Eradication of Helicobacter Pylori Infection Using Triple Drug Therapy: A Hospital Based Observational Study in Sikkim

Mona Dhakal[1], Om Prakash Dhakal[2], Dhurba Bhandari[3]

[1]Professor in Medicine, [2]Professor in Medicine, Department of Medicine,
[3]Tutor, Department of Microbiology, Sikkim Manipal Institute of Medical Sciences, Gangtok Sikkim

Abstract

Introduction: *Helicobacter pylori* infection is the important cause of various gastrointestinal. Variable resistance to treatment has been reported. This study was conducted to assess eradication rate of *h pylori* infection using the standard clarithromycin triple therapy.

Method: This retrospective observational study was conducted in Central Referral Hospital, Sikkim Manipal Institute of Medical Sciences. 100 consecutive patients in a period of one year from 2016-2017 who were found positive for *H pylori* infection by rapid urease test (RUT) or histology or both were included in the study.Assessment of the eradication of *H pylori* was carried out after 8 weeks of treatment using 14 days of clarithromycin containing standard triple regimen.

Results: Out of 100 patients,63 were males and 37 were females. Mean age of the patients was 38 years. Overall eradication rate was found to 63% after 8 weeks of treatment. Patients with gastric ulcer disease had worst eradication rate and it was statistically significant.[p=0.0143, OR 4.29(1.33-13.79)] .Out of these patients, eradication rate for *H pylori* was higher in duodenal ulcer patients than gastric ulcer patients. [p=0.0069, OR 6.5(1.6751-25.7798)].We found eradication rate of 63% in our study similar to these studies.7-10 days of triple therapy containing clarithromycin is reported to have around 90% eradication rate. (6) Of late, 7-10 days triple therapies have shown unacceptably low cure rates. We found eradication rate of 63% in our study similar to these studies.

Discussion: Triple therapy, a recommended first-line treatment of H. pylori infection is found to be one of the most effective eradication in Asia and Africa. Seven days administration of a PPI, amoxicillin or metronidazole and clarithromycin is well-tolerated and improves patient's compliance. 7-10 days of triple therapy containing clarithromycin is reported to have around 90% eradication rate.

Keywords: *H pylori, gastric ulcer, eradication, triple regime.*

Introduction

Helicobacter pylori infection is the important cause of various gastrointestinal diseases like gastritis, peptic ulcers, gastric adenocarcinoma and mucosa associated tissue lymphoma. This infection of stomach induces chronic inflammation. Production of ammonia by this urease producing bacteria and release of biochemicals such as proteases, vacuolating cytotoxin A and phospholipases are believed to contribute to its inflammatory and carcinogenic potential. Inflammation induced due to this bacterium causes various manifestations.[1] Although eradication of this infection is a debatable issue,[2] this remains central to the management of these illnesses.

Variable resistance to treatment has been reported in different parts of the world and eradication rate

Corresponding Author:
Dr. Om Prakash Dhakal
Professor in Medicine. Department of Medicine,
Sikkim Manipal Institute of Medical Sciences, Gangtok Sikkim
e-mail : dropdhakal@gmail.com

of the standard triple therapy is found to be as low as <80% or even less. This may be due to emergence of clarithromycinresistant strains of *H. pylori*.[3] Eradication close to 90% is acceptable. Diverse data are available in india where eradication rate using legacy triple therapy having clarithromycin is found to be low in some studies while some has shown high response rate.[4] A PPI, clarithromycin and amoxicillin or metronidazole containg triple therapy for 14 days remains a recommended treatment option in regions where *H. pylori* clarithromycin resistance is known to be <15% and in patients with no previous history of macrolide exposure for any reason. There is no treatment regimen which guarantees 100% cure of *H. pylori* infection. Indeed, there are currently only few regimens which consistently achieve eradication rates exceeding 90%.[5] This hospital based observational study was conducted to assess eradication rate of *h pylori* infection using the standard clarithromycin triple therapy in a north eastern part of India.

Method

This retrospective observational study was conducted in Central Referral Hospital, Sikkim manipal institute of medical sciences. It is a tertiary care hospital in Gangtok, Sikkim. 100 consecutive patients in a period of one year from 2016-2017 who found positive for *H pylori* infection by rapid urease test (RUT) or histology or both were included in the study. Informed written consent was taken and approval from the Institutional Ethical Committee was sought. Inclusion criteriabeing patients>12 yr of age, presenting with dyspepsia or symptoms such as malena, weight loss and anaemia and completed 14 days treatment of triple therapy. Patients previously treated for *H. pylori* infection or who gave a clear history of using proton-pump inhibitors or antibiotics within the past four weeks of endoscopy, refused consent or did not complete treatment due to any reason were excluded. Two biopsy samples each from the corpus and antrum were taken and subjected to RUT and histology. Infectionwas considered to be positive if either of two or both the tests were positive for the infection. The details of the patients and the findings were noted. Assessment of the eradication of *H pylori* was carried out after 8 weeks of treatment using 14 days of clarithromycin containing standard triple regimen. To confirm eradication, again two biopsy samples each from the corpus and antrum of the patients were taken and subjected to RUT or histology. Any one or both the tests positive were taken as positive test. Since CRH-SMIMS is the only tertiary care and medical college hospital in this remote north-eastern region of India, it caters to all the four districts of Sikkim.

Results

The study was conducted in 100 patients who completed 14 days clarithromycin containing triple therapy.Out of those 100 patients,63 were males and 37 were females. Mean age of the patients was 38 years. Overall eradication rate was found to 63% after 8 weeks of treatment. Gastritis was the most common finding in upper GI endoscopy in pretreatment group (N=37) whereas GERD and gastro esophageal growth was seen only in 1-1 patient.Gastric ulcer was seen in 15 patients and duodenal ulcer was present in 30 patients. Eradication rate of various GI manifestations was assessed. Patients with gastric ulcer disease had worst eradication rate and it was statistically significant.[p=0.0143, OR 4.29(1.33-13.79)] .Out of these patients, eradication rate for *H pylori* was higher in duodenal ulcer than gastric ulcer patients. [p=0.0069, OR 6.5(1.6751-25.7798)].

Table 1. Upper gastrointestinal lesions and Helicobacter pylori eradication in studied population

Endoscopic finding	n=100	Hpylori+Ve n=37 M=21 F=10	Hpylori-ve n=63 M=42 F=27	Eradication Rate (%)	P value	OR(95%CI)
Gastritis	37	12	25	67.56%	0.46	0.7(.3107-1.7131)
Antroduodenitis/duodenitis	13	6	7	53.84%	0.46	1.5(.4780-5.0160)
Gastric ulcer	15	10	5	33.33%	0.0143	4.29(1.33-13.79)
Duodenal ulcer	30	7	23	76.66%	0.6083	0.40(0.1539-1.0699)
Growth	1	1	0	0%	0.3155	5.2(0.2072-131.47)
GERD	4	1	3	75%	0.6065	0.55(0.0557-5.5447

Discussion

Triple therapy, a recommended first line treatment of *H pylori* infection is found to be one of the most effective eradication in Asia and Africa. Seven days administration of a PPI, amoxicillin or metronidazole and clarithromycin is well tolerated and improves patients compliance. 7-10 days of triple therapy containing clarithromycin is reported to have around 90% eradication rate.[6] Of late, 7-10 days triple therapies have shown unacceptably low cure rates.[7] Standard first-line triple therapy of two antibiotics and a proton pump inhibitor (PPI) failed to show consistent efficacy in various studies.[8]We found eradication rate of 63% in our study similar to these studies. Rapid metabolism of PPIs, antibiotic resistance and poor patient compliance are the probable causes of eradication failure.[9]However the major cause of eradication failure appears to be clarithromycin resistance.[10]According to a systemic review the rate of clarithromycin resistant strains worldwide ranged from 49% in Spain to 1% in The Netherlands.[11] Different ways have been recommended in to improve eradication rate of triple therapy like duration of treatment, effect of PPI on gastric acid secretion and using alternative regimens. One study has reported Esomeprazole to have more anti-secretory effects than other PPIs. Sequential and quadruple bismuth therapy has shown better eradication as compared to triple therapy.[12] A meta analysis trial in west asia suggested that 10-day Bismuth-Furazolidone/Metronidazole quadruple therapy, 14-day Clarithromycin-containing hybrid therapy and 14 day quadruple therapy including a proton pump inhibitor + Bismuth + Tetracycline (500 mg QID) + Metronidazole (500 mg TDS) are an effective first line options.[13] As per review article, bismuth-based furazolidone or clarithromycin containing quadruple therapies, hybrid regimen and concomitant therapy seem to be appropriate options among first line eradication regimens. 10-14 days course of Clarithromycin containing triple therapy has shown to be a good eradication therapy in Iran if local H pylori resistance to clarithromycin is known to be less than 15%.[14] According to one article, in regions with low (≤15%) clarithromycin resistance, 14 day hybrid (or reverse hybrid), 10-14 day sequential, 7-14 day concomitant, 10-14 day bismuth quadruple or 14 day triple therapy can achieve a high eradication rate (>90%) in the first line treatment of *H pylori* infection whereas in areas with high (>15%) if no recent data of local antibiotic resistances of *H. pylori* strains are available, universal high efficacy regimens such as 14 day hybrid (or reverse hybrid), concomitant or bismuth quadruple therapy can be adopted.[15] So in nut shell, it is still acceptable to employ a standard triple based therapy in areas with low clarithromycin resistance (<15%) to achieve eradication rate more than 90%, but it should be abandoned in areas with high clarithromycin resistance.

Quinolone based triple therapy can be effective in the first line therapy of *H pylori* infection.[16] Despite that, quinolonebased triple therapy is generally not recommended as first line therapy due to concerns about the rising prevalence of quinolone resistant strains.[17]

The prevalence of *H pylori* varies with different geographical locations, with high infection rates in the population in developing countries. In India, it is found to be over 80% in rural areas. The *H pylori* positivity in one study population was 61.85 %. [18] Only one prevalence study available in this part of India which showed relatively low prevalence of this infection.[1]

Treatment needs to be individualized on the basis of host polymorphisms, antibiotic resistance, demographic factors and co morbidity. Sequential therapy can be an alternative to the conventional triple therapy as first line therapy. Levofloxacin based triple therapy or a bismuth containing quadruple therapy can be employed as rescue treatment if the standard triple therapy or sequential therapy also fails. A levofloxacin based triple therapy is an acceptable alternative to metronidazole salvage. An empirical triple or quadruple therapy can be employed in case of unavailabity of culture guided antimicrobial sensitivity data. [3]

Conclusion

Since no studies are conducted in this part of India to show exact clarithromycin resistance, we used only standard triple therapy to eradicate *H pylori* in our patients. More studies especially comparative studies needs to be conducted using different regimes to assess clarithromycin resistance and to achieve good eradication rate of *H pylori* in this region.

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