Original Research Paper

Volume - 11 | Issue - 10 | October - 2021 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Gastroenterology

PREVALENCE OF SIBO IN IBS-D PATIENTS AND ROLE OF RIFAXIMIN IN THE MANAGEMENT

Dr V Venkata Ranga Reddy	Professor and Head of Department, Department of Gastroenterology, Kurnool Medical college.
Dr G Mohan Reddy	Associate Professor, Department of Gastroenterology, Kurnool Medical college.
Dr Rakesh Garlapati*	Resident, Department of Gastroenterology, Kurnool medical college. *Corresponding Author
Dr Nirdesh Chauhan	Resident, Department of Gastroenterology, Kurnool Medical college.

ABSTRACT **Background:** Irritable bowel syndrome (IBS) is characterized by the presence of abdominal pain associated with altered bowel movement. There is a paradigm shift from Brain-Gut axis disorder, as previously thought, to Gut-Brain axis disorder, which has shown increased importance to gut dysbiosis, including small intestinal bacterial overgrowth (SIBO). SIBO can be diagnosed as the presence of excess bacteria (either quantitative [>105 cfu/mL] or qualitative [excess bacteria of colonic origin] in the small intestine accompanied by intestinal or extra-intestinal symptoms thought to result from this excess. The gold standard test for SIBO has customarily been considered the quantitative culture of a jejunal aspirate. This, however, is invasive and costly as it generally requires endoscopy for sample collection. GHBT is a reliable test to diagnose SIBO with about 80-100% specificity and 40% sensitivity.

Method: This study was done in the department of gastroenterology, Kurnool medical college, Kurnool, to find the prevalence of SIBO in IBS-D patients by using the Glucose hydrogen breath test (GHBT) (LactoFAN2*) and response to Rifaximin. Eighty diagnosed cases of IBS-D (using ROME IV criteria) were subjected to GHBT using 100g of glucose in 250ml water and breath samples were taken at baseline and at 20 min interval for 2 hours. A hydrogen increase of ≥12 parts per million (ppm) over baseline is considered diagnostic of SIBO.

Results: Out of 80 patients, only 18 were positive for SIBO & were treated with rifaximin. After 14days, out of 18 patients, only 15 showed clinical improvement and repeat GHBT in these 15 patients was also negative.

Conclusion: The prevalence of SIBO in IBS-D patients is 22.5% using GHBT and use of rifaximin, was associated with good clinical response in treating SIBO in IBS-D patients.

KEYWORDS : IBS, SIBO, Rifaximin, GHBT

INTRODUCTION

Irritable bowel syndrome (IBS) is an important disease entity due to its high prevalence, substantial morbidity[1]. IBS is characterized by the presence of abdominal pain associated with altered bowel movements. Rome IV criteria, is useful in clinical practice and can be used to make a positive clinical diagnosis. Because of non-uniformity in the definition, IBS's prevalence varies from 1%-45% worldwide and in India prevalence is about 11%- 14%[2].

There is a rise in evidence showing that GI symptoms arise first, and a new-onset mood disorder develops later. The intestinal inflammation, the cytokine response, and the intestinal microbiome implicate in precipitating such gut-to-brain alterations. This paradigm shift from Brain-Gut axis disorder, as previously thought, to Gut-Brain axis disorder has shown increased importance to gut dysbiosis, including small intestinal bacterial overgrowth (SIBO)[4].

SIBO can be diagnosed as the presence of excess bacteria (either quantitative [$>10^5$ cfu/mL] or qualitative [excess bacteria of colonic origin] in the small intestine accompanied by intestinal or extra-intestinal symptoms thought to result from this excess.[3] The gold standard test for SIBO has customarily been considered the quantitative culture of a jejunal aspirate. This, however, is invasive and costly as it generally requires endoscopy for sample collection. GHBT is a reliable test to diagnose SIBO with about 80-100% specificity and 40% sensitivity.[5]

Very few studies showed a prevalence of SIBO specifically in IBS-D patients, and no study using recent ROME-IV criteria. Using ROME-IV criteria to diagnose IBS-D and Glucose hydrogen breath test for SIBO, we have conducted this study to find the prevalence of SIBO in IBS-D patients and the role of Rifaximin in treating these patients.

METHODS

This hospital-based prospective study was conducted in government general hospital, Kurnool, Andhra Pradesh. Patients visiting gastroenterology OPD who are fulfilling the ROME IV criteria for IBS-D were included in the study.

Individuals with predisposing conditions for SIBO (e.g., diabetes mellitus, scleroderma, prior small intestinal surgery, thyroid disorder) and patients who had taken systemic antibiotics, anti-fungal, anti-motility drugs, proton pump inhibitors in the previous month were excluded from breath testing.

Using Rome IV criteria, 80 patients (45female & 35male) were diagnosed with IBS-D. These patients were then subjected to GHBT while considering all pre-requisites. Breath samples were obtained at baseline and every 20 minutes up to 120 min following ingestion of 100 g of glucose dissolved in 250 mL of water. The baseline and post-glucose ingestion peak values for hydrogen were recorded for each patient. A hydrogen increase of ≥12 parts per million (ppm) over baseline is considered diagnostic of SIBO.

Patients, who were positive for SIBO, received rifaximin 400 mg every 8 hours for 14 days. These patients underwent a second GHBT after stopping therapy to assess the eradication of SIBO. At the same time, all patients were assessed by questionnaire for response to rifaximin to treatment.

Institutional ethical Committee has approved the study, and consent of each subject was taken.

RESULTS:

Among 80 IBS-D patients, 46 (57.5%) were male and 34 (42.5%) were female. Mean age among IBS-D patients was 31.06 years.

Out of 80 IBS-D patients, 18(22.5%) were SIBO-positive and 62(77.5%) were SIBO-negative. Out of these 18 SIBO-positive patients, 11 were male and 7 were female.

SIBO	Count	%
Positive	18	22.5%
Negative	62	77.5%
Total	80	100.0%

During initial HBT, mean baseline hydrogen level in patients who were diagnosed as SIBO-positive was 6.2ppm & mean peak hydrogen level was 19.56ppm while in SIBO- negative IBS-D patients, mean baseline hydrogen level was 5.31ppm & mean peak hydrogen level was 10.08ppm.

In SIBO-positive patients, initial mean baseline & peak hydrogen level were 6.22ppm & 19.56ppm respectively and after rifaximin therapy, mean baseline & peak hydrogen level were 4.28ppm & 7.94ppm respectively.

HBT Baseline and Peak	**Positive**		
	Male	Female	Total
Initial HBT baseline	6.00	6.57	6.22
Initial HBT Peak	19.27	20.00	19.56
Post-Rifaximin HBT Baseline	4.00	4.71	4.28
Post-Rifaximin HBT Peak	7.55	8.57	7.94

In comparison between initial and post-rifaximin in base line GHBT and peak GHBT, both of them were found to be significant at 95% confidence level. Probability value of pre and post base Line HBT is close to 0.000 and Peak HBT is close to 0.000. Both these values are less than the tolerance limit of 0.000. Hence it can be inferred that base line HBT and peak HBT have shown a significant difference in pre and post Rifaximin. Mean values of pre and post base line HBT is 6.22 and 4.28 and the mean value of pre and post peak HBT is 19.56 and 7.94

Paired Sample t-test												
		Descriptive Statistics				**Correlation**		**95% Confidence Interval of the Difference**		**T**	**df**	**Sig.**
		Mean	N	Std. Deviation	Std. Error Mean	Correlation	Sig.	Upper	Lower			
Base Line HBT	Initial	6.22	18	1.927	0.454	0.474	0.047	1.101	2.788	4.862	17	0.000
	Post-Rifaximin	4.28	18	0.958	0.226							
Peak HBT	Initial	19.56	18	1.580	0.372	0.010	0.969	10.465	12.757	21.377	17	0.000
	Post-Rifaximin	7.94	18	1.662	0.392							

DISCUSSION

In this study, only diarrhoea-predominant IBS patients were considered because symptoms of IBS-D overlap with SIBO. And also constipated subsets of IBS patients have methanogenic bacteria in the gut that consume hydrogen to produce methane[6] and can give a false negative result on a hydrogen breath test..80 patients were included in the study of which 47 were male, and 33 were female. There was no statistically significant gender difference in IBS-D patients. However, many studies have shown that men with IBS were more likely to report diarrhoea-related symptoms than women with IBS[7].

In this study, we used a glucose hydrogen breath test to check for SIBO in 80 diarrhoea- predominant IBS patients. Lactulose HBT has low specificity because of the difference in the mean mouth –to- cecum transit time among the different populations. Hence, lactulose HBT should not be used to diagnose SIBO. Even the double-peak criterion to diagnose SIBO on lactulose HBT has lower sensitivity than glucose HBT (31% vs. 40%). Therefore, glucose HBT should be used for diagnosing SIBO[5]. The glucose hydrogen breath test is highly specific but quite insensitive. Out of these 80, 18 patients were positive for SIBO that accounts for 22.5%.

For the eradication of SIBO, rifaximin is one of the most studied antibiotics. According to two placebo-controlled trials (TARGET 1 and TARGET 2) by Pimentel et al[10], rifaximin effectively relieves global IBS symptoms. In a recent meta-analysis, the efficiency of rifaximin (two studies) in eradicating SIBO was 64.1% compared to 41% with other systemic antibiotics (metronidazole or tetracycline, p=0.003).

Similarly, in this study, SIBO positive IBS-D patients were treated with 14 days of rifaximin therapy (400 milligrams TID). After 14 days, all 18 patients who were positive for GHBT initially came out negative, suggesting eradication of SIBO by rifaximin. But according to the response given by these 18 patients to the question **"regarding all your symptoms of IBS, as compared with the way you felt before you started the study medication, have you, in the past 2weeks, had adequate relief of your IBS symptoms?"** in yes/no, 15 out of 18 (83.3%) were responders and 3 out of 18 (17%) were non-responders. The reason for no response can be because of the multifactorial pathogenesis of IBS.

The baseline HBT and peak HBT have shown a significant difference in pre and post rifaximin therapy. Mean values of pre and post rifaximin therapy baseline HBT is 6.22 and 4.28, and the mean value of pre and post rifaximin therapy peak HBT is 19.56 and 7.94. This concludes that, after rifaximin therapy, Base Line HBT and Peak HBT have reduced to 4.28 and 7.94 from 6.22 and 19.56, respectively. This observation was also reported by Majewski et al. [1], where rifaximin was used at a dose of 800mg per day for 4 weeks.

CONCLUSION

A significant subset of IBS-D patients has SIBO. These are the patients who can be treated successfully by antibiotics like rifaximin. Rifaximin effective in eradicating SIBO and improving global IBS symptoms like abdominal pain, bloating and diarrhoea.

REFERENCES

1. Drossman D, Corrazziari E, Delvaux M, et al. Rome III: the functional Gastrointestinal Disorders. 3rd ed. McLean, VA: Degnon Associates; 2006.
2. Lovell RM, Ford AC. Global prevalence of and risk factors for irritable bowel syndrome: A meta-analysis. Clin Gastroenterol Hepatol 2012; 10:712-21.
3. Feldman, M., Friedman, L. and Brandt, L., 2020. *Sleisenger And Fordtran's Gastrointestinal and Liver Disease*. 11th ed. Philadelphia, PA: Saunders/Elsevier, pp.2008-2020.
4. Grover M, Kanazawa M, Palsson OS, et al. Small intestinal bacterial overgrowth in irritable bowel syndrome: association with colon motility, bowel symptoms, and psychological distress. Neurogastroenterol Motil 2008; 20:998-1008.
5. Ghoshal UC, Ghoshal U, Das K, Misra A. Utility of hydrogen breath tests in diagnosis of small intestinal bacterial overgrowth in malabsorption syndrome and its relationship with oro-cecal transit time. Indian J Gastroenterol. 2006; 25:6–10.
6. Saad RJ, Chey WD. Breath testing for small intestinal bacterial overgrowth: maximizing test accuracy. Clin Gastroenterol Hepato 2014;12(12):1964–72.
7. Adeyemo MA, Spiegel BM, Chang L. Meta-analysis: do irritable bowel syndrome symptoms vary between men and women? Aliment Pharmacol Ther. 2010 Sep;32(6):738-55.
8. Chang L, Heitkemper MM. Gender differences in irritable bowel syndrome. Gastroenterology. 2002 Nov;123(5):1686-701
9. Makharia GK, Verma AK, Amarchand R, Goswami A, Singh P, Agnihotri A, Suhail F, Krishnan A. Prevalence of Irritable Bowel Syndrome: A Community Based Study from Northern India. J Neurogastroenterol Motil 2011; 17:82-87
10. Pimentel M, Lembo A, Chey WD, et al. Rifaximin therapy for patients with irritable bowel syndrome without constipation. N Engl J Med. 2011; 364:22–32
11. Hartmann G, Honikel KO, Knusel F, et al. The specific inhibition of the DNA-directed RNA synthesis by rifamycin. Biochim Biophys Acta. 1967; 145:843–844