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## A RANDOMIZED OPEN LABEL COMPARATIVE CLINICAL STUDY OF VITAMIN C AND VITAMIN E AS AN ADD ON THERAPY TO STANDARD TREATMENT IN SYMPTOMATIC *HELICOBACTER PYLORI* INFECTION

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### Keywords:

*Helicobacter pylori*,  
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### ABSTRACT

**OBJECTIVE:** To evaluate the efficacy of anti-oxidants vitamin C and vitamin E as add on therapy to standard treatment in the eradication of *Helicobacter pylori* infection in Peptic Ulcer Disease compared to standard treatment. **METHODOLOGY:** The study was conducted in adult patients with confirmed *Helicobacter pylori* infection by Rapid Urease test and endoscopy attending Medical Gastroenterology department, Madras Medical College & Rajiv Gandhi Government General Hospital, Chennai between July 2012 to July 2013. Treatment period is 4 weeks and 4 weeks follow-up per patient. Sample size is 60 (30 patients-study drugs and standard treatment, 30 patients-standard treatment alone). The enrolled patients were randomized into either Control group (Standard Triple regimen: C. Amoxicillin 1 g BD, T. Metronidazole 400 mg TDS, C. Omeprazole 20 mg OD for 14 days) or Study group (standard treatment for 14 days plus T. Vitamin C 500 mg OD, C. Vitamin E 200 IU BD for 28 days) by simple randomization. **RESULTS:** 124 patients were screened out of which 60 patients were included in the study and all patients completed the study and were included in the analysis. The *Helicobacter pylori* eradication rate was 86.6% in study group compared to 56.6% in standard group (p value of 0.02) which is statistically significant with significant endoscopic and clinical improvement. **CONCLUSION:** Oxidative stress prevents complete eradication of H.pylori infection. Adding anti-oxidants Vitamin C and Vitamin E to standard triple regimen antagonises oxidative stress and is effective in eradicating *Helicobacter pylori* infection.

## 1.0 INTRODUCTION

*Helicobacter pylori* infection is one of the important causes of Peptic ulcer disease. Peptic ulcer disease causes significant morbidity and mortality, if untreated<sup>1,2</sup>. Peptic ulcer disease is a remitting and relapsing disease of the humans.

*Helicobacter pylori* is a gram negative, micro-aerophilic, helix shaped bacteria, 3×0.5 µm, inhabits gastro-intestinal tract, transmitted by faeco-oral route. If untreated *H.pylori* infection leads to Peptic ulcer disease and its complications<sup>3,4,5</sup> like perforation, bleeding and gastric cancer. Curing the infection not only heals the ulcer but prevents relapse.

Present treatment consists of combination treatment regimens consisting of two antibiotics (either of Amoxicillin, Clarithromycin, Tetracycline and Metronidazole) and proton pump inhibitor (Omeprazole, Lansoprazole or Pantoprazole) for fourteen days<sup>6,7</sup>. Despite various regimens treatment available, *H. pylori* eradication was suboptimal (70%)<sup>8,9</sup>. Thus demonstrating the need for development of new effective treatment.

*H. pylori* induces the production of reactive oxygen species which in turn causes inflammation of the gastric mucosa. This phenomenon of oxidative stress prevents complete eradication of Peptic ulcer. Therefore complete eradication of *H. pylori* is not possible with antibiotics alone<sup>10,11</sup>. Anti-oxidants like Vitamin C and Vitamin E can antagonize the oxidative stress, protect the gastric mucosa from damage caused by *H. pylori* infection by inhibition of lipid peroxidation and helps in healing of the ulcer<sup>5,12,13</sup>.

Alpha-Tocopherol, is a biological anti-oxidant, fat soluble vitamin<sup>14,15</sup>. Ascorbic acid another anti-oxidant is a water soluble vitamin<sup>16,17</sup>. In our study we have added Vitamin E and C to standard triple regimen as they have synergistic action, inhibits *H.pylori* induced oxidative stress in the gastro-intestinal tract, so that complete eradication of *H.pylori* can be achieved<sup>18,19,20</sup>.

## 2.0 METHODOLOGY

### 2.1 OBJECTIVE:

The prospective study was done to assess the therapeutic effect of combination of Vitamin C 500 mg OD and Vitamin E 200 IU BD along with triple regimen in comparison to the triple therapy alone (C.Amoxicillin 1 g BD, T.Metronidazole 400 mg TDS, C.Omeprazole 20 mg OD) in the complete eradication of *H. pylori* infection in Peptic ulcer disease patients.

## 2.2 STUDY DESIGN

This was a randomized, open label, prospective, parallel group two arm comparative study was done at Department of Medical Gastroenterology, Rajiv Gandhi Government General hospital, Madras Medical College, Chennai. The study was carried out from June 2012 to August 2013 for 8 weeks (4 weeks study period and 4 weeks follow up period) for each patient.

Adult patients with dyspepsia and *H. pylori* positive by Rapid Urease Test were the study population. Total number patients was 60 patients and 30 patients in each group (control and study groups).

## 2.3 SELECTION CRITERIA

### 2.3.1 INCLUSION CRITERIA:

- Age: 18-70 years
- Sex-Both genders
- Patients with dyspeptic symptoms with Rapid Urease Test positive for *H. pylori*
- Patients willing to participate in the study.

### 2.3.2 EXCLUSION CRITERIA

- Pregnant and lactating women
- Patients with intestinal obstruction, ulcer perforation.
- Patients already on proton pump inhibitor intake, antibiotics in the last two weeks
- Participation in another clinical study in the last three months
- Patients with any chronic systemic illness

## 2.4 STUDY PROCEDURE

The study was started after obtaining approval and clearance from the Institutional Ethics Committee (No.32072012). Information sheet and informed consent forms written in the regional language was provided to each patient and patient willing to participate in the study signed the required forms. 124 patients were screened and 30 patients in each group (control and study groups) who fulfilled the inclusion and exclusion criteria were recruited and randomized by odd number patients assigned to study group and even number patients to control group.

## 2.5 TREATMENT PLAN

30 patients in the control group received triple regimen (C.Amoxicillin 1 g BD, T.Metronidazole 400 mg TDS and C.Omeprazole 20 mg OD) for 2 weeks. 30 patients in the study group received

triple regimen( 2 weeks) with T. Vitamin C 500 mg OD and C.Vitamin E 200 IU BD for 4 weeks. Patients will be asked to return the empty packets during subsequent visits.

## 2.6 EVALUATION

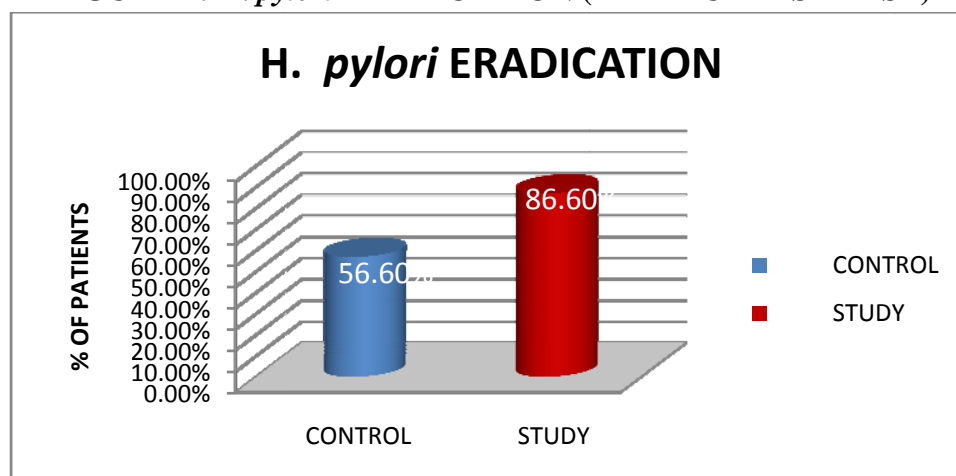
The collected data was analysed by statistical analysis. The difference within the group before and after treatment were analysed by using student paired t test and difference between control and study groups were analysed by ONE WAY ANOVA.

## 3.0 RESULTS

**TABLE 1: *H. pylori* ERADICATION (RAPID UREASE TEST)**

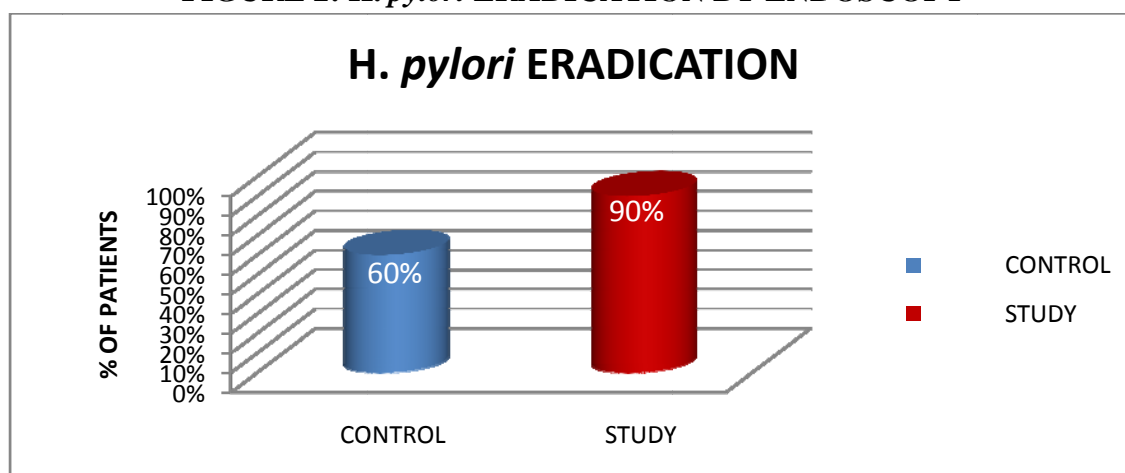
GROUPS	0 WEEKS				4 WEEKS				p value
	POSITIVE	%	NEGATIVE	%	POSITIVE	%	NEGATIVE	%	
CONTROL	30	100	0	0	13	43.3	17	56.7	<0.001
STUDY	30	100	0	0	4	13.3	26	86.7	< 0.001
p value	0.020								

**FIGURE 1: *H. pylori* ERADICATION (RAPID UREASE TEST)**

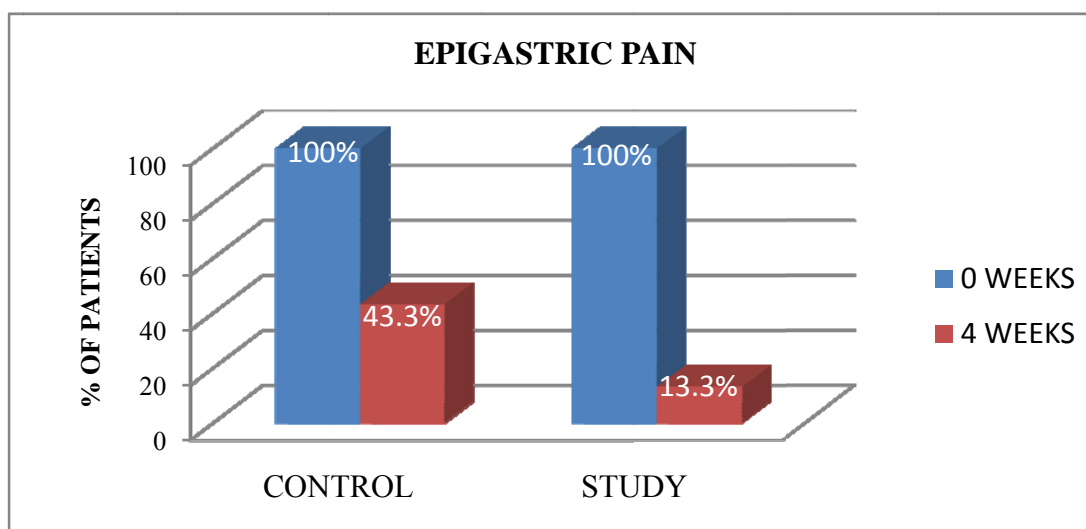


**TABLE 2: *H. PYLORI* ERADICATION BY ENDOSCOPY**

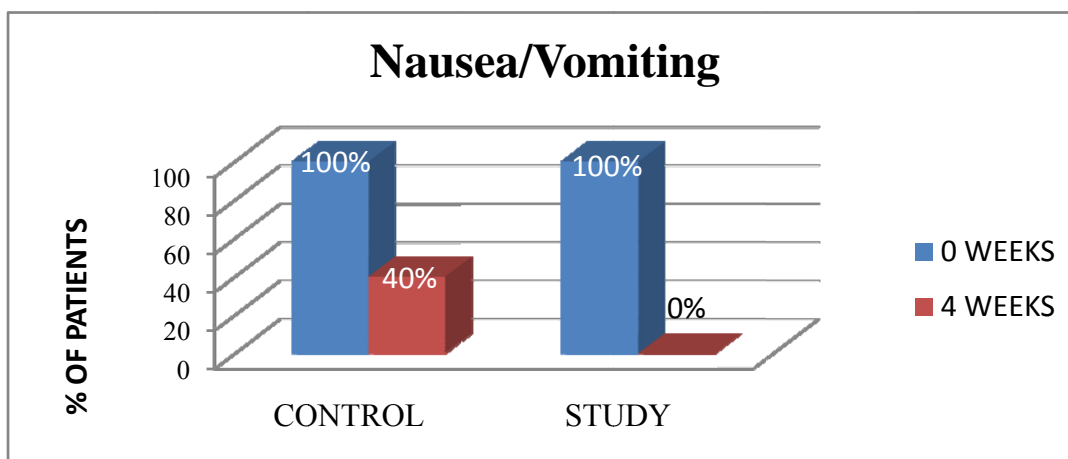
GROUPS	0 WEEKS		4 WEEKS		p value
	NO.	%	NO.	%	
CONTROL	30	100	18	60	0.0001
STUDY	30	100	27	90	<0.0001
p value	<0.0001		0.0005		

**FIGURE 2: *H. pylori* ERADICATION BY ENDOSCOPY****SYMPTOMATIC IMPROVEMENT AFTER 4 WEEKS OF TREATMENT****TABLE 3: EPIGASTRIC PAIN**

GROUPS	0 WEEKS				4 WEEKS				p value
	PRESENT	%	ABSENT	%	PRESENT	%	ABSENT	%	
CONTROL	30	100	0	0	13	43.3	17	56.7	<0.001
STUDY	30	100	0	0	4	13.3	26	86.7	<0.001
p value	0.020								

**FIGURE 3: EPIGASTRIC PAIN****TABLE 4: NAUSEA/VOMITING**

GROUPS	0 WEEKS				4 WEEKS				p value
	PRESENT	%	ABSENT	%	PRESENT	%	ABSENT	%	
CONTROL	30	100	0	0	12	40	18	60	<0.001
STUDY	30	100	0	0	0	0	30	100	<0.001
p value	<0.0001								

**FIGURE 4: NAUSEA/VOMITING****TABLE 5: ADVERSE DRUG REACTIONS MONITORING**

ADVERSE DRUG REACTION	CONTROL GROUP	STUDY GROUP
Diarrhoea	7 (23.3%)	2 (6.67%)
Metallic taste	4 (13.3%)	2 (6.67%)
Flatulence	3 (10%)	1 (3.33%)
Nausea	5 (16.6%)	2 (6.67%)

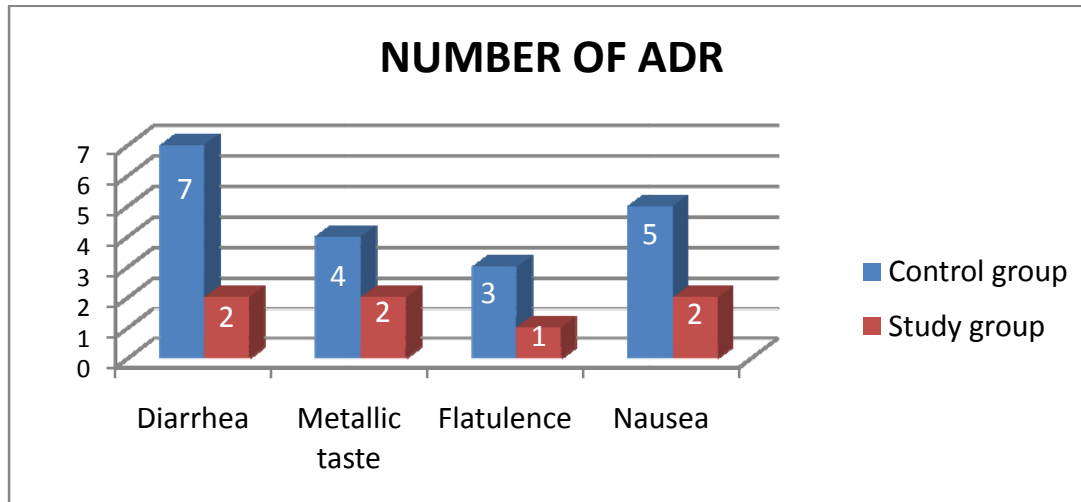
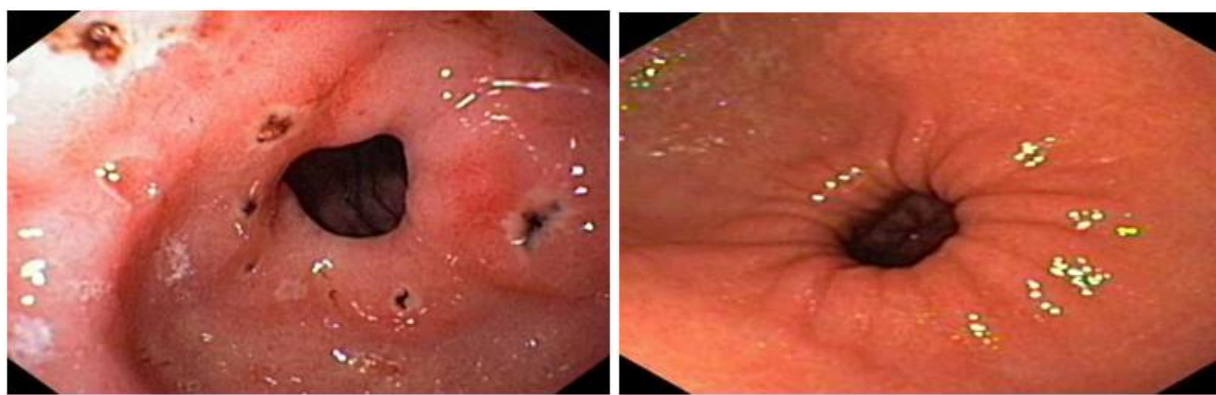
**FIGURE 5 ADVERSE DRUG REACTION MONITORING**

Figure 5 shows the adverse drug reactions in the control and study groups

**FIG 6 AND 7 SHOWS RAPID UREASE TEST AT 0 WEEKS AND 4 WEEKS****FIG 8 AND 9 SHOWS ENDOSCOPIC PICTURE AT 0 AND 4 WEEKS**

#### 4.0 DISCUSSION

The therapeutic efficacy of Vitamin C and Vitamin E with standard triple regimen in the eradication of *Helicobacter pylori* of Peptic ulcer disease was assessed in this study. *H. pylori* causes production of reactive oxygen species which in turn causes inflammation of gastric mucosa. Therefore complete eradication is not possible with antibiotics alone. Anti-oxidants helps to scavenge the free radicals produced by *H. Pylori* so that the antibiotics can eradicate *H. Pylori* completely. In addition to that anti-oxidants protect the mucosal layer cells from lipid peroxidation and helps in healing of ulcer<sup>21,22</sup>. In this study, anti-oxidants Alpha-tocopherol and Ascorbic acid were added to the triple regimen in Rapid urease test positive *H. Pylori* patients. Combination of anti-oxidants with triple regimen (study group) showed 86.6% eradication rate by Rapid urease test compared to 56.6% in the control group with significant p value of 0.02.



The endoscopic assessment showed almost complete healing of ulcer in the study group. The study group showed 90% eradication rate compared to 60% in the control group by endoscopic assessment. The epigastric pain due to Peptic ulcer was decreased to 13.3% in the study group compared to 43.3% in the control group. The nausea/vomiting also significantly decreased in the study group compared to control group. Among the adverse effects, the study group showed lesser incidence of 23% compared to 63% in the control group. The most common adverse effect was diarrhoea (23.3%) in the control group and nausea (6.7%) in the study group. These findings are consistent with other studies<sup>23,24,25</sup>. Addition of Vitamin E and C to the triple regimen have significantly contributed to the eradication of H. Pylori by its anti-oxidant, anti-inflammatory properties. In addition to this Vitamin C increases the synthesis of collagen and connective tissue which helps in the healing of ulcer.

## 5.0 CONCLUSION

In this study it has been proved that oxidative stress prevents the complete eradication of H. Pylori infection in Peptic ulcer disease. Combination of Vitamin E and C along with triple regimen provides novel therapeutic option for almost complete eradication of H. Pylori infection, enhances healing of ulcer and lessens the adverse effects. It also prevents the recurrence of Peptic ulcer and improves the quality of life of these patients.

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