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A COMPARATIVE STUDY TO ASSESS TOLERABILITY AMONG PATIENTS WITH OR WITHOUT SYNBIOTIC SUPPLEMENTATION IN H. PYLORI ERADICATION REGIMEN

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ABSTRACT

Background: Helicobacter pylori infection is a widespread disease leading to significant morbidity and mortality, requiring an appropriate therapeutic approach. Non-compliance to H. pylori eradication is mainly associated with side effects like diarrhea. Probiotics improve the antibiotic tolerability by reducing side effects which in-turn leads to improvement in quality of life of patients. **Objective:** To assess tolerability among patients with or without synbiotic supplementation in H. pylori eradication regimen. **Methods:** A prospective comparative study was conducted in 100 Peptic Ulcer Disease (PUD) patients diagnosed with H. pylori and the patients were randomly assigned into two treatment groups of 50 patients each. One group received Lansoprazole, Amoxicillin and Clarithromycin (LAC group) and other group received a synbiotic, Lansoprazole, Amoxicillin and Clarithromycin (SLAC group). Incidence of Adverse Drug Reaction(ADR) and tolerability was assessed using a standardized questionnaire given to the patient at the time of enrollment. **Results:** The total incidence of ADR was less in SLAC group compared to LAC group (30% vs 46%).SLAC group patients experienced less incidence of ADR in terms of of diarrhea(10% vs 30%), nausea (10% vs 36.66%) and taste disturbances(16.66% vs 40%) relative to LAC group patients. Tolerability was better in SLAC Group compared to LAC Group at day 14 but not statistically significant.

KEYWORDS: Synbiotics, Probiotics, H.pylori, ADR, tolerability.

INTRODUCTION

Helicobacter pylori infection is a widespread disease leading to significant morbidity and mortality, requiring an appropriate therapeutic approach.[1]

Effective treatment for H. pylori should achieve an eradication rate of over 90%.[2] Its eradication markedly reduces rate of ulcer relapse. Local prevalence of anti-microbial resistance should be known, so that the appropriate antibiotics can be combined. The other factors like cost, simplicity and tolerability should also be taken into account. Many meta-analysis studies have shown that two week regimens achieve better eradication rate than one week regimens.[3]

Triple therapy regimens with proton pump inhibitors, clarithromycin and amoxicillin or metronidazole are considered to be the most effective combinations for the treatment of H. pylori infections worldwide because of their safety, cost effectiveness and simplicity.[3,4] USFDA has recommended a regimen consisting of lansoprazole, amoxicillin and clarithromycin for 14 days. The same regimen used in south east Asian patients showed 87% eradication rate.[5]

The increasing prevalence of resistance to antibiotics combined with eradication failure and expense of currently used regimens means that there is a need to evaluate alternate agents for combination therapy of H. pylori infection.[6,7] In India, resistance to nitroimidazoles is high and therefore it is better to avoid this group of drugs.[8]

Long term intake of probiotics reduces the risk of development of disorders associated with high degrees of gastric inflammation. Non-compliance to H. pylori eradication is mainly associated with side effects like diarrhea and poor improvement of dyspepsia. Probiotics administration improve antibiotic tolerability by reducing side effects like diarrhea, bloating and taste disturbances.

Probiotics also improves H. pylori gastritis and decrease H. pylori density.[9]

A prebiotic is a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microflora, that confers benefits upon its hosts well-being and health. Synergistic combinations of pro- and prebiotics are called synbiotics.

Therefore, the present study was designed to compare the tolerability of two eradication regimen with or without synbiotic supplementation.

MATERIALS AND METHODS

After obtaining informed consent, 100 patients diagnosed with H. pylori infection by upper GI endoscopy, histopathological examination and rapid urease test were enrolled in the study.

They were randomly assigned into two different eradication treatment groups. One group received lansoprazole 30 mg, amoxicillin 1 gm, and clarithromycin 500mg twice a day for 2 weeks(LAC group) and other group received a regimen consisting of a synbiotic thrice daily, lansoprazole 30 mg, amoxicillin1 gm and clarithromycin 500mg(SLAC group) twice daily for 2 weeks.

Patients were followed up 2 weeks after starting the regimen. Incidence of ADR were assessed using a standardized questionnaire given to the patient at the time of enrollment and was filled in during treatment period, indicating the type and degree of interference with daily activity of the patient and also by clinically significant abnormal laboratory investigations. Tolerability was analyzed in all patients based on the side effects grading. At the end of two weeks when patient came for the 2nd visit treatment compliance was estimated by using a scale. Incidence of ADR and tolerability in both the groups were collected, analysed and results tabulated using appropriate statistical tests.

RESULTS

Study was conducted in Department of Surgical Gastroenterology, Bangalore medical college and research institute, Bangalore. 100 patients enrolled in the study and incidence of ADR and tolerability was assessed at the end of treatment regimen. 38 patients experienced side effects, 23(46%) in LAC Group and 15(30%) in SLAC Group. Occurrence of side effects were less in SLAC Group (P=0.099+).(Table 1)

Diarrhea was the common ADR seen in LAC group compared to SLAC group with statistical significance (p <0.05). Nausea, vomiting, abdominal pain, taste disturbances were other ADR noted in both the groups but not statistically significant. (Figure 1). Side effects stopped within one week after stopping the drug.

Tolerability grading was analyzed in both the groups and it was better in SLAC group compared to LAC group at day 14 but not statistically significant (Table 2). Comparison of Tolerability grading as excellent, good and poor at day 14 showed that SLAC group (80%) had excellent tolerance compared to LAC group (60%) and poor tolerance was more in LAC group (22%) compared to SLAC group (4%). This is due to reduced occurrence of side effects in SLAC group.(Table 3). Global evaluation of overall tolerability was better in SLAC group compared to LAC group.(Table 4). Excellent compliance was seen in SLAC group and 40% of LAC group.(Figure 2)

Table 1: Comparison of ADR (present/absent) on day 14 in two groups of patients studied (LAC Group Vs SLAC Group).

ADR	LAC Group	SLAC Group
Present	23(46.0%)	15(30.0%)
Absent	27(54.0%)	35(70.0%)

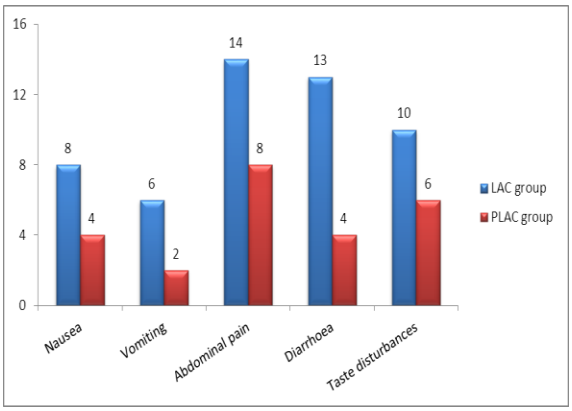

Figure 1: ADR at day 14 in two groups of patients studied (LAC Group Vs SLAC Group).

Table 2: Comparison of tolerability grading in two groups of patients studied (LAC Group Vs SLAC Group) on Day 14.

Tolerability grading	Day 14	
	LAC Group	SLAC Group
a. No side effects(A)	27(54.0%)	35(70.0%)
b. Slight discomfort, not interfering with daily activity (B)	3(9.0%)	5(10.0%)
c. Moderate side effects, sometimes interfering with daily activity (C)	9(18.0%)	8 (16.0%)
d. Severe side effects, work not possible(D)	10(20.0%)	2(4.0%)
e. Side effects severe enough to discontinue treatment (E)	1(2.0%)	0(0.0%)

Table 3: Comparison of tolerability in two groups of patients studied (LAC Group Vs SLAC Group) on day 14.

Tolerability grading	Day 14	
	LAC Group	SLAC Group
Excellent (A/B)	30(60.0%)	40(80.0%)
Good (C)	9(18.0%)	8(16.0%)
Poor (D,E)	11(22.0%)	2(4.0%)

Table 4: Distribution of Global Evaluation of Overall Tolerability in two groups of Patients studied (LAC Group Vs SLAC Group).

Global Evaluation of Overall Tolerability	LAC Group (n=50)		SLAC Group (n=50)	
	No.	%	No.	%
Patient assessment				
Excellent	30	60.0	40	80.0
Good	9	18.0	8	16.0
Poor	11	22.0	2	4.0
Physician assessment				
Excellent	30	50.0	40	70.0
Good	9	18.0	8	16.0
Poor	11	22.0	2	4.0

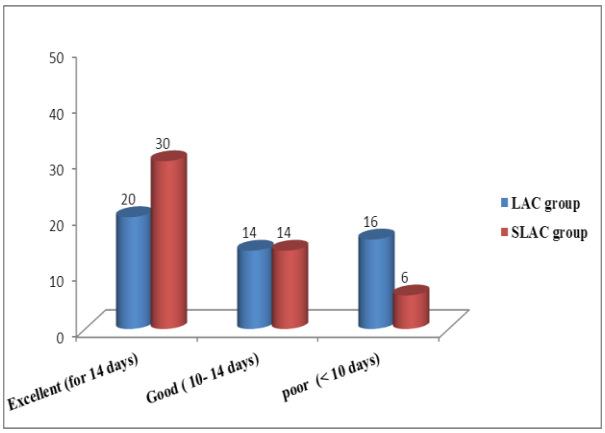

Figure 2: Compliance assessment in two groups (day14).

DISCUSSION

Achieving optimal efficacy with least side effects is desired in the treatment of H.pylori infection. Side effects associated with drug therapy is a major hindrance for medication compliance and thereby to eradication rates of H.pylori. Gastrointestinal side-effects due to antibiotics pose serious drawback of triple therapies[10]. Existence of high rates of ADR would demotivate patients who are willing to continue and complete the regimen duration. Discontinuation of antibiotic therapy will lead to development of antibiotic resistant strains of H.pyolri and making the therapy complicated.[11] Most common gastrointestinal side effects associated with antibiotic therapy are due to changes in gut microflora caused by unabsorbed or secreted antibiotics in the intestine. Net result is the suppression of growth of normal microflora and elevation of pathogenic microflora leading to gastrointestinal effects. Probiotics control overgrowth of pathogenic micro-organisms and may help to prevent or lower the incidence of antibiotic-associated side-effects.[12,13]

One of the studies on the effect of oral supplemention of Lactobacillus GG during Helicobacter pylori eradication therapy on antibiotic associated gastrointestinal side-effects revealed that diarrhoea, nausea and taste disturbance were signifcantly reduced in the Lactobacillus GG supplemented group. However, the overall assessment of treatment tolerability showed a signifcant difference in favour of the Lactobacillus GG supplemented group.[14] Our study also showed decrease in gastrointestinal side-effects with synbiotic supplemented group.

A randomized study conducted by Myllyluoma E et al showed an improved tolerance to the eradication treatment when total symptom severity was taken into account with probiotic supplementation.[15] Supporting the above facts metaanalysis done by Tong JL et al, Szajewska H et al and Zou J et al, have commented that probiotic supplementation reduces H.pylori therapy related side effects.[16,17,18]

Another metaanalysis has opined that impact on side effects remains unclear and more high quality trials on specific probiotic strains and side effects are thus needed.[19]

So in the conclusion, probiotic supplementation helps in reducing H.pylori therapy related side effects and improves patient compliance.

CONCLUSION

Supplementation with synbiotic in H.pylori eradication regimens increase patient compliance by decreasing drug related side effects and by improving patient tolerability.

LIMITATION

The present study was done only on 100 patients, and there is a necessary to do the same in larger population.

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