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Original Article

Meta-analysis of the efficacy of lansoprazole and omeprazole for the treatment of H.pylori-associated duodenal ulcer

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Abstract: Objective: To conduct a systematic evaluation of the efficacy of lansoprazole and omeprazole for the treatment of Helicobacter pylori-associated duodenal ulcer. Methods: Online databases, including CHKD, VIP, China Info, the National Digital Library of China, Google Scholar, PubMed, Lippincott Williams & Wilkins, and Wiley Online Library were searched for related studies. The quality of the studies was evaluated in accordance with the Cochrane Handbook for Systematic Reviews of Interventions, and relevant information was extracted from them. The studies were subjected to meta-analysis using RevMan5.3 software, and qualitative analysis was performed for studies, in which the data could not be merged. Results: A total of nine randomized controlled trials (RCTs) were included, all of which presented the possibility of bias. Meta-analysis showed no significant differences between patients treated with lansoprazole combinations and omeprazole combinations in terms of DU healing rate (RR = 1.04, 95% CI = 0.99~1.09, P = 0.93). There were significant differences between those treated by lansoprazole combination and omeprazole combination in terms of HP eradication rate (RR = 1.09, 95% CI = 1.01~1.18, P = 0.04), and there was no serious adverse reaction during the treatment process for both lansoprazole and omeprazole. Conclusion: Lansoprazole and omeprazole exhibit similar efficacy in the treatment of Helicobacter pylori associated duodenal ulcers.

Keywords: Lansoprazole, omeprazole, duodenal ulcer, HP infection, meta-analysis

Introduction

Data sources

CHKD, VIP, China Info, the National Digital Library of China, Google Scholar, PubMed, Lippincott Williams & Wilkins, and the Wiley Online Library were searched using the search terms Helicobacter Pylori (HP)-induced Duodenal Ulcer (DU) AND Lansoprazole (LAN) AND Omeprazole (OME); or Helicobacter Pylori (HP) AND Duodenal Ulcer (DU) AND Lansoprazole (LAN) AND Omeprazole (OME) in both Chinese and English, for all fields, including title, abstract, subject heading and full text up to SEPTEMBER 10, 2014, for studies comparing LAN and OME in DU patients who reported a formalized healing and eradication rates for duodenal ulcer.

Study selection

Nine studies met the inclusion criteria, comprising a total of 774 patients.

Data extraction

Efficacy, cognitive response, and remission outcomes were extracted from each publication or obtained directly from the authors.

Peptic ulcer, a lesion in the stomach and duodenum, is a common disease encountered in gastroenterology. Duodenal ulcer is the most common form of this disease and occurs frequently in China. Most lesions are in the duodenal bulb (95%) and are more likely to occur in the winter and spring. This disease is intimately linked with gastric acid secretion; Helicobacter (H.

pylori) infection; non-steroidal anti-inflammatory drug (NSAID) use; living and eating patterns; stress, smoking, and alcohol consumption; and mental and psychological factors. Current clinical treatments for duodenal ulcers include an H2 receptor antagonist (H2-RA) and proton pump inhibitor (PPI). PPI accelerates the healing rate, so it's the preferred medication for the treatment of duodenal ulcers. Commonly used PPIs include omeprazole, pantoprazole, lansoprazole, rabeprazole, esomeprazole, and Ai Pula. Omeprazole and lansoprazole are the first and second generations of PPIs, respectively, to specifically inhibit the proton pump h^+, k^+, and ATP enzyme activity of gastric parietal cells, resulting in the strong and continuous inhibition of gastric acid secretion and accelerated healing of ulcers [1]. Lansoprazole is a new proton pump inhibitor whose chemical structure is very similar to that of omeprazole. The difference between these PPIs is that lansoprazole contains an additional fluoride on its pyridine ring. After importing fluoride, lansoprazole is more physically and chemically stable and is more bioavailable [1]. However, there is no systematic review comparing the efficacy of lansoprazole and omeprazole for the treatment of HP-associated duodenal ulcers. Therefore, this comparative study of lansoprazole combination therapy with omeprazole combination therapy for the treatment of HP-associated duodenal ulcer includes a meta-analysis of all a randomized controlled trials (RCTs) conducted to date. A comparison of the efficacy and safety of omeprazole and lansoprazole therapies will provide a reference to aid in the clinical treatment of HP-associated duodenal ulcers.

Materials and methods

Inclusion criteria

(1) Study design: all studies included were randomized controlled trials (RCTs) that were not necessarily blinded. (2) Subjects: all subjects examined were diagnosed with HP-related duodenal ulcer, and their sex, age, and race were disclosed. (3) Interventions: controlled studies of both lansoprazole and omeprazole combined with the same drug that utilized clear evaluation criteria were included. (4) Outcome indicator: studies including DU healing rates, HP eradication rates and adverse reactions were included, while categorical variables used to judge ulcer healing included clinical symptoms and the completely or near-complete disappearance of the ulcer, with or without inflammation. (5) Consists of the clinical trials designed to compare two groups.

Exclusion criteria

(1) The study group and the control group were inconsistent in terms of combination therapy or treatment. (2) An association with stress ulcers; upper digestive tract bleeding; compound or other serious complications; patients with serious heart, liver and renal disorders; and pregnant and lactating women. (3) The experimental design was not reasonable or the research has failed to effectively extract statistically meaningful data. (4) The trials were non-randomized controlled clinical trials. (5) The study involved the use of non-Western medicine or the control group included clinical trials of other drugs. (6) Inappropriate statistical methods were used of the research was duplicated. (7) The research was non-original or included reviews and experiments on animals.

Retrieval strategies

Using computer-based retrieval methods, the Bibliographic database included data published in the academic literature in China (CHKD), the VIP scientific journal database, the digital record of periodicals in China, the National Digital Library of China, Google Scholar, PubMed, Lippincott Williams & Wilkins, and the Wiley Online Library. The retrieval was performed in August 2014 for articles unrestricted by language using the search terms Helicobacter Pylori (HP)-induced Duodenal Ulcer (DU) AND Lansoprazole (LAN) AND Omeprazole (OME), or Helicobacter Pylori (HP) AND Duodenal Ulcer (DU) AND Lansoprazole (LAN) AND Omeprazole (OME). All searches included title, abstract, subject heading and full text up to a publication date of September 10, 2014, for studies comparing LAN and OME in DU patients who reported formalized healing and eradication rates for duodenal ulcers. In total, sixty-nine articles were retrieved, and following the elimination of repeated titles and a number of studies according to the inclusion and exclusion criteria, nine studies remained, comprising a total of 774 patients (**Figure 1**).

Literature filtering and data extraction

Two researchers independently vetted the studies for inclusion and exclusion criteria, and in

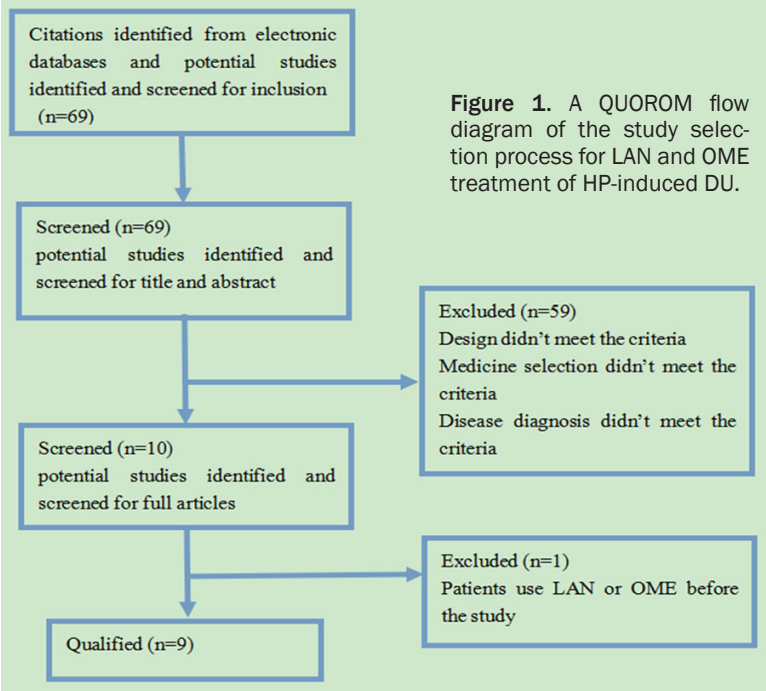

Figure 1. A QUOROM flow diagram of the study selection process for LAN and OME treatment of HP-induced DU.

the case of dissent during the extraction of data from the included studies, the two researchers discussed their differences and reached an agreement. The titles and abstracts of the retrieved documents were screen edprior to reading an article to determine whether it met the inclusion criteria. Third party opinions were solicited in the case of disagreement. Information extraction included: 1 the author's name, publication time and research type; 2 patient enrollment and exit, as well as group interventions; 3 time of therapy; and 4 evaluation indicators, DU healing rate, HP eradication rate, and ADR incidence rate.

Quality of literature evaluation

We assessed bias risk through the "bias of risk assessment tools" recommended by the Cochrane Collaboration network. RCT bias risk assessment was performed as follows: (1) random sequence generation (selection bias); (2) allocation concealment (selection bias); (3) researcherblinding (implementation bias); (4) outcome assessment blinding (observer bias); (5) data integrity (defaulters bias); (6) selective reporting (reporting bias); and (7) any others. The results of the literature evaluation are displayed using a graphic.

Data analysis

All statistical analyses were performed using RevMan 5.3 software, including the enumeration data (i.e., dichotomous variables), odds ratio (risk ratio, RR), 95% confidence interval (CI) analysis of therapeutic effect, and the heterogeneity analysis using the X^2 test. When statistically significant homogeneity was identified between studies ($P>0.10$, $I^2<50\%$), a fixed effect model was used for Meta-Analysis. While statistically significant heterogeneity between studies was observed ($P<0.10$, $I^2>50\%$), we analyzed the source of the heterogeneity via subgroup analyses for factors that may have caused the heterogeneity. If there was statistically significant heterogeneity between the two research groups but the clinical heterogeneity or difference was not statistically significant, the random effects model was used for analysis. If the heterogeneity was the result of low quality research, conduct sensitivity testing was used for analysis. If the heterogeneity between two groups was too great or we could not identify its source, only descriptive analysis was performed.

Results

Overview of included studies and quality assessment

Follow in group search criteria for document retrieval, 69 studies in total were deemed relevant. In light of the inclusion and exclusion criteria, nine articles were ultimately selected, reporting a total 774 cases as shown in **Table 1**. Of the included studies, three [2, 4, 5] that blinded participants and were of low risk, two [2, 5] case studies reported a number of withdrawals and a lack of follow-up, and only one [2] study reported the intentions of the researcher. The rest of the studies did not specify details regarding blinding, exits, missing cases, or intentionality analysis. We ultimately included nine [2-10] studies for which the data integrity was high. Risk assessment shows that for the included studies, there was some risk of bias. The results of this assessment are shown in **Figure 1** ("Risk of Bias").

Table 1. An overview of included studies

	Study design	The number of cases T/C	Exit numbers	Interventions		DU Healing rates (%)		HP Eradication rates (%)		ADR incidence of (%)		Outcome measures
				T	C	T	C	T	C	T	C	
Harris A.W 1998 [2]	RCT	64/75	29	LAN+AMO+ metronidazole	OME+AMO+ metronidazole	81.3	80.0	-	-	-	—	①②③④
Lorella Fanti 2001 [3]	RCT	21/22	0	LAN+ clarithromycin+ tinidazole, The successor LAN 3 Week	OME+ clarithromycin+ tinidazole, The successor OME 3 Week	100	100	-	-	4.8	4.5	①②③④⑤
Ormeci N 2003 [4]	RCT	54/54	0	LAN+AMO+ clarithromycin	OME+AMO+ clarithromycin	94.4	90.7	90.7	79.6	-	—	①②③④
Huang Xiaofeng 2005 [5]	RCT	21/20	2	LAN+AMO+ Clarithromycin	OME+AMO+ Clarithromycin	95.0	100	-	-	-	—	①②③④
Lin Hailing 2007 [6]	RCT	23/23	0	LAN+AMO+ Tinidazole	OME+AMO+ Tinidazole	87.0	82.6	95.7	82.6	13.0	13.0	①②③④⑤
Tao Lisheng 2011 [7]	RCT	28/28	0	LAN+AMO+ Furazolidone	OME+AMO+ Furazolidone	85.7	82.1	60.3	64.3	0	0	①②③④⑤
Xu Yuxiang 2012 [8]	RCT	84/84	0	LAN+AMO Qian 2 Week	OME+AMO Qian 2 Week	90.5	88.1	82.1	79.8	0	0	①②③④⑤
Ji Xiaoxia 2013 [9]	RCT	46/48	0	LAN+AMO+ Clarithromycin	OME+AMO+ Clarithromycin	89.1	87.5	84.8	83.3	-	—	①②③④
Yu Tao 2014 [10]	RCT	58/52	0	LAN+AMO Qian 2 Week	OME+AMO Qian 2 Week	77.6	67.3	86.2	69.2	0	0	③④⑤

① Ulcer healing rate; ② HP eradication rates; ③ Abdominal pain eased or disappeared; ④ Relapse rate; ⑤ Adverse reactions; LAN: Prevacid; OME: Omeprazole; AMO: Omeprazole.

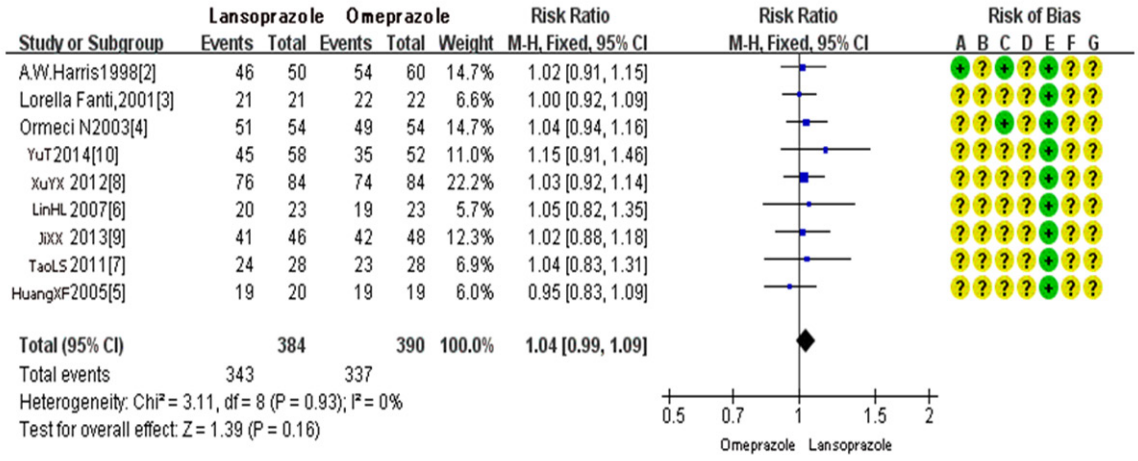

Figure 2. The amoxicillin and potassium clavulanate group VS the amoxicillin DU healing forest: Results of the Cochrane "bias of risk assessment tools" evaluation Cochrane "risk assessment of bias".

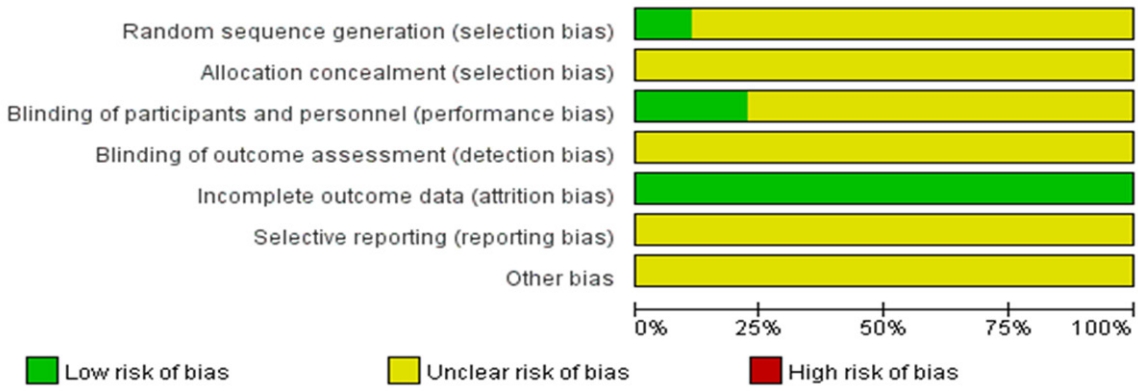

Figure 3. The amoxicillin and potassium clavulanate group VS the a moxicillin HP eradication rates of forest.

Meta-analysis

DU healing rate analysis: As we can see in **Figure 2**, the nine included clinical studies that were randomized controlled trials did not display statistically significant heterogeneity (I^2 = 0%, P = 0.93). Using the fixed effects model of combined statistics, the RR Value was found to be 1.04, 95% CI = [0.99-1.09]. The *P* value was 0.16, indicating that when comparing the omeprazole group with the lansoprazole group for the treatment of HP-related duodenal ulcers, no significant difference in healing rate was observed.

Rate of HP eradication: In **Figure 3**, we can see that of the included studies, six [4, 6-10] provide data on HP eradication. Analysis of these six studies revealed no statistically significant heterogeneity between the two groups (P = 0.57, I^2 = 0%). Using the fixed effects model of combined statistics, the RR Value was found to be 1.09, 95% CI = [1.01-1.18]. The *P* value was 0.04, indicating that the two groups' HP eradication rates were significantly different.

Analysis of adverse reactions

Only two studies [3, 6] reported cases of adverse reactions: one [6] study reported one

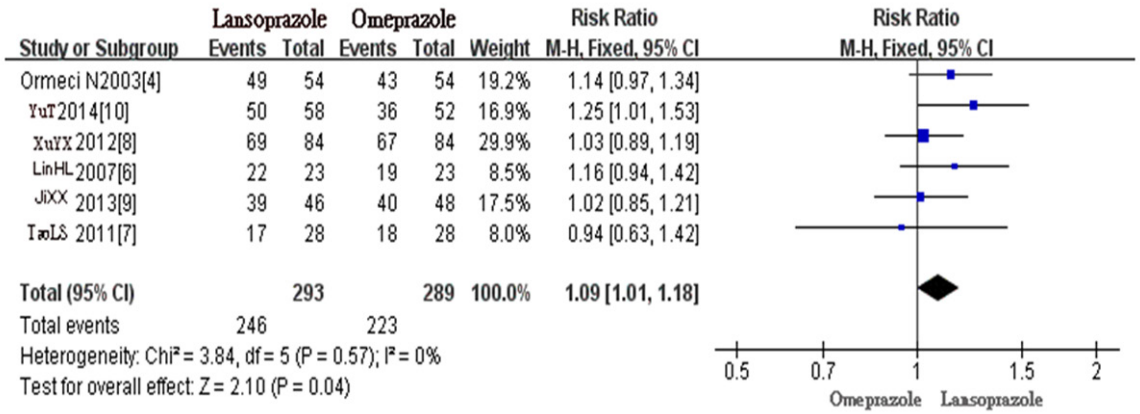

Figure 4. Included studies of DU healing rate on a funnel plot.

case of Anorexia in the lansoprazole group and two cases of weakness, dry mouth, while the omeprazole group contained two cases of dizziness and drowsiness and one case of dry mouth. In the other study [3], the lansoprazole group contained one case of mild diarrhea, while the omeprazole group had one case of stomatitis. One article [8] reported no adverse reactions within four weeks, but during the follow-up year there was one case of weakness and dizziness. Three studies [2, 5, 9] did not mention the incidence of adverse reactions. The rest of the articles reported no serious adverse reactions or only minor adverse reactions.

Sensitivity analysis

Using the fixed effect and random-effects models, we performed a meta-analysis to compare ulcer healing rate. The fixed effects model estimated the combined RR Value to be 1.04, 95% CI = [0.99, 1.09], and the random effects model's RR values and 95% CI were 1.02 and [0.98, 1.06], respectively. The difference between treatments was not statistically significant. Removing the maximum [8] and minimum [5] studies and applying the fixed effects model did not change the result of the analysis significantly (RR = 1.05, 95% CI = [0.98-1.12], suggesting the stability of the meta-analysis.

Release bias

Using a funnel plot to analyze the included studies, we found that poor graphical symmetry implicated a certain amount of publication bias (**Figure 4**).

Discussion

Epidemiological studies have shown that with the exception of those caused by non-steroidal anti-inflammatory drug (NSAID) use, nearly all duodenal ulcers are caused by HP infection. While a growing number of clinical studies have demonstrated that the recurrence of peptic ulcers is associated lingering or secondary HP infection. The eradication of Helicobacter pylori (HP) can significantly reduce the recurrence of duodenal ulcers [8]. In China, proton pump inhibitors combined with antibiotics are commonly used for the treatment of HP-associated duodenal ulcers. Omeprazole is one such clinical proton pump inhibitor used for the treatment of peptic ulcers, while Lansoprazole is the second most popular proton pump inhibitor after Omeprazole with a similar structure. Due to its four fluorideson the pyridine ringside chain, it has three fluoride ethyoxyl-replaced substituent groups, making it 30% more effective than Omeprazole [11]. Lansoprazole is more lipophilic than Omeprazole and can therefore penetrate the cell membrane more quickly to convert sulfonic acids and sulfonyl derivatives, thereby resulting in an acid-suppressive effect. Studies have reported that Lansoprazole exhibits a four-fold increase in bacteriostatic activity against Helicobacter pylori compared to Omeprazole [12]. Clinical use of Lansoprazole for the treatment of HP-associated duodenal ulcers was therefore assumed to be better than Omeprazole.

In this paper, nine randomized controlled studies were compared in a meta-analysis between

Omeprazole and Lansoprazole groups to assess their clinical efficacy. Although the six studies [4, 6-10] mentioning HP eradication rate showed a significant difference between groups (P = 0.04), the two groups showed no significant difference in healing rate (P = 0.16). Therefore, Omeprazole and Lansoprazole show no significant difference in the treatment of HP-associated duodenal ulcers. Thus, either Lansoprazole or Omeprazole canbe used to treat HP-associated duodenal ulcers.

Due to the small number of studies included in this meta-analysis, the majority of [3, 6-10] studies with blinding were not used. Furthermore, the sample size was relatively small, and we cannot guarantee the reliability of the studies. In addition, the asymmetry of our funnel plot analysis indicates a publication bias. This can be attributed to the included documents that were published, non-published or conference documents, or may be connected to the limitations of our literature search strategy and the design of the inclusion and exclusion criteria. As a result, we cannot draw conclusions with absolute certainty. We look forward to analyzing a larger sample assessed in multicenter, high quality randomized controlled trialsin the future to have reliable data for the evaluation of Lansoprazole for the treatment of HP-associated duodenal ulcer.

Disclosure of conflict of interest

None.

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