Print ISSN: 2321-6379
Online ISSN: 2321-595X
DOI: 10.17354/ijss/2018/3

Original Article

Comparative Analysis of Anti Versus Probiotic in Patients with Irritable Bowel Syndrome

Vinod Mitla[1], Surinder Sharma[2], Syed Arshad Mustafa[3], Mohd. Ismail[4]

[1]Lecturer, Department of Internal Medicine, Government Medical College, Jammu, Jammu and Kashmir, India, [2]Medical Officer, Department of Health and Medical Education, Government District Hospital, Gandhinagar, Jammu, Jammu and Kashmir, India, [3]Associate Professor, Radiation Oncology, Government Medical College, Srinagar, Jammu and Kashmir, India, [4]Associate Professor, Internal Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India

Abstract

Background: Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder with high prevalence. It imposes a significant economic burden to the health-care system worldwide. Earlier IBS was thought to be a disease hard to categorize, difficult to diagnose and impossible to treat, but over the years, the pathophysiology and clinical paradigm of IBS have been well elucidated so are the therapeutic options and diagnostic strategies.

Objective: In our study, we tried to analyze the efficacy of antibiotic (rifaximin) versus probiotic (VSL#3) in alleviating symptoms of IBS.

Materials and Methods: Comparative efficacy of anti-biotic versus pro-biotic was assessed in 220 IBS patients with regard to improvement in global IBS symptoms. The study was conducted in the postgraduate Department of Medicine, Government Medical College, Srinagar, from February 2012 to September 2013 and all the enrolled patients had given informed consent before conducting this study.

Results: There was a significant improvement in global IBS symptoms in both the groups even after switchover of drugs in both the cohorts. The safety profile of both drugs was the same.

Key words: Irritable bowel syndrome, Rifaximin, VSL#3

INTRODUCTION

Irritable bowel syndrome (IBS) is a chronic gut disorder characterized by recurring symptoms of abdominal pain, bloating, and altered bowel function in the absence of any organic abnormality.[1] The prevalence of non-GI symptoms such as lethargy, poor sleep, backache,

nocturia, sense of incomplete bladder emptying, and early satiety is also seen more in patients of IBS.[2] IBS is seen to be slightly more prevalent in females,[3] whereas age and race do not seem to have any consistent effect on the symptoms.

Access this article online

www.ijss-sn.com

Month of Submission : 07-2018
Month of Peer Review : 09-2018
Month of Acceptance : 09-2018
Month of Publishing : 10-2018

The exact cause of IBS is not yet known, but factors likey implicated in its etiology include genetic influences, food intake habits, endocrine disturbances, malabsorption, post-operative changes, and stress.[4,5]

Disorders in gut motility have been observed in the stomach, small intestine, colon, and rectum of IBS patients.[6] Studies have pointed to a disturbance in cyclic pattern of gut motility involving greater frequency of the high frequency of high amplitude prolonged contractions and greater pre-prandial colonic motility.[7] Small bowel bacterial overgrowth has emerged as a possible cause of IBS.[8] In an analysis of 202 patients with IBS, around 78% of the patients were found to have bacterial overgrowth.[9]

Role of antibiotics has emerged in recent years due to good response of these drugs in symptom improvement and normalization of abnormal breath testing.[10] Patients with IBS are supposedly have an alteration in intestinal microbiota.[11] Hence, various antibiotics have been

Corresponding Author: Dr. Syed Arshad Mustafa, Associate Professor, Radiation Oncology, Government Medical College, Srinagar, Jammu and Kashmir, India. E-mail: syedarshad07@gmail.com

incriminated in the treatment of IBS including neomycin and rifaximin albeit with mixed results.[10,12]

Manipulation of intestinal microflora by probiotics has shown some symptomatic improvement in some studies[13] lending support to the evidence that intestinal microflora of IBS patients is different from that of healthy individuals.[14] This study was undertaken to evaluate the efficacy of rifaximin (a broad spectrum poorly absorbed antibiotic) with VSL#3 (Probiotic) in reducing symptoms in patients with IBS without constipation.

MATERIALS AND METHODS

This study was conducted in the Department of Internal Medicine Government Medical college, Srinagar, from February 2012 to September 2013. It was a monocentric, prospective, randomized study involving 220 patients. All the patients' fulfilling diagnostic criterion for IBS (ROME II CRITERIA) Table 1 were enrolled after obtaining proper informed consent. Eligible patients were rated for their abdominal pain on a 7 point Likert scoring system (with 0 indicating no pain at all; 1, hardly; 2, somewhat; 3, moderate; 4, a good deal; 5, a great deal; and 6, a very great deal) and for average daily consistency of their stools on a 5 point scale (1 indicating very hard stool; 2, hard; 3, formed; 4, loose; and 5 watery) over the course of at least 07 days.

Patients with constipation-predominant IBS were excluded from the study as were patients with inflammatory bowel disease, diabetes, uncontrolled thyroid disease, previous surgery, HIV infection, uncontrolled hepatic and renal disease, patients on antispasmodics, tegaserod, antipsychotics, pre-probiotics, and rifaximin.

Patients were randomized into two groups of "A" and "B" comprising 116 and 104 patients, respectively. The study was carried out in two phases whence in Phase 1, Group A received VSL#3 once daily for 2 weeks, and Group B rifaximin twice a day for 2 weeks. Patients were weekly monitored for 10 weeks for symptom improvement. After completion of Phase 1, Phase 2 study was carried out after a washout period of 4 weeks to eliminate the residual effect of Phase 1 drugs before starting Phase 2, crossover was done between two groups. Group A now received rifaximin and Group B received VSL#3.

Table 1: Rome II criteria

A	Continuous or recurrent abdominal pain	>12 weeks
B	>2 of the following	Relief with defecation Change in stool frequency Change in stool form
C	Onset of clinical symptoms	>1 year before diagnosis

The primary endpoint in both the groups was relief of IBS symptoms.

OBSERVATIONS AND RESULTS

None of the demographic parameters with respect to age, sex, and symptomatology were significant statistically [Table 2].

Majority of the patients (57%) in this study were in the age group of 21–40 years, as consistent with world literature [Table 3].[15]

Neither the difference in the number of patients in the two groups nor the duration of symptoms in two phases was statistically significant [Table 4].

In the Phase-1, there were 60 patients in the probiotic group and 32 patients in the rifaximin group who did not respond to treatment. Of the responders, there were 56 in the probiotic group while as 72 in rifaximin group [Table 5].

The response was sustained in 33 patients in the probiotic group and 46 patients in rifaximin group until the end of the study which was significant statistically.

Sustained response during the 3rd month was seen in 21 patients in the probiotic group while it was seen in 44 patients in rifaximin group in Phase 2. This finding was statistically significant. In this phase, 36 patients in the rifaximin group and 58 patients in the probiotic group did not respond to treatment [Table 6].

DISCUSSION

IBS with a prevalence of 10–20% of the general population globally[16] and 24.9% in the Kashmir valley[17] reduces the quality of life and imposes a significant economic burden to the health-care system.

Specific peripheral mechanisms like intraluminal intestinal irritants such as maldigested carbohydrates or fats, excess of bile acids, gluten intolerance, alterations in the microbiome, and genetic susceptibility to inflammation are thought to result in symptoms of IBS.[18] Other pathophysiological mechanisms that are considered in IBS are abnormalities intrinsic to the smooth muscle of the gut, visceral hypersensitivity, and central nervous system hypervigilance.[19-21] To reestablish the balance of nature within the intestinal flora to correct the disruption caused by antibiotic treatment, physicians in the past had done fecal microbiota transplantation in the patients with fulminant, life-threatening pseudomembranous colitis

Table 2: Baseline patient characteristics

Demographic parameters	Rifaximin	VSL3#	Remarks
No. of patients	104	116	NS
Age	39±13.559	39.22±11.248	NS
Age group (%)			
<50	83 (79.8)	97 (83.6)	NS
>50	21 (20.2)	19 (16.4)	
Sex (%)			
M	65 (62.5)	66 (56.9)	NS
F	39 (37.5)	50 (43.1)	
Average daily score			
Global IBS score	3.5±0.6	3.4±0.7	NS
IBS related bloating	3.4±0.7	3.4±0.8	NS
IBS related pain	3.3±0.7	3.2±0.8	NS
Stool consistency	3.9±0.3	3.8±0.8	NS
Average daily bowel movement	3.0±1.2	3.0±1.5	NS
Days with stool urgency (%)	81±22.5	81.9±22.6	NS
Duration of IBS symptoms	6.16±4.56	5.28±2.89	NS

IBS: Irritable bowel syndrome

Table 3: Distribution of patients in two groups in two phases of the study

Phase of study	Group		Total	Remarks
	Probiotic	Rifaximin		
	n (%)	*n* (%)	*n* (%)	
Phase-1	116 (52.7)	104 (47.3)	220 (100)	NS
Phase-2	96 (49.2)	99 (50.8)	195 (100)	
Total	212 (51.1)	203 (48.9)	415 (100)	
	100	100	100	

NS: Not significant; Chi-square - 0.159; *P* value - 0.695

Table 4: Distribution of duration of symptoms (years) in patients in two groups

Group	No. of pts	Mean±SD	Minimum age	Maximum age	remarks
Probiotic	116	5.28±2.89	1.0	15.0	NS
Rifaximin	104	6.16±4.56	1.5	30.0	NS

NS: Not significant ; *P* Value - 0.085. SD: Standard deviation

caused by Clostridium difficile and reported dramatic responses.[22] Rifaximin; a minimally absorbed antibiotic and probiotics are currently being used to restore the balance in the gut flora in patients of IBS. This study was conducted to evaluate the efficacy of two frontline modalities of treatment of IBS, i.e., antibiotic (rifaximin) versus probiotic (vsl3#). Functional gut disorders have predominantly been seen to be prevalent in the younger age group and female sex,[23] but in our study the majority of the patients (59.5%) were males.

Although diarrhea-predominant IBS has been seen to be more in men than in women,[24] in our study the observation

Table 5: Durability of relief of global IBS symptoms during the entire study period in the two groups in Phase-1

Months	Global IBS Symptom response		Total
	Probiotic *n* (%)	Rifaximin *n* (%)	
No response	60 (51.7)	32 (30.8)	92 (41.8)
1	56 (48.3)	72 (69.23)	128 (58.18)
2	44 (37.9)	58 (55.7)	102 (46.36)
3	33 (28.4)	46 (44.2)	79 (35.9)

Chi-square-14.041;*P* value 0.003. IBS: Irritable bowel syndrome

Table 6: Durability of relief of global IBS symptoms during the entire study period in the two groups in Phase-2

Months	Global IBS symptoms response		Total
	Rifaximin *n* (%)	Probiotic *n* (%)	
No response	36 (36.4)	58 (60.4)	94 (48.2)
1	63 (63.6)	38 (39.6)	101 (51.8)
2	51 (51.5)	27 (28.1)	78 (40.0)
3	44 (44.4)	21 (21.9)	65 (33.3)

Chi-square - 19.899; *P* value<0.0001. IBS: Irritable bowel syndrome

of association of constipation and gender in IBS was extended to indicate the female to male ratio significantly increases according to the severity of constipation

relative to the severity of diarrhea. As far as smoking is concerned, it has not been seen to be a factor implicated in IBS,[25] as is consistent in our analysis too. IBS comes with frequent relapses which could be managed by a short course of rifaximin as reported by studies that more patients in the rifaximin group had statistically significant ($P < 0.001$) relief of global IBS symptoms as compared to placebo in case of relapses.[26] In the VSL#3 group proportion of patients having satisfactory relief of IBS symptoms compared to placebo is not statistically significant.[27] The key secondary endpoint - adequate relief of IBS related bloating for at least 2 of the first 4 weeks after treatment was achieved in 47.1% of rifaximin group and 29.3% of the probiotic group in Phase 1 and 51.5% of rifaximin group and 34.4% of probiotic group in Phase 2 (after crossover).

Hence, rifaximin proved superior to probiotic in achieving both primary and secondary endpoints with sustained response at 12 weeks in a significant proportion of patients (nearly 49%).

Studies conducted by Pimentel and Kim have concluded that rifaximin and probiotic have significantly reduced bloating symptoms as compared to placebo ($P < 0.001$).[26,27]

No comparative study is available between rifaxim and probiotic vis a vis bloating is concerned. In daily global IBS symptoms 11.5% and 11.1% of the patients in the

rifaximin group and 9.5% and 7.3% patients in the VSL#3 group, hardly had any response to treatment in Phase 1 and Phase 2 (after crossover), respectively. However, 38.5% and 41.4% of patients in the rifaximin group and 23.3% and 27.1% of patients in the VSL#3 group reported their response to treatment as somewhat in Phase 1 and Phase 2, respectively. This was statistically significant.

In a worldwide analysis pertaining to the durability of response to rifaximin, it was concluded that the response was more over a course of 3 months on the basis of daily assessments.[26]

CONCLUSION

The primary endpoint was attained in 51% and 49.5% of the patients in rifaximin group and 37.1% and 34.4% in the VSL#3 group in Phase 1 and 2, respectively, with $P = 0.04$ in both the phases. The key secondary endpoint was attained in 47.1% and 51.5% of patients in the rifaximin group and 29.3% and 34.4% of patients in the VSL#3 group in Phase 1 and 2, respectively. The respective p values in Phase 1 and 2 were 0.008 and 0.021, respectively.

REFERENCES

1. American College of Gastroenterology Task Force on Irritable Bowel Syndrome, Brandt LJ, Chey WD, Foxx-Orenstein AE, Schiller LR, Schoenfeld PS, *et al.* An evidence-based position statement on the management of irritable bowel syndrome. Am J Gastroenterol 2009;104 Suppl 1:S1-35.
2. Triadafilopoulos G, Simms RW, Goldenberg DL. Bowel dysfunction in fibromyalgia syndrome. Dig Dis Sci 1991;36:59-64.
3. Heaton KW, Radvan J, Cripps H, Mountford RA, Braddon FE, Hughes AO, *et al.* Defecation frequency and timing, and stool form in the general population: A prospective study. Gut 1992;33:818-24.
4. Camilleri M. Management of the irritable bowel syndrome. Gastroenterology 2001;120:652-68.
5. Cann PA, Read NW, Cammack J, Childs H, Holden S, Kashman R, *et al.* Psychological stress and the passage of a standard meal through the stomach and small intestine in man. Gut 1983;24:236-40.
6. van Wijk HJ, Smout AJ, Akkermans LM, Roelofs JM, ten Thije OJ. Gastric emptying and dyspeptic symptoms in the irritable bowel syndrome. Scand J Gastroenterol 1992;27:99-102.
7. Vassallo MJ, Camilleri M, Phillips SF, Steadman CJ, Talley NJ, Hanson RB, *et al.* Colonic tone and motility in patients with irritable bowel syndrome. Mayo Clin Proc 1992;67:725-31.
8. Vantrappen G, Janssens J, Hellemans J, Ghoos Y. The interdigestive motor complex of normal subjects and patients with bacterial overgrowth of the small intestine. J Clin Invest 1977;59:1158-66.
9. Pimentel M, Chow EJ, Lin HC. Eradication of small intestinal bacterial overgrowth reduces symptoms of irritable bowel syndrome. Am J Gastroenterol 2000;95:3503-6.
10. Pimentel M, Chow EJ, Lin HC. Normalization of lactulose breath testing correlates with symptom improvement in irritable bowel syndrome. A double-blind, randomized, placebo-controlled study. Am J Gastroenterol 2003;98:412-9.
11. Ringel Y, Carroll IM. Alterations in the intestinal microbiota and functional bowel symptoms. Gastrointest Endosc Clin N Am 2009;19:141-50, vii.
12. Majewski M, Reddymasu SC, Sostarich S, Foran P, McCallum RW. Efficacy of rifaximin, a nonabsorbed oral antibiotic, in the treatment of small intestinal bacterial overgrowth. Am J Med Sci 2007;333:266-70.
13. George J, Hunt M, Kornbluth A, Legnani P. An open label pilot trial of high dose rifaximin in the treatment of patients with constipation predominant irritable bowel syndrome. Gastroenterology 2006;130 suppl4:A515.
14. Balsari A, Ceccarelli A, Dubini F, Fesce E, Poli G. The fecal microbial population in the irritable bowel syndrome. Microbiologica 1982;5:185-94.
15. Waehrens R, Ohlsson H, Sundquist J, Sundquist K, Zöller B. Low prevalence of irritable bowel syndrome in primary health care in four swedish counties. Scand J Prim Health Care 2013;31:132-7.
16. Everhart JE, Renault PF. Irritable bowel syndrome in office-based practice in the united states. Gastroenterology 1991;100:998-1005.
17. Iqbal S, Mir TA, Iqbal A, Malik GM. A study of prevalence of stress related functional gastrointestinal disorders in urban/rural civilian population and paramilitary population in Kashmir valley. Int J Curr Res2018;10:67022-6.
18. Camilleri M. Peripheral mechanisms in irritable bowel syndrome. N Engl J Med 2012;367:1626-35.
19. Lynn RB, Friedman LS. Irritable bowel syndrome. N Engl J Med 1993;329:1940-45.
20. Horwitz BJ, Fisher RS. The irritable bowel syndrome. N Engl J Med 2001;344:1846-50.
21. Mayer EA. Irritable bowel syndrome. N Engl J Med 2008;358:1692-69.
22. Eiseman B, Silen W, Bascom GS, Kauvar AJ. Fecal enema as an adjunct in the treatment of pseudomembranous enterocolitis. Surgery 1958;44:854-9.
23. Drossman DA, Li Z, Andruzzi E, Temple RD, Talley NJ, Thompson WG, *et al.* U.S. Householder survey of functional gastrointestinal disorders. Prevalence, sociodemography, and health impact. Dig Dis Sci 1993;38:1569-80.
24. Herman J, Pokkunuri V, Braham L, Pimentel M. Gender distribution in irritable bowel syndrome is proportional to the severity of constipation relative to diarrhea. Gend Med 2010;7:240-6.
25. Farzaneh N, Ghobaklou M, Moghimi-Dehkordi B, Naderi N, Fadai F. Effects of demographic factors, body mass index, alcohol drinking and smoking habits on irritable bowel syndrome: A case control study. Ann Med Health Sci Res 2013;3:391-6.
26. Pimentel M, Lembo A, Chey WD, Zakko S, Ringel Y, Yu J, *et al.* Rifaximin therapy for patients with irritable bowel syndrome without constipation. N Engl J Med 2011;364:22-32.
27. Kim HJ, Camilleri M, McKinzie S, Lempke MB, Burton DD, Thomforde GM, *et al.* A randomized controlled trial of a probiotic, VSL#3, on gut transit and symptoms in diarrhoea-predominant irritable bowel syndrome. Aliment Pharmacol Ther 2003;17:895-904.

How to cite this article: Mitla V, Sharma S, Mustafa SA, Ismail M. Comparative Analysis of Anti Versus Probiotic in Patients with Irritable Bowel Syndrome. Int J Sci Stud 2018;6(7):15-18.

Source of Support: Nil, **Conflict of Interest:** None declared.