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Research Article

A comparative prospective study in the management of *Helicobacter pylori* infection using *Lactobacillus reuteri* Vs conventional therapy

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Abstract

Background: *H*elicobacter *pylori* (*H. pylori)* infection has become a remarkable worldwide health problem. The eradication of H. pylori has become a challenge. Probiotics have proven beneficial in reducing the side effects and increases patient compliance. *Lactobacillus reuteri* (*L. reuteri*) is frequently used probiotic and considered safe for human consumption. The aim of this study was to compare the effectiveness of a probiotic and conventional antibiotic triple therapy in the management of *H. pylori* infection.

Methods: This was a prospective observational study carried out for a period of six months. Patient data were extracted from their medical records. Treatment outcome was evaluated based on the report of Rapid Urease Test (RUT). Symptoms were assessed using Gastrointestinal Symptom Rating Scale (GSRS). Descriptive statistics were used to summarize patient characteristics. T-test, chi square test and one way ANOVA were used wherever appropriate.

Results: A total of 105 patients with confirmed *H. pylori* infection were included, of which 42% were males and 58% were females. The mean age of three group patients were 38.03±10.68, 34.00±13.36 and 36.11±13.37 years. Eradication rate noted in *Lactobacillus reuteri* only treatment was 86%, eradication rate noted in *Lactobacillus reuteri*+ ppi was 86% and in antibiotic group was 92%. Patients with three different treatments have shown significant improvement in gastrointestinal symptoms ($p < 0.001$).

Conclusion: The overall data suggest that *L. reuteri* is recommended for a better eradication rate and reduced gastrointestinal symptoms. Though conventional triple therapy of *H. pylori* has shown an increased eradication rate and significant improvement in gastrointestinal symptoms, there was no great difference when compared with *L. reuteri* treated patients.

Keywords: *H. pylori*, Triple therapy, *L. reuteri,* Eradication, Gastrointestinal symptoms

BACKGROUND AND AIM

Helicobacter pylori (*H. pylori*) is a widespread microaerophilic, gram-negative, spiral- shaped bacterium that infects at least 50% of the global population. *H. pylori* can withstand the acid environment of the stomach because of its ability to adhere to the gastric mucosa, colonizing the mucosal lining of the stomach[1,2]. The majority of *H. pylori* carriers remain asymptomatic. But it is associated with many gastrointestinal diseases such as peptic ulcer, gastric cancer, and rarely mucosa-associated lymphoid tissue lymphoma. *H. pylori* infection has become a remarkable worldwide health problem[3]. The prevalence of *H. pylori* infection differs between regions of the developing world. In some developing countries, the prevalence of *H. pylori* is about 80–90%[4].The eradication of H. pylori has become a challenge in many parts of the world. Therapeutic options for *H. pylori* infection include different combinations of proton pump inhibitors associated with two or three antibiotics for the purpose of eradication. Alas, this approach has higher risks of side effects that lead to poor compliance and this demands the introduction of new antimicrobial agents. Few researchers proved the use of probiotics during the first-line *H. pylori* therapy that improved the patient's compliance and dropped gastrointestinal symptoms[5,6].

A probiotic is defined as a living microbial species that shows a constructive effect on bowel microecology on administration. The most studied probiotics are lactic acid-producing bacteria, particularly *Lactobacillus*[7]. Probiotics have proven beneficial in reducing the side effects of antibiotics and increases patient compliance. *Lactobacillus reuteri* (*L. reuteri*) is one species of lactobacillus which is safe for human consumption and also exerts an inhibitory effect on the settlement of human gastric mucosa by *H. pylori*[8]. This strain acts against *H. pylori* in the stomach by specifically binding and co-aggregating. Binding to *L. reuteri* masks surface structures of *H. pylori* and severely impedes its motility. The aggregated *H. pylori* no longer adhere to the gastric mucosa and the *Lactobacillus- Helicobacter* complexes are flushed out of the stomach[9]. Several studies reported supplementation with *L. reuteri* in both symptomatic and non-symptomatic *H. pylori* infected subjects shown a clear reduction of infection load after 4 weeks of use and improvement in symptoms

associated with the infection. In addition to this, certain revealed *L. reuteri* strains together with proton pump inhibitors (PPI) in the absence of antibiotics, may eradicate H. pylori infection at least in 50% of the treated patients[10,11].

The aim of our study was to compare the effectiveness of a probiotic and conventional antibiotic triple therapy in the management of helicobacter pylori infection in patients with severe gastrointestinal manifestations.

METHODS

The present prospective observational study was carried out at the Department of Gastroenterology, Princess Esra Hospital, Shah Ali Banda, Hyderabad for a period of six months. People with the following criteria were allowed to participate in this study: a) Confirmed H. pylori infection; b) Age of 18 to 70 years. Patients with the following criteria were excluded: a)Chronic diseases such as renal failure and cirrhosis, pan gastritis, peptic ulcers; b) Malignancies; c) Gall bladder disorders; d)Prior upper digestive tract surgery; e)Prior probiotic therapy in the last month; f) Antibiotics, PPIs and H2RA therapy in the previous 4 weeks; g) Known allergy to antibiotics.All patients gave written informed consent before participation. A complete history of the patients, laboratory investigations, treatment chart were extracted from their medical records and documented in a suitably designed individual case record form. This included their age, gender, gastrointestinal symptoms, report of Rapid Urease Test (RUT), drug chart. The changes in symptoms were recorded using the Gastrointestinal Symptom Rating Scale (GSRS) at baseline and post treatment.

Study outcomes

The primary outcome was comparing the effectiveness of probiotic (*L. reuteri*) and conventional triple therapy in the suppression of the bacteria confirmed by a RUT performed post-treatment. The secondary endpoint was to assess the improvement in the gastrointestinal symptoms using the GSRS.

Statistical analysis

The data was analyzed using Microsoft Excel and Statistical Package for Social Service (SPSS) Version 20. Means and standard deviations (SD) were calculated for continuous variables, while frequencies and percentages were calculated for categorical variables. A dependent t-test was used to compare the mean scores before and after treatment. One-way analysis of variance (ANOVA) was used to compare the mean scores of three different groups. A chi-square test was carried out for the analysis of categorical variables. P values less than 0.05 were considered statistically significant at a 5% level of significance with a confidence interval of 95%.

RESULTS

Baseline characteristics

A total of 105 patients with confirmed *H. pylori* infection, of which 42% were males and 58% were females participated in the study. They were randomized into three study groups namely Group I, II and III. Each group consists of 35 patients. Patients in Group I treated with *L. reuteri* alone. Group II patients treated with *L. reuteri* and PPI. Patients of Group III treated with conventional triple therapy. The mean age of three group patients were 38.03±10.68, 34.00±13.36 and 36.11±13.37 years. The three treatment groups were similar in their baseline characteristics [Table 1& Figure 1-2].

Table 1: Baseline Characteristics

Characteristic	Treatment Group			P value
	I	II	III	
Age (years)				
Mean ± SD	38.03±10.68	34.00±13.36	36.11±13.37	0.4079
Range	(18-64)	(18-61)	(17-75)	
Gender, frequency (%)				
Male	15(43)	12(34)	17(49)	0.4755
Female	20(57)	23(66)	18(51)	

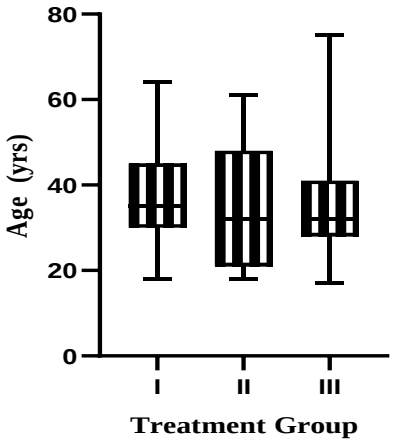

Figure 1: Age Wise Distribution

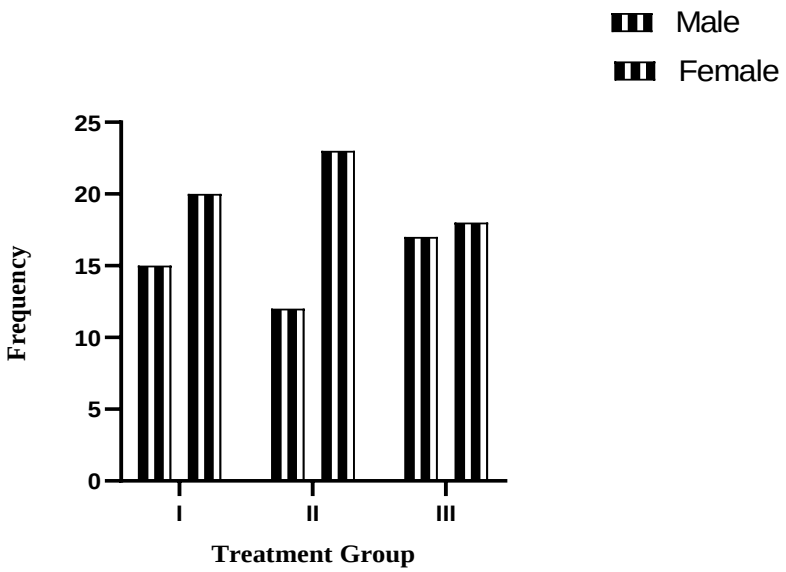

Figure 2: Distribution Based on Gender

Comparison of treatment efficacy

All patients were tested positive before treatment in rapid urease test. Only 12% were tested positive and 88% of patients were tested negative post -treatment. Eradication rate noted in *L. reuteri* only treatment was 86%, eradication rate noted in *L. reuteri*+ ppi was 86% and in antibiotic group was 92%.At the end of therapy there was no significant difference in the report of rapid urease test between three groups (p = 0.7039) [Table 2& Figure 3]

Table 2: Report of RUT after Treatment

Treatment Group	Rapid Urease Test		P value
	Positive	Negative	
Group 1	5(14)	30(86)	0.7039
Group II	5(14)	30(86)	
Group III	3(9)	32(91)	

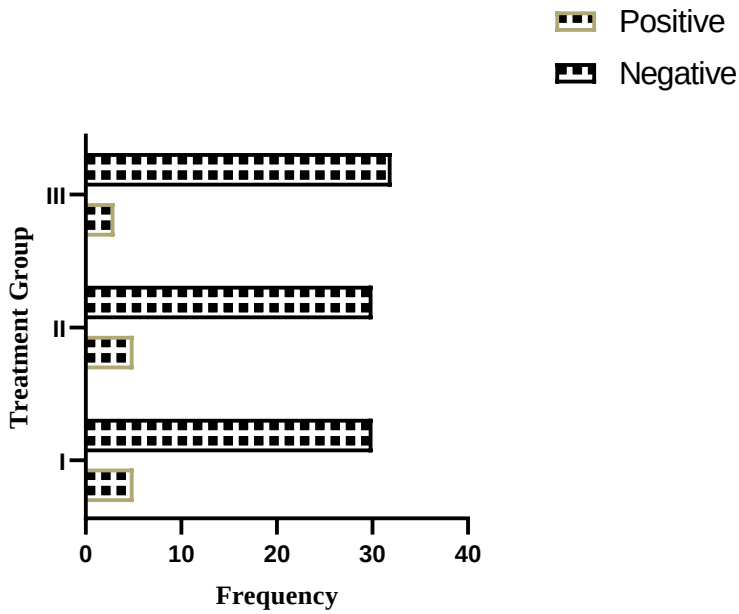

Figure 3: Rapid Urease Test

Assessment of gastrointestinal symptoms using GSRS

The baseline GSRS scores for three different groups were 2.73±0.49, 2.39±0.65 and 2.57±0.53 respectively [Table 3 & Figure 4] with no significant difference (p = 0.0568).

Table 3: Comparison of Baseline GSRS Score

Treatment Group	Minimum	Maximum	Mean ± SD	P value
Group 1	1.80	4.13	2.73±0.49	0.0568
Group II	1.60	4.33	2.39±0.65	
Group III	1.86	4.20	2.57±0.53	

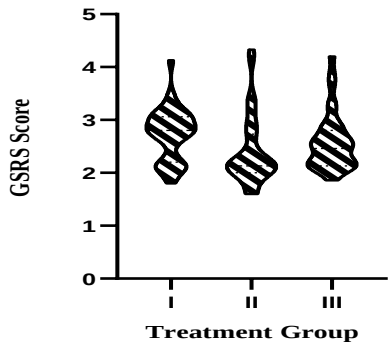

Figure 4: Comparison of Baseline GSRS Score

After treatment, GSRS scores for three treatment groups were 2.03±0.43, 1.81±0.59 and 1.83±0.46 respectively [Table 4& Figure 5-7]. Patients with three different treatments have shown significant improvement in gastrointestinal symptoms (p < 0.001). When the percentage of improvement in symptoms were evaluated, we found that patients receiving conventional triple therapy marked higher improvement (29%) whereas the other two groups (Group I & II) shown 26% and 24% of improvement. Three different treatment patterns were well tolerated by all patients and no serious adverse events were reported during the period of intake.

Table 4: Comparison of GSRS Score before and after Treatment in Group I

Treatment Group	Review	Minimum	Maximum	Mean ± SD	P value
I	Before treatment	1.80	4.13	2.73±0.49	<0.0001
	After treatment	1.40	3.33	2.03±0.43	
II	Before treatment	1.60	4.33	2.39±0.65	<0.0001
	After treatment	1.13	3.73	1.81±0.59	
III	Before treatment	1.86	4.20	2.57±0.53	<0.0001
	After treatment	1.26	3.33	1.83±0.46	

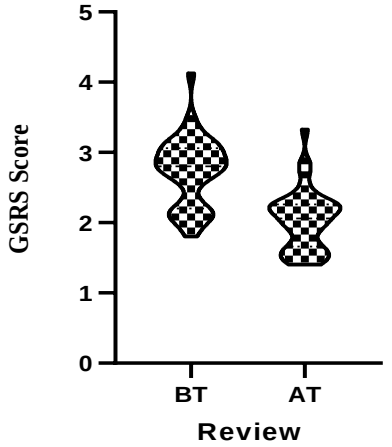

Figure 5: Comparison of GSRS Score before and after Treatment in Group I

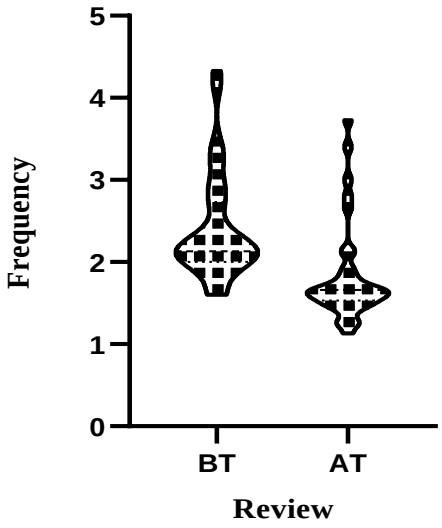

Figure 6: Comparison of GSRS Score before and after Treatment in Group II

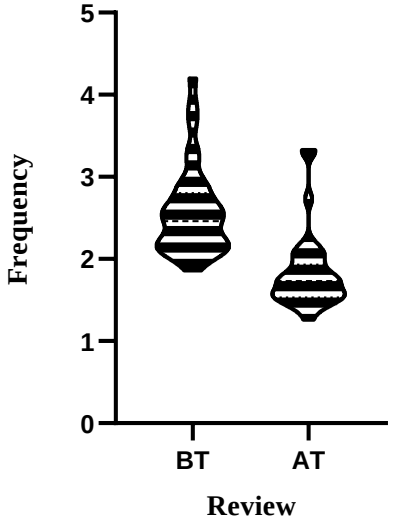

Figure 7: Comparison of GSRS Score before and after Treatment in Group III

DISCUSSION

H. pylori infection is considered endemic in many countries. Even though various therapeutic regimens (dual therapy, triple therapy, quadruple therapy, and sequential therapy) are available currently, failure of treatment remains a major problem in medical practice[12]. There are several factors that plays a role in eradication failure. Among those, the most pertinent is patient's poor compliance and antibiotic resistance. Probiotics were studied to lower the frequency of adverse events related to *H. pylori* therapy thereby it improves the patient's compliance[13]. Therefore, it is essential to include probiotics as an adjunct therapy to the current treatment regimen of *H. pylori* infection to achieve higher eradication rates.

Microorganism belongs to the genera *Bifido bacterium, Lactobacillus, Saccharomyces,* and *Bacillus* were the commonly used probiotics in humans. Based on the evidence, the most considered probiotics are lactic acid bacteria especially *Lactobacillus* and *Bifido bacterium.* The favourable effects of the above probiotics seem to be strain-specific and dose-dependent[14].In the present study, we have used *L. reuteri* since the administration of *L. reuteri*is considered safe in children as well as in adults and also diminishing the severity of gastrointestinal symptoms. In addition to this, there are certain indirect effects like decrease of inflammatory cytokines, restoration of IL-10, suppression of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kappa B) activation in most of the cases[15]. Hence, *L. reuteri* is promising when aiming at achieving the reduction of bacterial levels, modulating the immune response, controlling inflammation, or inhibiting the adherence of *H. pylori* to the gastric epithelium by reducing its motility.

Our study compared the effectiveness of three treatment patterns of *H. pylori* infection i.e., *L. reuteri* alone, *L. reuteri* with PPI, and conventional triple therapy. We analyzed the existence of *H. pylori* infection in patients of different ages and observed that the incidence of *H. pylori* infection varies with age. However, a significant difference doesn't exist between the groups. Several studies showed that the prevalence of *H. pylori* infection increased with age in the general population in developed and developing countries[8]. Our study demonstrates a female predominance in H. pylori positivity and is similar to Agah S et al[16] which reported female gender was one of the significant factors that predicted H pylori infection in gastric ulcer patients.

The rapid urease test is an indirect popular diagnostic test that is simple, rapid, and cheap that is commonly used in clinical practice. The RUT detects the presence of *H. pylori* based on the presence of urease in or on the gastric mucosa[17]. Our study compared the outcome of treatment based on RUT report that was taken post-treatment. The overall *H. pylori* eradication was achieved in 88% of the patients treated. Group I & II have shown 86% of eradication rate whereas Group III had shown 91% of eradication rate which is higher than reported by Adeyemi EO et al[18].

Interestingly, there was a statistically significant decrease in GSRS score after 15 days and 28 days of treatment. Refinement of clinical manifestations is a marker of successful therapy. All the three treatment groups showed improvements in the GSRS after therapy, but the conventional triple therapy group showed more but with a difference of only 3%. These improvements of symptoms should promote patients for more compliance to treatment.

This is a prospective observational study to generate a hypothesis further clinical trail and large multicentre studies are needed to evaluate better current *H. pylori* therapy with *L. reuteri*as adjuvant therapy.

CONCLUSION

Our study concluded that *L. reuteri* has the potential to suppress *H. pylori* infection, and also may lead to an improvement of gastrointestinal symptoms associated with *H. pylori*. Though conventional triple therapy of *H. pylori* has shown an increased eradication rate and significant improvement in gastrointestinal symptoms, there was no great difference when compared with *L. reuteri*treated patients.The overall data suggests that *L. reuteri* is recommended for a better eradication rate and reduced gastrointestinal symptoms. Hence, further studies on a larger number of patients are required to explain the real clinical application of *L. reuteri*. In addition to this, future studies should concentrate on elucidating an ideal duration of *L. reuteri* administration.

Ethical approval

This study was conducted as per the protocol and principles of the Declaration of Helsinki. The study was approved by the Ethical Committee of Deccan College of Medical Sciences with IRB project No.2021/32/003

Conflicts of interest

Authors have declared that no conflict of interests exists.

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