

Prospective Study on Anti-Helicobacter Pylori Therapy and Endoscopic Biopsy Following Surgery in Cases of Peptic Perforation

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Abstract

Background: The most common causes of peptic ulcer disease (PUD) are Helicobacter pylori infection and use of nonsteroidal anti-inflammatory drugs (NSAIDs), and the PUD leads to perforation. Perforation of gastric or duodenal ulcer is one of the most serious and overwhelming catastrophes that can befall on human being. The incidence of peptic ulcer disease has decline in worldwide in recent years following judicious use of wide spectrum and highly effective ulcer healing drugs. Despite the widespread use of gastric antisecretory agents and H. pylori eradication therapy the incidence of perforated peptic ulcer has changed little.

Aim: The current study aims to check the involvement of the H. pylori in peptic perforations and whether by eradicating the bacterium H. pylori can we prevent the ulcer recurrence in post operative peptic perforation patients.

Materials and Methods: After the confirmation of peptic perforation and detecting the H. pylori infection patients were subjected to graham's repair by both open and laparoscopic method. Then after recovery they were included in the trial category. This study also involves the comparison between effectiveness of triple therapy regimen over esomeprazole alone therapy in post-operative periods. The patients were advised to follow up upto 1 year and ulcer recurrence was observed.

Results: Study was conducted on 128 patients, out of which 68 were excluded and remaining 60 patients were included in the study. 30 patients were included in triple therapy group and 30 to only esomeprazole therapy group. After 1 yr. follow up it was found that 25(83.3%) out of 30 patients and 5(16.6%) out of 30 patients has H. pylori eradication. Ulcer recurrence occurred 3.3% in case triple therapy and 36.6% in case of only esomeprazole therapy.

Conclusions: In this study it was found that in cases of peptic perforations triple therapy (anti-helicobacter pylori therapy) is superior to esomeprazole alone in the eradication of H. pylori. Triple therapy also prevents long term recurrence of ulcer in post operative peptic perforation in 1 year follow up study.

Keywords: Acid suppression therapy, Graham's omental patch, *H. pylori*, Malignancy, Perforated peptic ulcer, Peritonitis, Triple therapy, Ulcer recurrence, Vagotomy

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Introduction

Perforation is one of the common complications of a peptic ulcer. Modern techniques are available to deal such type of incidence still it is a life-threatening condition.

In case of peptic perforation, after simple patch repair immediate definitive surgery is advice as there is chance of ulcer relapse. Now a days for severe and bleeding peptic ulcer *H. pylori* eradication therapy is recommended. Recently in perforated peptic ulcer patient *H. pylori* status was found to be high. There is possibility that by eradicating *H. pylori* bacterium after simple patch repair ulcer recurrence can be prevented and hence immediate definitive surgery can be obviate[1].

In case of omental patch repair in peptic perforation the long-term result is dissatisfying, ulcer recurrence was noted repeatedly [2,3]. So after the simple patch repair to prevent ulcer relapse some suggest the immediate definitive surgery[3,4]. This is safe in selective patients but in this procedure, there is increase in perioperative complication and death [5]. Meanwhile only fewer surgeons are able to masters in definitive surgery inspite of the complications. Still simple patch repair remains an attractive and lifesaving procedure as it takes less time to operate, and peptic perforation is an “out of hour” emergency procedure.

The treatment for peptic ulcer disease has now changed as *helicobacter pylori* found to be one of causative organism. The ulcer relapse and uncomplicated peptic ulcer can be treated by anti-helicobacter pylori therapy. For uncomplicated and bleeding peptic ulcer treatment *H. pylori* eradication therapy is found to be an excellent option as it is suggested by National institute of

health conseus meeting and Maastricht meeting of europe [6].

The relation in between *H. pylori* and peptic ulcer disease still now on experimental studies. In serological testing the *H. pylori* infection rate found to be 47% [6] and in biopsy studies it was found to be 80% [7,8]. To know the relationship in between *H. pylori* and peptic ulcer perforation, we performed a prospective study by treating few postoperative patient with anti-helicobacter pylori regimen and and few patient with only proton pump inhibitor and observing the improvement and ulcer relapse with a given period of time.

Aims and Objectives

To study and identify the most common etiological risk factors among patients with gastroduodenal perforations and effect of anti-helicobacter pylori therapy in post-operative peptic perforations cases at our institution.

Materials and Methods

This study was conducted in the department of general surgery, M.K.C.G. Medical College and Hospital, Berhampur with IEC approval. After admission the detail history was carefully elicited from the patient and his attendants. All consecutive patients from both sex and <75yrs. age group who were undergo the Graham’s closure of the peptic perforation, in the Department of General Surgery, M.K.C.G. Medical College & Hospital, Berhampur, Odisha from July 2019 to June 2021.

Inclusion criteria: Age group <75 yrs., Patient who will undergo Graham’s closure of the peptic perforation, those patients gave consent for treatment and willing to follow up for 1 year.

Exclusion criteria: Patients doesn’t undergo immediate surgery and was treated

conservatively from the beginning, Previous gastrectomy or vagotomy, pregnancy, perforated ulcer due to drugs that are used for other medical diseases i.e., Steroid induced, Burn, Hypergastrinemia. Case of malignant perforation, Age group > 75 yrs.

Procedure

After the confirmation by chest x-ray immediate plan for surgery was done. During surgery peptic perforation was confirmed by direct visualisation, then flexible gastroscopy was introduced to obtain biopsy samples. Seven biopsy samples were taken: three samples for histological examination, three samples for gram stain and one for rapid urease test.

Detection of *H. pylori* positive: patient is said to be *H. pylori* (+)ve when rapid urease test is found to be positive or helical microorganism present in histological section.

Surgery: Perforations <1 cm in diameter were repaired by simple omental patch. In >1cm of perforation gastrectomy or other definitive surgery is performed. After repair of perforation peritoneal toiletting is done and postoperative antibiotic therapy and proton pump inhibitor were prescribed until oral intake.

Assignment to the treatment group: postoperative and *H. pylori* positive patient

were included in the trial. After resuming the oral diet odd group of patient assigned to triple therapy and even group of patient were assigned to only esomeprazole therapy.

Triple Therapy: Tab amoxicillin (1000mg) twice daily, Tab clarithromycin (500 mg) twice daily, Tab Esomeprazole (20mg) twice daily for 14 days. Compliance with treatment course was checked by phone inquiry. Follow-up endoscopy was scheduled on interval of 3 months, 6 months, 9 months and 1 year and additional biopsy samples were collected. Repeat endoscopic will be performed whenever patients are symptomatic.

Sample Size and Statistical Analysis: Anticipating a default rate around 10%, we had decided to recruit 30 patients approximately into each treatment group. Intention to treat analysis is used to find differences in ulcer healed and ulcer recurrence between the triple therapy and esomeprazole alone groups of patients. Patients who unable to appear for follow-up were treated by phone. Data was collected, compiled and analysed using Microsoft excel® for windows. The result was evaluated and compared using Univariate analyses (Chi-square, Students t-test). The statistical data was carried out by IBM SPSS® version 20.

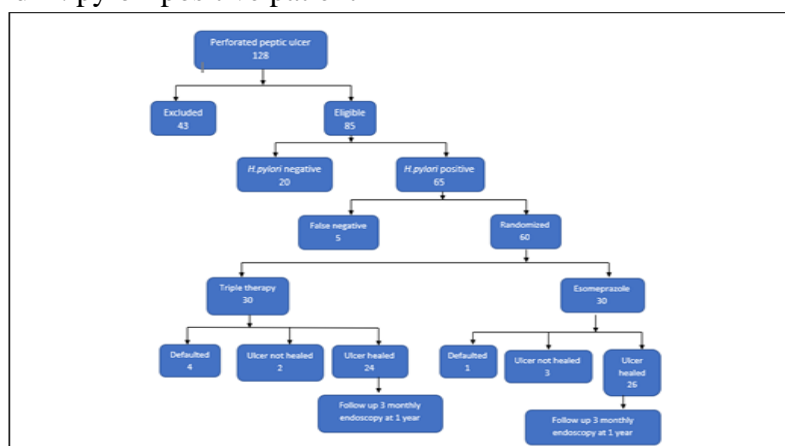


Figure 1: Trial profile

Observations and Result

From July 2019 to June 2021, 128 patients (98 men and 30 women) with a mean age of 51.2 years (S.D. = 18.12) were certain to have peptic ulcer perforation during laparoscopy or laparotomy. 43 patients were excluded from the study. Rest 85 patients, 65 (76.5%) were *H. pylori* positive. 5 patients were not included in the randomization trial because the rapid urease test and histology results were falsely negative.

In endoscopic biopsy (H and E stain):

- *H. pylori* was demonstrated in 87% cases (65 patients) overlaying the surface epithelium (Fig-2).
- Antral mucosa showed infiltration of inflammatory cells (Neutrophils and lymphocyte) In the lamina propria (Fig -3).
- Serrated appearance, mucin depletion, nuclear enlargement and focal loss of nuclear polarity were observed in varying proportion in all the positive case (Fig-4).
- The two groups were compared in age, sex, smoking, nonsteroidal anti-inflammatory drugs (NSAIDs) use, ulcer history, size of perforation,

peritoneal contamination severity, and method of repair (Table-6). 55 patient came at 3 month for endoscopy.

- *H. pylori* eradication rate of triple therapy group was significantly higher than that of the esomeprazole alone group (83.32% vs. 16.65%, $P < .001$) (Table-7).
- Initial healing of peptic ulcers was compared between the two groups. Complete ulcer healing was found in 24 patients in triple therapy and 26 patients in only esomeprazole therapy ($P = 0.58$) in early outcome (Table-7). Patients with registered healed ulcer were scheduled for follow-up according to the study protocol. After 1 year follow-up 1 patients in the triple therapy group and 11 patients in the esomeprazole alone group had ulcer recurrence (Table-9). Ulcer recurrence difference in between the triple therapy regimen group and the control group was statistically significant (4.81% vs. 38.12%, $P = .0001$, intention-to-treat) (Table-8) with a relative risk of 0.18 (95% confidence interval 0.04–0.69). 8 of these 12 ulcer recurrences were associated with continuous *H. pylori* infection: 11 in the esomeprazole group and 1 in the triple therapy group.

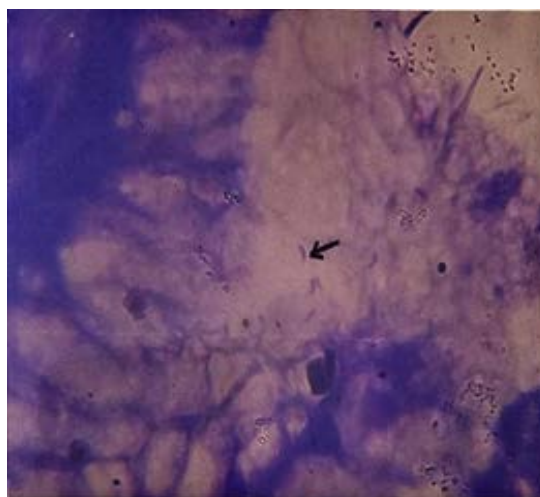


Figure 2: Presence of *H. pylori* in Surface Epithelium (H&E x 1000)

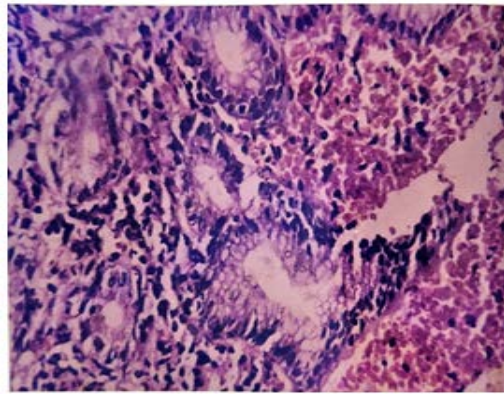


Figure 3: Antral Mucosa Showing Vascular Congestion and Infiltration by Inflammatory Cells in the Lamina Propria. (H&E x 100)

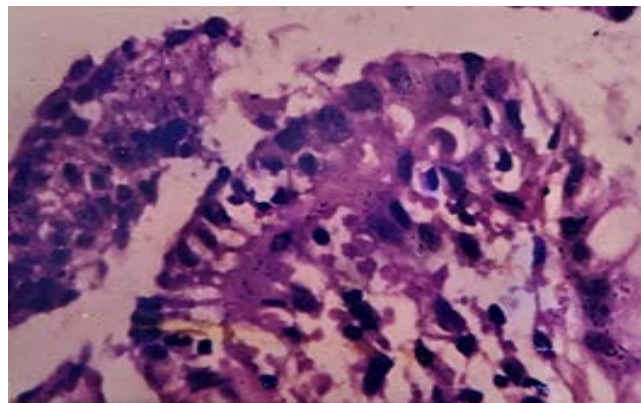


Figure 4: Surface Epithelium showing a Serrated Appearance, Mucin Depletion, Nuclear Enlargement and Focal Loss of Nuclear Polarity (H&E x 400)

Table 1: sex incidence

Sex	No. of patients	Percentage
Male	98	77%
Female	30	23%
Total	128	100%

98 male and 30 female were present in this study, out of 128 cases male:female ratio was 3:1

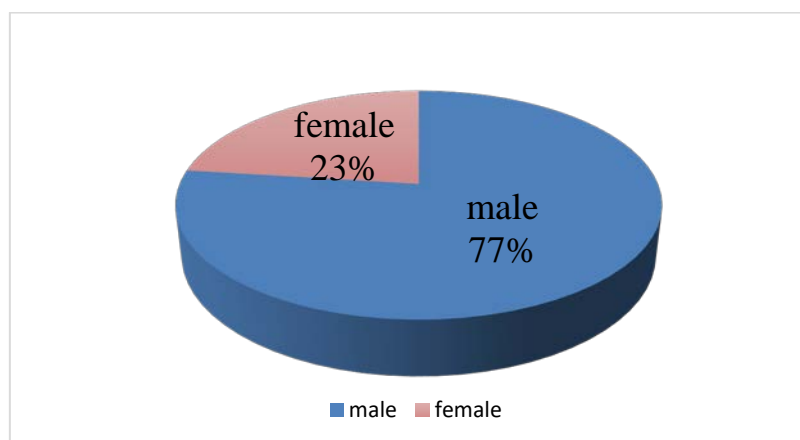


Figure 5: Sex Incidence

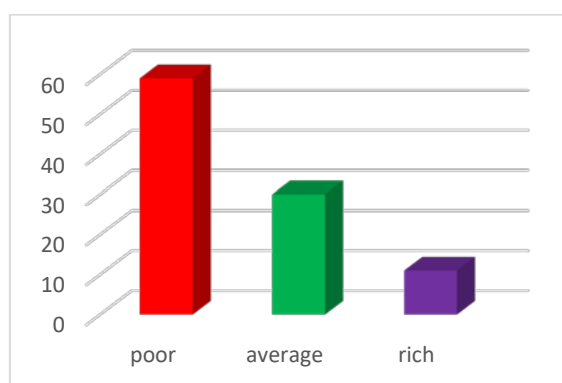
Table 2: Age Distribution

AGE IN YEARS	TOTAL CASES	PERCENTAGE
11-20	2	1.5%
21-30	28	21.8%
31-40	28	21.8%
41-50	38	29.6%
51-60	32	25%
TOTAL	128	100%

Table 3: Socioeconomic Status

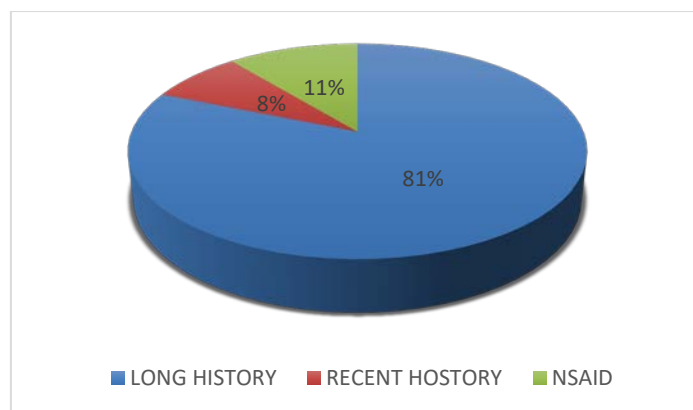
SOCIOECONOMIC STATUS	NO. OF CASES	PERCENTAGE
POOR	76	59
AVERAGE	38	30
RICH	14	11
TOTAL	128	100

The highest incidence was recorded in the poor socioeconomic status which comprised 59%, least incidence was recorded in the rich i.e. 11%. 30% cases were found in middle group strata.

**Figure 1: Socioeconomic Status****Table 4: Peptic Ulcer History**

ULCER HISTORY	NO. OF CASES	PERCENTAGE
LONG HISTORY	104	81
RECENT HISTORY	10	8
NSAID USE	14	11
TOTAL	128	100

Previous history of peptic ulcer disease ranging from 3 months to 10 yrs. was present in 104 (81%) and 10(8%) had no previous history of peptic ulcer but had history of dyspepsia less than 3 months. In 14 cases (11%) history of NSAID was present.

**Figure 2: Peptic Ulcer History****Table 5: Criteria of Excluded**

Reason	No. Of patients	No. With HP status determined	No. With positive HP status	No. With use of NSAID
> 75 years	17	12	4	7
Failure in biopsy sample obtaining	11	-	-	1
Definitive surgery indicated				
Truncal Vagotomy & drainage	4	1	1	0
Partial gastrectomy	6	5	1	3
Non-ganjam residence	3	2	2	0
gastric surgery history	1	1	1	1
malignancy	1	0	0	0

HP-*Helicobacter pylori*, NSAID – Nonsteroidal anti-inflammatory Drug.

Table 6: Aspects of Patients

	Triple Therapy (n = 30)	Esomeprazole Therapy (n = 30)	P Value
Age (years)	44 ± 14	45 ± 15	.73
Sex			
Female	9	4	.90
Male	21	26	
Cigarette smoking			
Not smoke or Ex- smoker	17	14	.08
4-8 packs/week	23	22	
> 8 packs/week	11	4	
NSAID intake	10	9	.88
Dyspepsia > 3 months	26	27	.43
Ulcer history	15	10	
ulcer complications history	7	6	
Severity of peritonitis			
Mild	6	5	.50
Moderate	16	21	
Severe	8	4	
Size of perforation (mm)	4.2 ± 1.3	4.6 ± 1.5	.72

Operation approach			
Open method	22	23	.92
Laparoscopic method	08	7	

Table 7: Outcomes in 3 Months

	Triple Therapy (n =30)	Esomeprazole Therapy (n = 30)	P Value*
Patients who underwent initial follow-up endoscopy	26 (86.6%)	29(96.6%)	.16
H. pylori eradicated	25(83.3%)	5 (16.6%)	<.001
Complete ulcer healing	24 (80%)	26 (86.6%)	.58

*Chi-square analysis with Yates correction (intention-to-treat).

Table 8: Outcomes of Patients at 1-Year Follow-Up

	Triple Therapy	esomeprazole Alone	P Value*	Relative Risk (95% CI)
Patients with complete ulcer healing on initial endoscopy	30	30	-	-
All Ulcer recurrence	1 (4.8%)	11 (38.1%)	< .001	0.18 (0.04-0.69)
Duodenal	1	9	-	-
Gastric	0	1	-	-
Gastric + duodenal	0	1	-	-
Symptomatic ulcer recurrence	1 (2.4%)	6 (21.4%)	.02	0.18 (0.03-1.17)
Pain	1	7	-	-
Bleeding	0	1	-	-
Obstruction	0	1	-	-

* Two-tailed Fisher exact test, intention-to-treat.

Table 9: Ulcer Recurrence

Regimen	Total Cases for Follow Up	Ulcer Recurrence	Percentage
Triple Therapy	30	1	3.3%
Esomeprazole Alone	30	11	36.6%

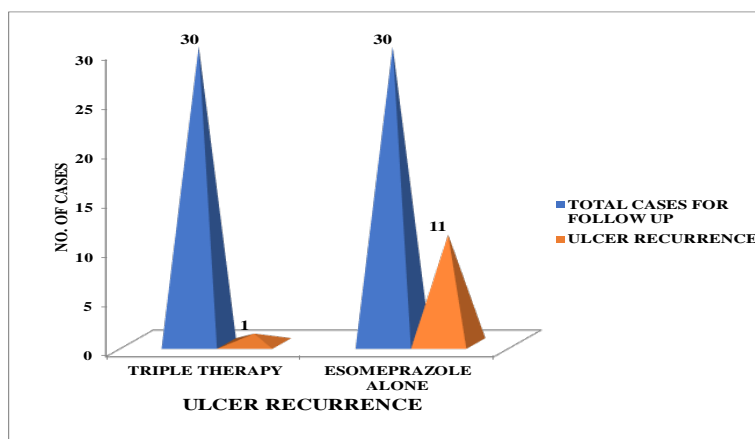


Figure 3: Ulcer Recurrence

Discussion

The surgical treatment of choice for perforated peptic ulcer has been controversial. Simple repair is the outmost best procedure since its popularization by Graham in 1937 [9]. On long-term follow-up of Graham's repair patient shows ulcer relapse after 1 year [10].

In our study we have determined that whether the peptic perforated patient are related to *H. pylori* infection and after the postoperative period by implementing triple therapy can we eradicate the *H. pylori*. Reduction in the postoperative complication after simple repair and reduction in ulcer relapse can be achieved by anti-helicobacter pylori therapy.[11] Triple therapy is the more desirable option than definitive surgery in cases of peptic perforation to prevent ulcer relapse in long term basis. After *H. pylori* elimination and without any proton pump inhibitor, 96% of patients found to be ulcer-free at 1-year follow-up. Simple repair either by laparotomy or laparoscopic, is the procedure of choice for peptic ulcer perforation. *H. pylori* status is checked either by endoscopic biopsy or serology and the bacterium should be eradicated in positive cases.

Conclusion

Among adults, peptic perforations were more common in 21 to 45 age groups. The incidence was more common among male patients with male to female ratio of 3:1. Duodenal perforations which is more common than gastric perforations occurred mainly in first part of duodenum and is mostly found in lower socioeconomic groups. *H. pylori* is the common etiological risk factor for peptic perforations among 15 to 45 age groups, followed by smoking and psychological stress. In this study it was found that in cases of peptic perforations triple therapy (anti- *helicobacter pylori* therapy) is superior to esomeprazole alone in the eradication of *H. pylori*. Triple therapy also prevents long term recurrence

of ulcer in post operative peptic perforation in 1 year follow up study.

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