Comparison of Five Different Treatment Regimens for H. Pylon Eradication

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Huma Qureshi,Waqaruddin Ahmed,Ghazala Mohyuddin Arain,Itrat Mehdi,S. Ejaz Alarn (PMRC Research Centre, Jinnah Postgraduate Medical Centre, Karachi.)

Abstract

Aim: Treatment response to five different H. Pylori eradication regimens were evaluated to see which is the best regimen in our setup.
Methods: Patients presenting with upper GI symptoms of acid peptic disease underwent upper GI endoscopy and an antral CLO test. All those with a positive CLO test were included in the study. The study was carried out over a year and one trial was followed by another. The treatment regimens comprised of (1) Omeprazole 20mg once a day, colloidal bismuth subcitrate 120mg three times a day, Metronidazole 200 mg three times a day (18 cases). (2) Colloidal bismuth subcitrate three times a day, furazolidone 100mg three times a day, metromdazole 200mg three times a day (28 cases). (3) Omeprazole 20mg once a day, Clarithromycin 500mg twice a day (21 cases). (4) Lansoprazole 30mg once a day, Amoxycillm 500mg three times a day (21 cases). (5) Lansoprazole once a day, Amoxycillin 500mg three times a day and Roxithromycin 150mg twice a day (14 cases). Therapy for all 5 groups comprised of 14 days. Endoscopy and CLO test were done prior to the entry in the trial and at 28 days to see the response.
Results: Meta analysis was done for all the 5 regimens. For the purpose of analysis patients were divided into 2 groups, i.e., those with peptic ulcer and positive CLO (peptic ulcer disease (PUD) and those without peptic ulcer but positive CLO test (Non ulcer dyspepsia (NUD). PUD was seen in 14 of 18 cases in group T, 18 of 28 cases in group 2, 16 of 21 cases in group 3, 6 of 21 cases in group 4 and 3 of 14 cases in group 5. In PUD after 14 days of therapy, lesions healed ahd CLO became negative in 50% cases each in group 1 and 2, 56% in group 3, 83% in group 4 and all in group 5, while in NUD, 25%, 60%, 80%, 47% and 82% respectively showed H. Pylori eradication.
Conclusion: Of the different therapies one proton pump inhibitor with two antibiotics gave best results in ulcer healing and H. pylon eradication in ulcer and non ulcer dyspepsia OPMA 49:278, 1999).

Introduction

Various drug combinations have been introduced for the eradication of Helicobacter pylon but none has been found ideal[1-6]. In developing countries there is high (70-80%) occurrence of this pathogen[1] creating confusion as to whom to treat and whom to ignore, but a high recurrence after eradication (30% at 1 year)[3] and high cost of therapy also contribute significantly to problems in its eradication. The present study was done to evaluate as to which drug combination is best for H. pylon eradication in our setup.

Patients, Methods and Results

Patients presenting with symptoms of peptic ulcer disease i.e., pain in the epigastrium, vomiting, indigestion, nocturnal pain, bloating etc seen at the gastroenterology centre were examined clinically and checked for protozoal/parasitic disease by getting fresh stool examination at the centre and an ultrasound of abdomen for gall bladder or liver disease. Those with negative tests and presistent

symptoms were included in the study. A standardized protocol was made and each subject was entered in the same protocol. This study was run over a year and completion of one trial was followed by commencement of another study. Upper 0.1. Endoscopy was done in a fasting state using topical anesthesia and olympus XQ 20 scope. After performing complete examination of the upper G.1. tract an antral biopsy was taken and embedded in the CLO gel for H. pylon detection. Change in the color of the gel within 15 minutes from yellow to magenta was taken as a positive test and no change or delayed reaction were taken as negative test.

Patients with upper G.I. bleeding, malignancy, previous surgery on the stomach, pregnant and lactating females, those who had received H2 blockers, proton pump inhibitors or antibiotics in the past 10 days were excluded. Patients coming from far-flung areas with possibility of non-compliance to follow-up endoscopy were also excluded. This is a meta analysis of 5 different trials run one after the other over a year. For the purpose of analysis patients with peptic ulcer i.e., those with duodenal ulcer, gastric ulcer or gastritis and a positive CLO test were classified as peptic ulcer disease (PUD) and with a positive CLO test but a normal endoscopy as non-ulcer dyspepsia (NUD). The drugs were supplied for 14 days and compliance checked on day 7 and 14 by counting the number of tablets or capsules present in the pack. Endoscopy and antral CLO test were repeated on day 28. In PUD cases response was taken as the healing of the lesion and a negative CLO test while persistence of ulcer or positive CLO test was a non-response, in NUD negative CLO was taken as a response and positive CLO as non-response. No cross over therapy was done.

Drugs in group 1 consisted of 20 mg of Omeprazole (Zaprole) once a day, Colloidal Bismuth (Cebes) three times a day and Metronidazole 400 mg three times a day, group 2 consisted of Colloidal Bismuth (Cebes) three times a day with Furazolidone (Furoxone SK&B) 100 mg three times a day and Metronidazole 400 mg three times a day. Group 3 comprised of 20 mg of Omeprazole (Losec Astra) with Clarithromycin (Klaricid-Abbott) 500 mg twice a day, group 4 consisted of 30 mg of Lansoprazole (LanzolPharmatec) with Amoxycillin (SK&B) 500 mg three times a day and group 5 consisted of 30 mg Lansoprazole (Lanzol) with Amoxycillin (SK&B) 500 mg three times a day and Roxythromycin (Rulid-Hoechst-Marion Roussel) 150 mg twice a day.

A total of 102 cases entered the trial of whom 18 were in group 1, 28 in group 2, 21 in group 3, 21 in group 4 and 14 in group 5. Peptic ulcer disease was found in 14 of 18 cases in group 1, 18 of 28 in group 2, 16 of 21 in group 3, 6 of 21 in group 4 and 3 of 14 in group 5. After 14 days of therapy, ulcer healed and CLO became negative in 7 (50%) cases in group 1, 9 cases (50%) in group 2, 9 cases (56%) in group 3, 5 (83%) in group 4 and all 3 in group 5. In non-ulcer dyspepsia group CLO negativity rates were 25%, 60%, 80%, 47% and 82% in the five respective groups. Non response rates in PUD were 50%, 50%, 44%, 17% and none in the five groups respectively, and were 75%, 40%, 20%, 53% and 18% in NUD respectively.

When the type of therapy was compared to the response it was found that group 1 and 5 received one proton pump inhibitor with two antibiotics (Omeprazole 20 mg + Colloidal Bismuth + Metronidazole = group 1, Omeprazole 20 mg + Amoxycillin + Roxithromycin = group 5) and group 2 and 4 received one proton pump inhibitor with one antibiotic i.e., Clarithromycin or Amoxycillin. In both PUD and NUD the response to two antibiotics was much better (100% and 82%) in those receiving Amoxycillin and Roxithromycin (group 5) than those receiving Bismuth and Metronidazole (50% and 60% group 2). Using one antibiotic Amoxycillin had an edge over Clarithromycin in PUD (82% vs 47%) while Clarithromycin was better in NUD (83% vs 56%).

Comments

We compared the efficacy of 5 different drug combinations for the eradication of H. pylori and obtained best results when a proton pump inhibitor (Lansoprazol) was used with 2 antibiotics i.e.,

Amoxicillin and Roxithromycin.

For H. pylori eradication initial studies suggested the use of Colloidal Bismuth with 2 antibiotics for 28 days with over 80% response rates[1,2,7]. Similar results were seen at our centre when Bismuth was used with Metronidazole and Amoxicyllin for H. pylori associated duodenal ulcer[3]. Changes in drug combination and duration were suggested internationally due to poor compliance and more side effects due to a larger number of tablets to be taken daily. Later studies showed that proton pump inhibitors produced a more rapid ulcer healing and addition of broader range of antibiotics (macrolides) also contributed significantly to ulcer healing and H. pylon eradication in a shorter span of time. Now twice a day proton pump inhibitor with dual antibiotics twice a day for 7-10 days is recommended for H. pylon eradication[6].

H. pylon does not get resistant to Bismuth, Tetracyclin and Furazolidone[7]. In the present study Colloidal Bismuth with Furazolidone and Metronidazole were used to reduce the cost of therapy and improve the response rate; but the response rates were 50% for PUD and 60% for NUD which are below the acceptable standards. In appears that Metronidazole resistance might be contributing to these poor figures[4,6,8].

When response to therapy of a proton pump inhibitor plus one antibiotic was compared with two antibiotics it was found that although the cost of therapy escalated to almost twice of that with single antibiotic but response was much better with two antibiotics. It has been found in one of our studies that even different brands of Omeprazoles have different response rates[9]. This concern was confirmed in one of the studies from UK where different brands of Omeprazoles from 13 countries were checked for their stability and quality and it was found that appearance of the drug was an excellent predictor of the level of decomposition products in each formulation. They reported that any discoloration which was more than pale brown contained significant level of decomposition products[10]. Similar results were found in another study comparing 32 copy products of Omeprazole of whom only 4 had acceptable potency[11]. Poor response with some brands of Omprazoles might be due to this reason also. It is concluded that for better ulcer healing and H. pylori eradication standard brands of medications should be used which should include a proton pump inhibitor with two antibiotics of which one should be a Macrolide and other either Amoxycillin or Metronidazole. When choosing the brand a high initial cost is probably better than poor or no response at the end of the therapy.

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