

Two Weeks Triple Therapy with Lansoprazole, Amoxicillin and Roxithromycin is better than dual Therapy with Lansoprazole and Amoxicillin for H. pylori Infection: A Randomised, Clinical Trial

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Abstract

Aims: To compare the efficacy of 2 weeks of dual therapy of Lansoprazole and Amoxicillin with triple therapy of Lansoprazole, Amoxicillin and Roxithromycin for H. pylori eradication.

Subjects: Twentyfive suffering from dyspepsia and found H. pylori positive (CLO) during upper GI endoscopy.

Methods: Patients were divided into 2 groups, one group received Lansoprazole (30mg) once a day, and amoxicillin (500mg) three times a day (group I), while the second group received Lansoprazole and amoxicillin in similar dosage with the addition of Roxithromycin (150mg) twice a day (group II). H. pylori status was confirmed on endoscopy using CLO test at entry to the protocol and then at 4 weeks.

Results: H. pylori eradication was 57% in group I and 86% in group II with healing of lesions in all cases. Conclusion: Better response with triple therapy (group II) indicates enhanced eradication of the pathogens with triple therapy while using roxithromycin (JPMA 50:157, 2000).

Introduction

Various drug combinations have been used for H. pylori eradication with varied results¹⁻³. Generally triple therapy using a proton pump inhibitor with two antibiotics gives satisfactory results⁴⁻⁵. In one study omeprazole combined with amoxicillin alone or with amoxicillin and metronidazole were found equally effective in H. pylori eradication⁵ while omeprazole plus clarithromycin and tetracycline gave poor results⁶ but similar combination with tinidazole gave better results⁶. There is a general fear that metronidazole tolerance is decreasing and its resistance increasing world over^{4,7-9}. Therefore most new combinations are replacing metronidazole with macrolides like clarithromycin¹⁰ or roxithromycin^{5,8}. Most antibiotics are able to kill H. pylori when it is in a dividing state because during this state some specific proteins are produced to which antibiotics are sensitive (Amoxicillin and Clarithromycin)¹¹. Proton pump inhibitors increase the pH of gastric mucosa and make the non dividing non protein producing H. pylori into dividing H. pylori and thus increase and enhance the H. pylori's sensitivity to antibiotics like Amoxicillin and Clarithromycin¹¹. Metronidazole attacks on the DNA therefore its effect is not related to the pathogen's dividing status's.

In the present study two antibiotics (Roxithromycin and or Amoxicillin) were used with a proton pump inhibitor to see if the effect of two antibiotics is enhanced when compared with a single antibiotic.

Patients, Methods and Results

Adult patients undergoing upper G.I. endoscopy for symptoms of acid peptic disease were included in the study. Patients already on antibiotics or anti ulcer treatment, upper G.I. bleeders and those with malignancy or chronic liver or renal disease were excluded from the study.

Upper G.I. endoscopy was done in a fasting state using Olympus or Fujinon scopes. After complete examination of the esophagus, stomach and duodenum, an antral biopsy was taken and embedded immediately in the CLO gel using a disposable needle. The color change of the gel from yellow to

magenta within 15 minutes was taken as a positive test while late positives and those that remained yellow were taken as negative. Irrespective of the presence or absence of lesion on endoscopy, all cases that were CLO positive within 15 minutes of embedding were given H. pylori clearance therapy after informed consent. Two drug combinations were used i.e. Lansoprazole 30 mg (Lanzol) once a day before breakfast with Amoxicillin 500mg three times a day (Group I) or Lansoprazole with Amoxicillin in the same dose plus Roxithromycin (Rulid) 150mg twice a day (group II), using systematic randomization. Drugs were given for 14 days and endoscopy plus CLO test were repeated at 28th day. Those cases in whom CLO remained negative at 15 minutes were taken as respondents while those whose CLO showed a color change within 15 minutes were labelled as non respondents. Relief of symptoms was also evaluated at the end of the study.

A total of 4 cases were enrolled for the study of whom 8 were lost to followup and I has yet to complete the therapy leaving 36 cases for evaluation.

There were 26 males and 10 females whose ages ranged from 28 to 35 years (mean 28 years). On endoscopy 26 cases had no lesion. 6 had gastritis or duodenitis and 4 had duodenal ulcer. CLO was positive in all cases. Using systematic randomization, 23 cases in group 1 and 22 in group II received the drug but at the end of the study after excluding the lost to followup cases, 22 had received Lansoprazole with Amoxicillin (group I) and 14 Lansoprazole. Amoxicillin with Roxithromycin (group II).

After 2 weeks of therapy 13 cases (57%) in group I and 12 cases (86%) in group II cleared infection with H. pylori by showing negative CLO test, while 9 cases (43%) in group I and 2 cases (14%) in group II were still CLO positive. H. pylori clearance rate was better in group II (not significant) suggesting that addition of Roxithromycin either potentiated the effect of amoxicillin or acted synergistically and produced better H. pylori clearance.

Comments

H. pylori plays a major role in the occurrence of gastroduodenitis and duodenal ulcer. Its eradication not only results in healing of the lesion and also prolongs the remission of the disease especially in duodenal ulcer^{6,12-14}. Eradication of this pathogen was initially tried with Bismuth preparation plus metronidazole and another antibiotic like amoxicillin or tetracycline'. Resistance to metronidazole^{7,9,15} and other commonly used antibiotics' and lack of compliance to longer duration of therapy (4 weeks) and too many drugs (9 tablets daily) lead to revising the treatment strategy. Newer antibiotics like Clarithromycin and macrolides like Roxithromycin with proton pump inhibitors were used with an attempt to not only reduce the chances of resistance but also produce better compliance, rapid healing and early eradication by disturbing the environment of H. pylori. Goh⁶ reported 79% and 86% H. pylori eradication when using 40mg of Omeprazole once a day with Amoxicillin alone or in combination with Metronidazole and they suggested that dual therapy is not only effective but also well tolerated. Similar results were reported with a one week's therapy of omeprazole plus clarithromycin and tinidazole⁶ but poor response was achieved when low dose Tetracycline was used instead of Tinidazole⁶. Higher dose i.e., 500mg Tetracycline four times a day gives better results. History of smoking and previous use of H₂ blockers have been failure. Moreover short term triple therapies do not seem to produce reproducible results worldwide and it reported to be associated with short term triple therapy is generally accepted that good eradication results are difficult to achieve with short term dual or triple therapies⁶. therefore two weeks of dual or triple therapies are recommended for H. pylori eradication.

Using a similar but twice a day regimen of lansoprazole 30mg, clarithromycin in 500mg and amoxicillin 1gram for 2 weeks, Schawtz et al⁵ reported a 94% eradication of H. pylori. but this figure dropped to 57% and 53% respectively for patients receiving dual therapy of lansoprazole and clarithromycin or lansoprazole and amoxicillin. It is also reported that primary resistance to

clarithromycin is around in Europe^{16,17}, while secondary resistance develops less frequently when proton pump inhibitors are used in clarithromycin and another antibiotic. as compared with proton pump inhibitor and clarithromycin¹⁸.

In the present study two weeks triple therapy comprising of Lansoprazole, amoxicillin and Roxithromycin showed better response (86%) than that achieved with dual therapy (57%) in H. pylori eradication. Addition of Roxithromycin had a synergistic antibiotic effect on the bacterium thereby improving the response. In the present study though the cost of therapy was exceptionally high but better eradication of H. pylori was achieved when compared with dual therapy.

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