REVIEW ARTICLE

Drugs 2005; 65 Suppl. 1: 83–96
0012-6667/05/0001-0083/$39.95/0

Potent Gastric Acid Inhibition in *Helicobacter pylori* Eradication

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Abstract

At present, antisecretory drugs — foremost among them the proton pump inhibitors (PPIs) — represent a keystone in *Helicobacter pylori* eradication therapy. The present article shall first compare the role of PPIs as compared with histamine H_2 receptor antagonists, both of them in the role of antibiotic-associated antisecretory therapy, and shall then address the contribution of each of the various PPIs that have been developed until the present time to the *H. pylori* eradication therapies. In summary, it may be concluded that PPIs are more effective overall than H_2 receptor antagonists when the two groups of antisecretory drugs are given at the usual standard doses together with antibiotics with the intention of eradicating *H. pylori* infection. However, all PPIs (omeprazole, lansoprazole, pantoprazole, rabeprazole, and esomeprazole) are equivalent when given together with two antibiotics to cure the infection.

1. Introduction

Helicobacter pylori infection is the fundamental cause of chronic gastritis and gastro-duodenal ulcer disease, and plays a fundamental role in the development of gastric cancer.[1] *H. pylori* eradication in patients with peptic ulcer is associated with undoubted benefits, such as speeding of ulcer healing, prevention of recurrences and decrease of haemorrhagic complications.[2] At present, antisecretory drugs, foremost among them the proton pump inhibitors (PPIs), represent a keystone in eradication therapy. The present chapter shall first compare the role of PPIs with that of histamine H_2 receptor antagonists, both of them in the role of antibiotic-associated anti-secretory therapy, and shall then address the contribution of each of the various PPIs that have been developed until the present time to the *H. pylori* eradication therapies.

As in all the other articles in this issue, the scientific evidence will be categorised according to the proposals of the Centre for Evidence-Based Medicine, Oxford, UK (see Introduction — Potent Acid Inhibition, by Ponce and Mearín). As the results assessed in the present article are derived exclusively from systematic reviews and meta-analyses of randomised clinical trials (with homogeneous results), the level of evidence for the derived conclusions shall be categorised as '1a'. Therefore, in all cases the degree of recommendation should and must be categorised as 'A' ('very highly recommendable', the highest degree).

2. PPIs *versus* Histamine H_2 Receptor Antagonists

Eradication therapy for *H. pylori* is based on the combination of two antibiotics plus one antisecretory drug.[3] Multiple studies and trials have been published that include the H_2 receptor antagonists as anti-secretory agents, with relatively encouraging results.[4–12] The first thing to do is thus to

consider whether the PPIs are superior to the anti-H_2 in this indication. On the one hand the PPIs possess, different to the H_2 receptor antagonists, intrinsic antibacterial activity against *H. pylori*,[13] besides producing a synergic pharmacokinetic interaction with the antibiotics.[14,15] On the other hand, the PPIs have a greater anti-secretory capacity than that achieved when using standard-dose H_2 receptor antagonists.[14,15] It may thus be postulated that, combined with antibiotics, PPIs will be more effective in *H. pylori* eradication than H_2 receptor antagonists. And yet, in this context, only but few studies have directly compared PPIs *versus* H_2 receptor antagonists as the eradication efficacy against *H. pylori*, with contradictory results.

Some years ago a meta-analysis was carried out in which both types of anti-secretory drugs were compared; at that time no statistically significant differences were demonstrated.[16] However, that meta-analysis was published only as a 'Letter to the Editor' in a German-language journal, and it furthermore suffered from a number of serious limitations, such as the small number of studies assessed (and the small number of patients included in each study) or the suboptimal quality of the methodologic aspects, thus considerably limiting the validity of the conclusions. For this reason, an updated systematic review and meta-analysis has been recently carried out in which the *H. pylori* eradication efficacy of both groups of anti-secretory drugs, when administered together with antibiotics, was assessed.[17] To this purpose, all those published randomised studies were selected in which PPIs and H_2 receptor antagonists were compared when administered together with the same two antibiotics. Twenty studies were identified[18–37] and, overall, a greater efficacy of PPIs *versus* H_2 receptor antagonists was evidenced (eradication rate of 74% *vs* 69% in the 'intention to treat' analysis). The odds ratio (OR) for this comparison was 1.31, with a 95% confidence interval (95% CI) of 1.09–1.58, as graphically represented in figure 1.

A number of arguments might be put forward for explaining the better results achieved with PPIs as compared with H_2 receptor antagonists.[38,39] Thus, the *in vitro* efficacy of antibiotics against *H. pylori* depends on a number of factors, such as drug adherence to the gastric mucosa and to the mucus layer, their stability within the gastric environment and their antibacterial activity. All these factors are

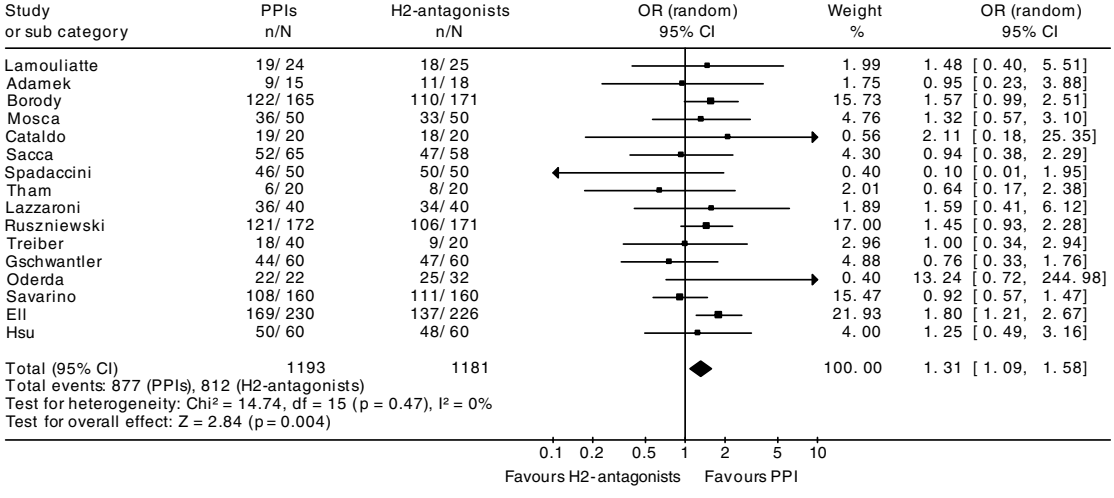

Fig. 1. Meta-analysis of the studies comparing proton pump inhibitors (PPIs) and histamine H_2 receptor antagonists (H2-antagonists) in combination with antibiotics in *Helicobacter pylori* eradication therapy. Intention-to-treat analysis.[18–37] **OR** = odds ratio; **95% CI** = 95% confidence interval.

in turn influenced by the intragastric acidity level and thus by the potency of the associated anti-secretory drugs.[13,40] It is well known that PPIs possess a more marked anti-secretory effect than H_2 receptor antagonists when both are prescribed at the usual standard doses.[14,15] One recent study randomised a group of *H. pylori*-infected patients to receive two antibiotics (amoxycillin and clarythromycin) plus one of the following regimes for 7 days: (a) no anti-secretory drug, (b) ranitidine 150 mg b.i.d., (c) ranitidine 300 mg b.i.d., and (d) omeprazole 10 mg b.i.d.[28] The *H. pylori* eradication rates were 33%, 59%, 79% and 83%, respectively, suggesting that the eradication efficacy correlates with the degree of acid secretion inhibition and that it is similar in patients receiving high doses of ranitidine or normal ('standard') doses of omeprazole. In this context, in two of the discordant studies in the aforementioned meta-analysis,[17] which showed even better results (albeit without achieving statistical significance) with the H_2 receptor antagonists than with the PPIs, very high doses of the former were prescribed that were notably higher (in relative terms) than those prescribed in the case of PPIs.[23,36] Thus, when a subanalysis of the data was performed excluding those discordant studies, the therapeutic benefit of PPIs over H_2 receptor antagonists became even more evident (the OR increased from 1.31 to 1.37, and the between-study heterogeneity vanished).

On the other hand, the hypochlorhydria induced by anti-secretory drugs impairs the survival of *H. pylori* within the stomach, as the growth of this microorganism depends on intragastric pH.[41] As some antibiotics require *H. pylori* to be in active division for exerting their antibacterial activity, maintaining the pH above a given threshold might be fundamental for allowing the bacterium to be in a state of division that will render it susceptible to the action of antibiotics.[13] PPIs possess *in vitro* an additive, even synergistic, effect to that of a number of antimicrobials;[42,43] for instance, the activity of amoxycillin against *H. pylori* increases with increasing pH.[44] In fact, amoxycillin given alone is only able to induce a transient 'clearance' of the infection, but only exceptionally does it achieve true eradication of the microorganism *in vivo*.[38] The addition to amoxycillin of standard doses of H_2 receptor antagonist achieves eradication rates some 15% higher than those seen with the antibiotic alone. Prescribing higher doses of ranitidine or omeprazole, both in combination with amoxycillin, has been associated with eradication rates in the order of 60%.[38] A number of studies have suggested that the use of high doses of omeprazole increases the amoxycillin concentration in the gastric juice,[45] and that higher PPI doses improve the *H. pylori* eradication rates when a dual therapy with PPI and amoxycillin is prescribed.[46–49]

It has been demonstrated that the level of gastric acidity achieved while a dual therapy is being given exerts a clear influence on the final eradication rate. Thus, during dual therapy with omeprazole and amoxycillin, the patients in whom *H. pylori* eradication was finally achieved were those evidencing a more alkaline intragastric pH.[50,51] However, these results have not been confirmed by other authors[52–54] so it is possible that increasing the PPI dose beyond a given level, with the intention of achieving a neutral pH over the 24 h of the day, may not be really useful.[33] In this context, and contrary to the previously mentioned studies, some authors have observed that the degree of acid secretion inhibition is not a decisive factor for *H. pylori* eradication when a dual therapy is used.[18,37]

Another one of the clinically relevant antibiotics, clarithromycin, is the most acid-labile among those antibiotics habitually used in treating *H. pylori* infection. The activity of this antibiotic against *H. pylori* increases with increasing pH.[13] Joint administration of omeprazole and clarithromycin increases the plasma and mucous concentrations of the antibiotic.[13] Finally, metronidazole is highly stable in the gastric juice at a pH range between 2 and 7.[55] Thus, the bioavailability and the pharmacokinetic features of the nitroimidazoles do not seem to be influenced by the acid secretion inhibition induced by PPIs.[13] Furthermore, and in contrast to other antibiotics, no synergistic effect (as to *H. pylori* eradication efficacy) has been

described between PPIs and metronidazole.[40] A recent meta-analysis has demonstrated greater efficacy of eradicative triple therapies including amoxycillin (i.e., PPI–amoxycillin–clarithromycin) when the PPI is given at double-dose twice daily instead of once daily.[56] Another meta-analysis with the aim of comparing the efficacy of once-daily PPIs (the standard dose once daily) as compared with double-dosing (the standard dose twice daily) in the context of triple therapies demonstrated a higher eradication rate with the double dose;[57] concretely, the beneficial effect of the higher dose of PPI (and its consequent greater anti-secretory effect) was restricted to the triple therapy combination containing clarithromycin and amoxycillin, but was not observed when the antibiotics prescribed were clarithromycin and metronidazole.[57–59]

Another possible explanation for the better results achieved with the PPIs as compared with the H_2 receptor antagonists might be the different direct effect on *H. pylori* the PPIs may have. Thus, while the H_2 receptor antagonists have no intrinsic antibacterial effect against *H. pylori*, the PPIs have been shown to have, *in vitro*, a remarkable bactericidal activity, with a minimum inhibitory concentration (MIC) similar to that described for the bismuth salts.[60,61] Nevertheless, it is debatable whether this antibacterial effect also applies *in vivo*, as the plasma PPI concentration is appreciably lower than that required for achieving an antibacterial effect *in vitro*.[13,62] Thus, the administration of omeprazole alone renders the detection of *H. pylori* impossible immediately after concluding therapy in up to 50% of the cases; but when the same diagnostic methods are used 4 weeks after the end of therapy, eradication of *H. pylori* is only confirmed in less than 5% of the patients.[38]

Besides the therapeutic efficacy aspects, other variables of interest, such as the safety profile or the cost of therapy, should also be borne in mind when comparing PPIs and H_2 receptor antagonists. The tolerability profile of the two groups of antisecretory drugs (together with antibiotics) has been similar in a number of studies, no differences having been reported in the incidence of adverse side effects.[20,21,26,27,33,35,36,63] A cost–benefit study has been carried out in which the decision analysis model, considering both the direct and indirect costs, has demonstrated that the therapies including PPIs and H_2 receptor antagonists are approximately similar in cost-effectiveness.[64] However, the sensitivity analysis, which particularly considered the fluctuations in the eradication rates, suggests that the PPI-containing regimes might finally be more cost-effective, underscoring the idea that the most relevant fact on which the final cost of a therapeutic strategy depends is its *H. pylori* eradication efficacy. Other studies have demonstrated that, although improved results might be achieved with high-dose ranitidine (as compared with reduced doses of omeprazole), this benefit is associated with considerably higher costs, as not less than 600 mg ranitidine would have to be given twice daily.[36]

In summary, and based on the discussed data, it may be concluded that PPIs are overall more effective than H_2 receptor antagonists when the two groups of antisecretory drugs are given at the usual standard doses together with antibiotics, with the intention of eradicating *H. pylori* infection.

3. Role of the Various PPIs in *H. Pylori* Eradication Therapy

3.1 Lansoprazole

The first studies on triple therapies used omeprazole, as this was initially the only available PPI. Further drugs, such as lansoprazole, belonging to the same therapeutic group later appeared in the market and began being used in eradication therapy. A review specifically addressing the role of lansoprazole in *H. pylori* eradication demonstrated, some time ago, that the efficacy of lansoprazole and omeprazole in this indication was similar.[65] Some time later, the I Spanish Consensus Conference on *H. pylori* eradication therapy again examined the issue of whether lansoprazole was as effective as omeprazole, concretely in the context of triple therapies using

a PPI together with two antibiotics for 7 days, and the answer was affirmative.[2] Thus, the mean efficacy (analysis of the data as per intention to treat) of the combination of lansoprazole, clarithromycin and a nitroimidazole was 85%, while when the latter antibiotic was replaced by amoxycillin the resulting mean efficacy was 81%.[2]

3.2 Pantoprazole

Pantoprazole was the third PPI to be introduced and, similar to the other drugs in the group, demonstrated itself to be very effective in achieving symptomatic relief and healing of oesophagitis and peptic ulcer, with therapeutic success rates similar to those previously reported for omeprazole and lansoprazole. One particular difference of this drug as compared with the foregoing PPIs is its lesser affinity for the hepatic cytochrome P450, and thus its potential (albeit of doubtful clinical relevance) advantages regarding pharmacologic interactions.[62,66–73]

As previously stated, PPIs possess *in vitro* antibacterial activity against *H. pylori*, but differences do exist in this aspect depending on the type of PPI. Thus, again *in vitro*, pantoprazole is less effective against *H. pylori* than omeprazole or lansoprazole.[74–76] Lansoprazole, for instance, inhibits *H. pylori* urease activity more intensely than pantoprazole. However, it has been suggested that intrinsic antibacterial activity might have only limited clinical relevance in the achievement of eradication, whereas the fundamental effect of PPIs would be related to the intragastric pH increase they induce, which in turn would increase the efficacy of the associated antibiotics.[62] Even though a number of comparative studies on acid secretion inhibition achieved with various PPIs have suggested that pantoprazole has the same or similar potency to omeprazole when given at the same dosage, pantoprazole 40 mg (i.e., the standard dose) has been shown to be more effective than omeprazole 20 mg (again, the standard and usually prescribed dose) for increasing intragastric pH.[77]

Thus, it might be postulated (and questioned, and debated) whether the efficacy of the two PPIs — omeprazole and pantoprazole — is also different when they are combined with antibiotics with the intent of eradicating *H. pylori* infection. One systematic review and meta-analysis has recently been carried out that might help answer this question.[78] Thus, it is in the first place manifested that the combination of pantoprazole and amoxycillin given for 14 days (i.e. dual therapy) has only slight therapeutic efficacy, about 60%. However, triple therapies comprising two antibiotics together with pantoprazole achieve considerably higher healing rates. In this way, the mean eradication rate with the combination of pantoprazole–clarithromycin–amoxycillin given over 7 days is 78%, and the rate is 84% with the combination of pantoprazole–clarithromycin–nitroimidazole given over the same period. These results are similar to those achieved previously with other PPIs such as omeprazole or lansoprazole.[56,79–82] Furthermore, the aforementioned systematic review has shown that some randomised comparative studies have achieved better results with 7 days' triple therapy than with 14 days' dual therapy.[83–86]

Even though the requirement to increase the pH during *H. pylori* eradication therapy is well established, the optimum dose of PPIs to be given is still subject to debate. Lamouliatte et al.[87] have compared, in a randomised study, the efficacy of a double dose of pantoprazole (standard dose b.i.d.) and of a single daily dose of this PPI, given in the context of triple therapy together with amoxycillin and clarithromycin over 7 days. The *H. pylori* eradication rate with the double dose of the PPI (pantoprazole 40 mg b.i.d.) was 75% *versus* only 56% with the single pantoprazole dosage (40 mg once daily). Other PPIs, such as omeprazole or lansoprazole, have also been shown to be more effective in *H. pylori* eradication when given at double doses.[57] However, in a recent randomised study comparing pantoprazole 40 mg once daily with pantoprazole 40 mg b.i.d. in a triple therapy with clarithromycin and metronidazole — instead of amoxycillin — over 1 week, Bardhan et al.[58] reported exactly the same eradication rate (84%) in

both groups. They concluded that when these two antibiotics (clarithromycin and metronidazole) are used in *H. pylori* eradication therapy, the PPI may be prescribed only once daily at the usual dosage.

These results have been recently confirmed in one meta-analysis,[57] wherein the beneficial effect of a double-dose PPI was restricted to the combination including clarithromycin and amoxycillin. These differences might and may be due to the antibiotic combinations used; thus, amoxycillin is, as previously pointed out, highly acid labile, and the regimes including this antibiotic will therefore be those most pH dependent. This might also explain why when combining PPIs with clarithromycin and metronidazole the required dose of the antisecretory drug is lower, whereas when amoxycillin is prescribed instead of metrinidazole higher doses of the PPI are required for achieving the maximum therapeutic benefit.[87]

The major result of the aforementioned meta-analysis comparing pantoprazole with other PPIs (such as omeprazole or lansoprazole) as eradication therapy against *H. pylori* is that the results are the same regardless of the PPI used.[78] Thus, as graphically presented in figure 2 derived from the seven studies[88–94] included in the meta-analysis in which 534 patients received pantoprazole and 603 patients received other PPIs, the mean *H. pylori* eradication rate was 83% and 81%, respectively. The OR for this comparison was exactly 1 (95% CI, 0.61–1.64). However, a certain degree of statistical heterogeneity between the studies was demonstrated, and this forced some subanalyses (which had been planned *a priori*) according to a number of variables. Thus, separate analyses were carried out on those studies using one concrete PPI type or one concrete dose of such drugs; this solved the heterogeneity problem and confirmed the presented results of therapeutic equivalence.

3.3 Rabeprazole

The development and marketing of rabeprazole represented a further step in the already long and highly sloped stairway of acid secretion inhibition. The results achieved with this new PPI in both gastro-oesophageal reflux disease and peptic ulcer disease have been at least similar to those previously reported for other 'older' PPIs such as omeprazole or lansoprazole.[63,95–98] Yet rabeprazole has a higher anti-secretory potency and is associated with a faster onset of action than other PPIs such as omeprazole at equivalent doses.[62,95–99] However, this PPI has shown itself to have a greater anti-secretory potency and is associated with a faster onset of action than other PPIs (such as omeprazole) at equivalent doses.[62,95–99] This PPI has been shown to have high anti-secretory efficacy in *H. pylori*-infected subjects.[100] On the other hand, a number of studies have shown that rabeprazole shows greater

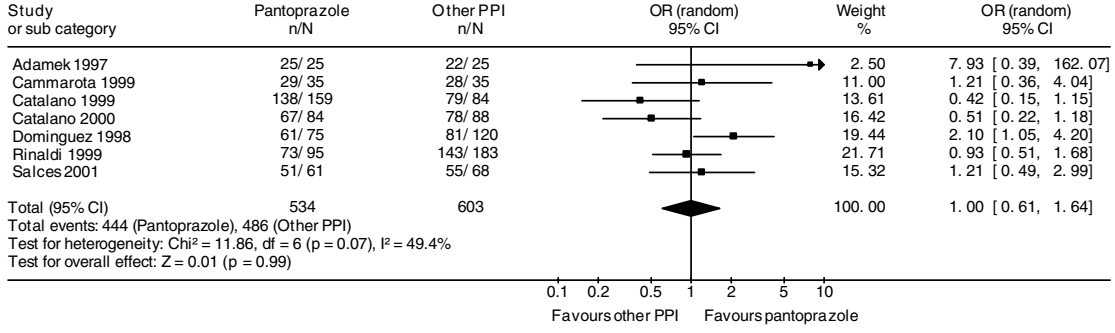

Fig. 2. Meta-analysis of the studies comparing pantoprazole with other proton pump inhibitors (PPIs) in combination with antibiotics in *Helicobacter pylori* eradication therapy. Intention-to-treat analysis.[88–94] **OR** = odds ratio; **95% CI** = 95% confidence interval.

antibacterial activity against *H. pylori* than other PPIs.[97,101–107] Thus, the MIC range against *H. pylori* for rabeprazole is considerably lower than that previously reported for omeprazole or lansoprazole.[97,101–108] Furthermore, *in vitro*, rabeprazole inhibits *H. pylori* motility[105,106] and urease activity.[109,110] However, but for some exceptions, rabeprazole monotherapy has not been able to eradicate *H. pylori* infection.[111]

Thus, once again rabeprazole must be directly compared with other PPIs in order to establish whether the aforementioned differences translate into a therapeutic benefit *in vivo* in terms of *H. pylori* eradication. In this case, the systematic review of the available literature shows that the eradication rate with rabeprazole and amoxycillin (dual therapy) for 14 days is rather low, about 70%.[112] However, triple therapies (i.e., rabeprazole together with two antibiotics) achieve therapeutic success more frequently. For instance, the combination rabeprazole–amoxycillin–clarithromycin given during 7–14 days is able to eradicate the infection in 75–98% of cases,[112] and the eradication success rate with the combination rabeprazole–clarithromycin–nitroimidazole is 85% — success levels that are similar to those previously reported for other PPIs.[2,56,79–81] Furthermore, a meta-analysis of the comparative studies[112] demonstrates that rabeprazole is equivalent to other PPIs when given together with two antibiotics, as shown in figure 3. From the results of the studies included in that meta-analysis,[113–123] with 1076 patients treated with rabeprazole and 1150 treated with other PPIs, mean eradication efficacies of 79% and 77%, respectively, were calculated. The OR for this comparison was 1.15 (95% CI, 0.93–1.42), the results being statistically homogeneous.

One final consideration concerns the fact that PPIs experience considerable hepatic biotransformation. In the liver, these drugs are metabolised to variable degrees by various isoenzymes [cytochromes (CYP) P450], themselves categorised into subfamilies based on a number of genetic polymorphisms. One of the main isoenzymes involved in PPI metabolism is CYP2C19, and a number of mutations have been described in this enzyme that may be responsible for genetic polymorphisms and for consequent modifications in the metabolism and in the pharmacokinetic profiles of the PPIs.[112] It was initially demonstrated that the *H. pylori* eradication rate achieved with other PPIs, such as omeprazole or lansoprazole, depended on the patient's CYP2C19 genotype.[124,125] It has been later suggested that the metabolism of rabeprazole is less dependent on that genotype, as this last PPI is

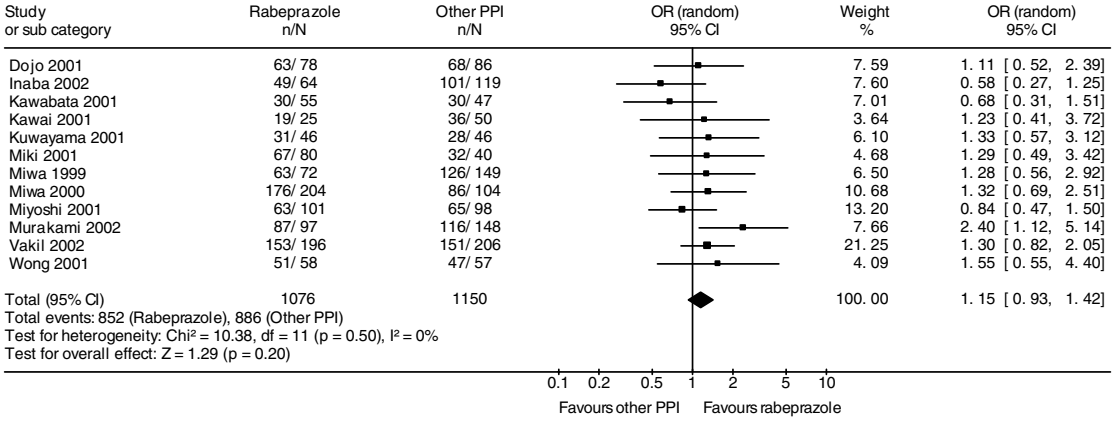

Fig. 3. Meta-analysis of the studies comparing rabeprazole with other proton pump inhibitors (PPIs) in combination with antibiotics in *Helicobacter pylori* eradication therapy. Intention-to-treat analysis.[113–123] **OR** = odds ratio; **95% CI** = 95% confidence interval.

metabolised mainly through a non-enzymatic pathway that is largely independent from CYP2C19.[126–128] It would therefore be expected that the *H. pylori* eradication efficacy with rabeprazole might be greater than that with omeprazole or lansoprazole in patients with complete CYP2C19 expression, in whom the latter PPIs would be extensively metabolised. A number of studies have therefore examined the effects of the CYP2C19 genotype, as assessed by polymerase chain reaction techniques, on the *H. pylori* eradication rates achieved with various different rabeprazole-based therapies, both dual[120,124,125,129] and triple.[113–115,117,125,130,131] While some studies have shown that regimes including omeprazole are affected by the patient's CYP2C19 genotype to a greater degree than those including rabeprazole,[125,126] most authors have failed to demonstrate any difference related to this genotype in therapeutic efficacy between rabeprazole and other PPIs.[113,115,117,120,131,132] These data thus indicate that the role of the CYP2C19 in the *H. pylori* eradication efficacy is not at all demonstrated, and stress the need for further studies that may clarify this aspect.

3.4 Esomeprazole

Esomeprazole is the *S* isomer of omeprazole, which is itself a racemic mix of the *S* and *R* optic isomers.[133–138] This new PPI achieves better control of intragastric pH than omeprazole, lansoprazole, pantoprazole or rabeprazole.[133–138] In consequence, esomeprazole induces a greater healing rate of erosive oesophagitis and more rapid symptomatic relief than omeprazole in patients with gastro-oesophageal reflux disease.[133–135,137] Furthermore, esomeprazole evidences *in vitro* activity against *H. pylori* superior to that of other PPIs such as omeprazole.[139] A recent study demonstrated that the 50% MIC and the 90% MIC against *H. pylori* were 16 mg/L and 32 mg/L, respectively, for esomeprazole *versus* 32 mg/L and 64 mg/L, respectively, for omeprazole. Thus, the greater *in vitro* antibacterial potential of esomeprazole might, at least in theory, contribute to improving the eradication efficacy against this microorganism *in vivo*.

In order to examine this aspect, a systematic review and meta-analysis has been quite recently carried out comparing esomeprazole with other PPIs.[140] From the results of the studies assessing the eradication efficacy of combinations of esomeprazole and antibiotics[141–145] an eradication rate (intention to treat) of 82% for triple therapies was calculated. It can thus be concluded that esomeprazole-based combinations are effective in treating *H. pylori* infection, with eradication rates that are comparable with those previously reported for other PPIs.[146] In this context, the Food and Drug Administration has recently approved the combination including esomeprazole (40 mg once daily), amoxycillin (1 g b.i.d.) and clarithromycin (500 mg b.i.d.) given for 10–14 days for eradication therapy against *H. pylori*.[134,135]

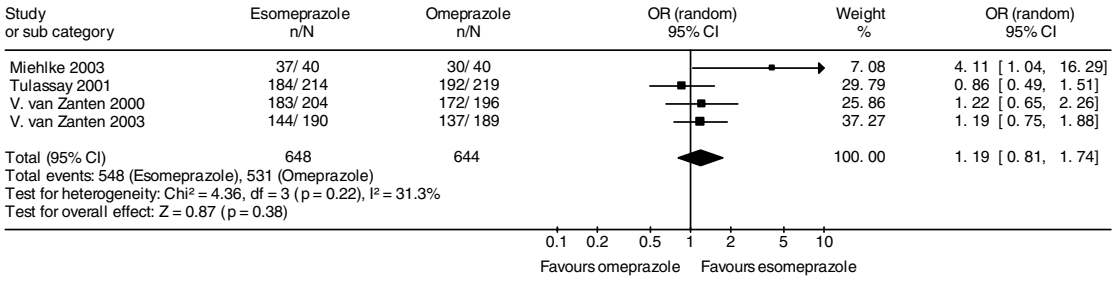

Fig. 4. Meta-analysis of the studies comparing esomeprazole and omeprazole in combination with antibiotics in *Helicobacter pylori* eradication therapy. Intention-to-treat analysis.[142,144,145,147] **OR** = odds ratio; **95% CI** = 95% confidence interval.

As previously stated, and bearing in mind that esomeprazole achieves better control of intragastric pH[133–138] and evidences greater activity against *H. pylori* than other PPIs,[139] it might at least in theory be more effective in the eradication of the microorganism *in vivo*. However, the results of the meta-analysis comparing esomeprazole and omeprazole do not confirm this hypothesis, as they evidence no statistically significant differences between the two anti-secretory drugs.[140] This meta-analysis included four studies in which esomeprazole was compared with omeprazole.[142,144,145,147] Overall, and as per intention to treat, 648 patients received esomeprazole and 644 patients received omeprazole. The results of the meta-analysis are shown graphically in figure 4. The eradication rate with esomeprazole was 85%, very similar to the 82% rate achieved with omeprazole (OR, 1.19; 95% CI, 0.81–1.74; statistically homogeneous results). However, as all comparative studies used esomeprazole at a dosage of 20 mg b.i.d., it would be desirable to have further studies available using the standard dose for this PPI (40 mg) given b.i.d. Finally, the drop-out rates because of adverse side effects in the randomised double-blind studies were identical for both drugs, lending further support to the concept that esomeprazole and omeprazole are equivalent in *H. pylori* eradication.[142,144,145]

4. Conclusion

In summary, it may be concluded that PPIs are overall more effective than H_2 receptor antagonists when the two groups of anti-secretory drugs are given at the usual standard doses together with antibiotics, with the intention of eradicating *H. pylori* infection. However, all PPIs (omeprazole, lansoprazole, pantoprazole, rabeprazole, and esomeprazole) are equivalent when given together with two antibiotics to cure the infection.

Acknowledgement

Supported in part by a Grant from the Instituto de Salud Carlos III (C03/02).

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