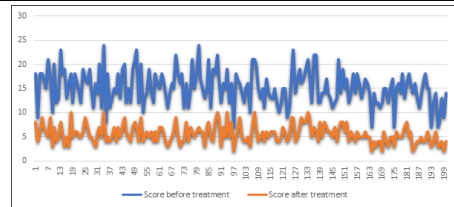


Figure 4: Symptomatic scores before and after rifaximin treatment.

Here blue graph indicates the symptomatic score before rifaximin treatment and the orange graph indicates the symptomatic score after rifaximin treatment.

Table VI : Distribution Based On Prescribed Dose And Duration

INDICATIONS	DOSE	DURATION
Irritable bowel syndrome	400 mg BD	14 Days
Small intestinal bacterial overgrowth	400 mg BD	14 Days
Clostridium difficile infection	400 mg BD	14 Days
Chronic liver disease	550 mg BD	14 Days
Inflammatory bowel disease	400 mg BD	14 Days
Traveller's diarrhoea	200 mg TID	7 Days
Spontaneous bacterial peritonitis	400 mg BD	14 Days
Subacute intestinal obstruction with abdominal pain	400 mg BD	14 Days
Diverticular disease	200 mg TID	14 Days

DISCUSSION

Rifaximin is gaining attention for its potential effectiveness in a multitude of gastrointestinal diseases. Patients who had received rifaximin showed improved symptoms after treatment in the current study and continued to receive rifaximin. No serious adverse events or deaths were reported in this study. Patients receiving rifaximin demonstrated a lower rate of all-cause hospitalization.

During 6 months duration we found 34.5% of CLD patients, 16.5% of IBS patients, 16.5% of Traveller's diarrhoea patients, 12.5% of IBD patients, 11% of SIBO patients, 4.5% of SBP patients, 2.5% of Sub acute intestinal obstruction patients, 1.5% of Diverticular disease patients and 0.5% of Clostridium difficile infection patients.

Significant improvements in overall symptomatic scores were observed after 1 month of rifaximin treatment compared to baseline. Patients in the rifaximin group reported notably greater mean enhancements in scores across various symptoms such as abdominal pain, bloating, epigastric pain, bloating, hematemesis, diarrhea, constipation, flatulence, vomiting, belching, heartburn. Rifaximin demonstrated good tolerance, with a similar incidence of adverse events.

In study, the mean symptomatic score before treatment was 15.21 and the mean symptomatic score after treatment was 5.60. Following rifaximin treatment, the mean score reduced to 5.60. The composite results showed a positive outcome for all 200 patients, with a significant reduction in the mean score from 15.21 to 5.60, indicating substantial improvement. This illustrates the enhanced therapeutic efficacy of prescribing rifaximin. The level of significance for symptomatic score before and after treatment was found to be 0.0001.

CONCLUSION:

The study unequivocally established that rifaximin, when given in appropriate doses and duration, significantly improved symptomatic scores in patients afflicted with gastrointestinal and liver disorders. Patients administered rifaximin reported a considerable improvement in quality-of-life scores for various symptoms. A questionnaire was used to assess symptoms and the results substantiated a significant

improvement in mean scores from the baseline in the particular duration of treatment.

Declarations

Funding : No funding source

Conflict Of Interest : None declared

Ethics Committee Approval Number: RP/24/2023 (Yashoda Academy of Medical Education And Research)

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