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# *Effects of rabeprazole, 20 mg, or esomeprazole, 20 mg, on 24-h intragastric pH and serum gastrin in healthy subjects*

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## SUMMARY

*Aim*: To compare the antisecretory effects of rabeprazole and esomeprazole in an open, randomized, two-way crossover, clinical pharmacology study.

*Methods*: Twenty-four healthy subjects (14 men, 10 women; mean age 26.8 years) received rabeprazole 20 mg or esomeprazole 20 mg daily on days 1–5, with a 14-day 'wash-out'. Intragastric pH was recorded continuously, and serum gastrin measured, on days 0, 1 and 5.

*Results*: On day 0, mean intragastric pH *AUC* was significantly higher before the esomeprazole than before the rabeprazole treatment in four of the five time intervals analysed. On days 1 and 5, mean intragastric pH *AUC* was higher after rabeprazole than esomeprazole during 5–11, 14–24 and 0–24 h after dosing. Mean pH *AUC* in the first 5 h after dosing on day 5 was higher after esomeprazole than rabeprazole ($P = 0.012$). On day 1, mean per cent times pH > 3 and > 4 were significantly greater after rabeprazole than esomeprazole during 0–14, 14–24 and 0–24 h. On day 5, mean serum gastrin $AUC_{0\text{-}4}$ was higher ($P = 0.017$) after rabeprazole than esomeprazole (335 vs. 316 pg/mL.h).

*Conclusion*: In this clinical pharmacology study, rabeprazole 20 mg daily was more effective than esomeprazole 20 mg daily in increasing intragastric pH and maintaining pH > 3 and > 4. On day 5, mean pH *AUC* was higher after esomeprazole than rabeprazole.

## INTRODUCTION

Rabeprazole is a proton pump inhibitor for the treatment of patients with duodenal ulcer, gastric ulcer, or gastro-oesophageal reflux disease (GERD).[1, 2] In healthy volunteers, rabeprazole 20 mg had a faster onset of antisecretory action than did omeprazole 20 mg, and yielded a higher intragastric pH, and longer times for which pH > 3 and > 4, during the 24 h after the first dose.[3] After 8 days' dosing, the differences in times for pH > 3 and > 4 persisted, but there was no difference in 24 h acidity. A similar advantage of a single dose of rabeprazole 20 mg over omeprazole 20 mg, lansoprazole 30 mg, and pantoprazole 40 mg has also been reported.[4] Rabeprazole 20 mg was as effective as omeprazole 20 mg in patients with GERD,[5] duodenal ulcer,[6] or gastric ulcer.[7] Rabeprazole 10 and 20 mg daily were both equivalent to omeprazole 20 mg daily in preventing relapse of erosive GERD.[8]

Esomeprazole magnesium is the (*S*)-enantiomer of omeprazole and accounts for 50% of the administered dose of omeprazole.[9] In patients with symptomatic GERD, esomeprazole 20 and 40 mg daily both increased intragastric pH to a greater degree than did omeprazole 20 mg daily, but there was no difference between the two esomeprazole doses.[10] In patients with erosive GERD, esomeprazole 20 and 40 mg daily produced a higher healing rate than omeprazole 20 mg, although again there was no difference between the two esomeprazole doses.[11] In maintenance therapy for GERD, esomeprazole 20 and 40 mg daily prevented relapse to a similar extent, whereas a 10-mg dose was less effective.[12]

Both rabeprazole and esomeprazole are highly effective in suppressing acid secretion. Increasing intragastric pH

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is a stimulus for gastrin production by G cells in the antrum of the stomach.[13] High gastrin concentrations produce enterochromaffin-like cell hyperplasia, which leads to gastric carcinoid tumours in rats.[14] However, in humans, long-term treatment with proton pump inhibitors has not been shown to cause tumour formation.[15] The elevation in serum gastrin is viewed as a physiological response to gastric acid suppression, and is a biomarker for the effect of antisecretory agents.[16]

Our study was designed to compare the antisecretory effects of single and repeated once-daily doses of rabeprazole 20 mg and esomeprazole 20 mg in healthy *Helicobacter pylori*-negative subjects, by measuring intragastric pH and serum gastrin concentrations. For rabeprazole, 20 mg is the recommended 'healing' dose, but it is the recommended maintenance dose for esomeprazole. Nevertheless, we chose to study the same dose of each drug, to ensure that we would be able to determine which was the more pharmacologically potent.

## SUBJECTS AND METHODS

### *Subjects*

Subjects were healthy, nonsmoking men and women aged 18–45 years, with a body mass index of 18.0–30.9 kg/m$^2$. All were negative for *H. pylori* by serology and $^{13}$C-urea breath test (Pylobactell kit, Bureau of Stable Isotope Analysis, UK; samples analysed by BSIA with European Scientific Tracermass Isotope Ratio Mass Spectrometer and RoboPrep G Automatic Breath Sampler). None of the subjects had a history of dyspepsia, gastrointestinal disorder affecting drug absorption, or drug or alcohol abuse. They used no prescription medication (except oral contraceptives) in the 4 weeks before the study, nor over-the-counter medication within 7 days of its start.

### *Ethics*

This study proposal was approved by the Brent Medical Ethics Committee. All subjects gave written informed consent.

### *Study design*

The study was an open-label, randomized, two-way crossover design. The subjects were resident at the study unit for two 6-day periods that were separated by a wash-out period of at least 14 days. After an overnight fast, we gave the subjects either rabeprazole 20 mg or esomeprazole 20 mg with 100 mL of water once daily, in the mornings of days 1 through 5. The order of treatment with rabeprazole or esomeprazole was randomized using a SAS program (SAS for Windows, version 6.12). We measured intragastric pH and serum gastrin from pre-dose until 24 h after dosing on days 1 and 5, and at the corresponding times on day 0. The subjects had standard meals and drinks at 1, 4 and 10 h after dosing on days 1 and 5, and at the corresponding times on day 0. Alcoholic drinks, caffeinated beverages, smoking and strenuous exercise were not allowed during the interval from 48 h before day 0 until the end of each study period. We discharged the subjects on day 6 of each period, and they returned 5–10 days later for a follow-up medical examination.

### *Measurement of intragastric pH*

We recorded intragastric pH on days 0, 1 and 5. On day 0, after anaesthetizing the subject's nostril with lignocaine (lidocaine) hydrochloride spray, we inserted a disposable antimony internal reference pH electrode with surface markings of 1 cm (Zinetics Medical, UT). We monitored pH during passage of the electrode down the oesophagus, through the gastro-oesophageal sphincter and into the stomach. We confirmed the entry of the electrode into the stomach by a sharp fall in pH, usually to less than 3.2. Next, we withdrew the electrode slowly to about 40 cm; a sharp rise in pH identified the point at which the electrode crossed the sphincter. We then advanced the electrode to a final position 8–10 cm (depending on the subject's height) beyond the point at which the pH fell below 3. The electrode was positioned 54–62 cm from the nostril. We recorded intragastric pH every 6 s using a Flexilog 2020 96-h recorder (Oakfield Instruments, Oxford, UK), which had been pre-calibrated using buffers of pH 4 and 7 before passage of the electrode. We uploaded the recorded data to a computer, and analysed it using Flexisoft II software (Oxford Instruments).

We removed the pH electrode on the morning of day 2, at least 48 h after we had inserted it. About 1 h before dosing on day 5, we inserted a pH electrode again and removed it 24 h after dosing, on the morning of day 6.

*Measurement of serum gastrin concentration*

We collected blood samples (4 mL) in plain glass tubes via a Teflon venous cannula in the subject's forearm on days 1 and 5 at 0, 1, 2, 3 and 4 h after dosing, and at the corresponding times on day 0. Samples were centrifuged within 15 min of collection, at 800 ***g*** for 10 min at 4 °C. The serum was transferred to polypropylene tubes and stored at −20 °C or below until assay. Serum gastrin concentrations were measured using a commercial, validated radioimmunoassay (DiaSorin Inc., Wokingham, Berkshire, UK), by the Analytical Unit, St. George's Hospital, London. This assay had a lower limit of quantification of 25 pg/mL, a within-assay coefficient of variation < 10% and a between-assay coefficient of variation < 9%.

*Statistical analysis*

The data were analysed using SAS for Windows, version 6.12; the null hypothesis was rejected if *P*-values were 0.05 or less. The primary analysis of the pharmacodynamic data was done on the per protocol population, which included all randomised subjects who completed a full course of each antisecretory therapy and had no appreciable loss of pH data, and excluded any with major protocol violations. The area under the intragastric pH vs. time curve (*AUC*) was calculated over the intervals 0–5, 5–11, 11–14, 14–24 and 0–24 h on days 0, 1 and 5, using a linear trapezoidal method. Serum gastrin *AUC* was calculated over the interval 0–4 h. The percentage of the time that the intragastric pH was > 3 and > 4 was calculated over the intervals 0–14, 14–24 and 0–24 h.

To test for differences between treatments in intragastric pH, an analysis of variance (ANOVA) of intragastric pH *AUC* and of percentage of time with pH > 3 and > 4 was carried out. Percentages were arcsine-transformed before the analysis to normalize the distribution of the data. A separate ANOVA was done on data from days 0, 1 and 5, with effects for subject, period and treatment in the model. Because the intragastric pH on day 0 (baseline) differed significantly between treatments, a *post hoc* analysis of covariance (ANCOVA) was done in which the day 0 AUC, or the percentage of time with pH > 3 and > 4 over 24 h, was included in the model as a covariate.

Serum gastrin $AUC_{0\text{-}4}$ was analysed using an ANOVA model with effects for subject, period and treatment. Each day was analysed separately, and the *AUC* values were log-transformed before analysis. The 95% confidence interval of the mean difference between treatments was calculated and then back-transformed to give the ratio as a percentage. The effect of the treatment on the serum gastrin *AUC* was not formally tested for significance because it was an expected outcome of treatment and plainly evident.

## RESULTS

*Subjects*

Twenty-six subjects, 15 (58%) men and 11 (42%) women, entered the study. Their mean age was 26.8 years (range: 20–43 years), weight 70.3 kg (51.5–98.7 kg), height 174 cm (149–195 cm), and body mass index 23.2 kg/m$^2$ (19.4–30.8). Twenty-four subjects completed the study in accordance with the protocol; all had pH data that was ≥ 98% complete. A female subject withdrew for personal reasons after receiving four doses of esomeprazole during the first study period, and a male subject was excluded from the per protocol evaluation owing to incomplete pH data.

*Intragastric pH*

Plots of median intragastric pH over 24 h on days 0, 1 and 5 are given in Figures 1a–c; meal times are also indicated. Means, standard deviations (s.d.) and medians of the pharmacodynamic variables are given in Tables 1 and 2; differences that are statistically significant are indicated. Adjusted means of pharmacodynamic variables are given in Table 3.

The effect of study period on intragastric pH *AUC* and percentage of time with pH > 3 and > 4 was not statistically significant in any of the analyses, indicating that the carryover of treatment effects from the first period to the second was negligible.

On day 1, mean intragastric pH *AUC* was significantly higher during rabeprazole than during esomeprazole treatment in the 5–11, 11–14, 14–24 and 0–24 h intervals after dosing (Table 1, $P = 0.028$). On day 5, that difference between treatments remained in all intervals except 11–14 h after dosing. There was no difference between treatments in mean intragastric pH *AUC* in the first 5 h after dosing on day 1; however, on day 5 mean $AUC_{0\text{-}5}$ was significantly higher during

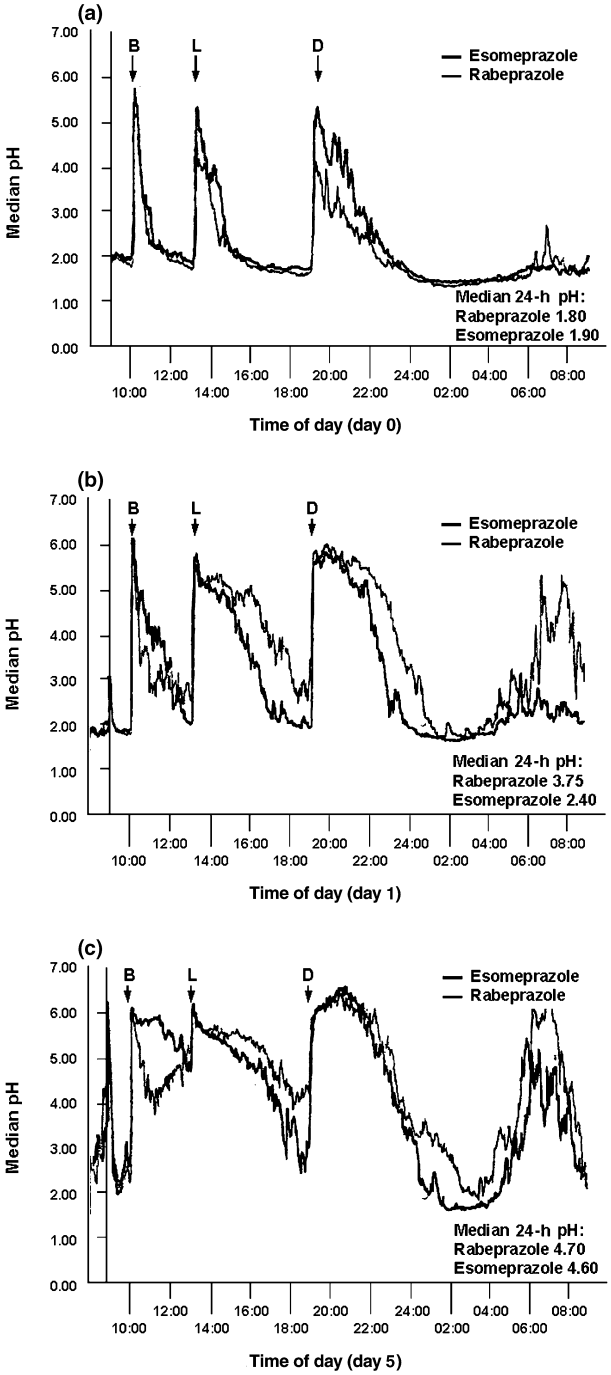


Figure 1. Median intragastric pH. (a) Over 24 h at baseline (day 0). (b) After treatment with rabeprazole or esomeprazole on day 1. (c) After rabeprazole or esomeprazole on Day 5. B = breakfast, L = lunch, D = dinner.

esomeprazole than during rabeprazole treatment ($P = 0.012$).

On day 0, mean intragastric pH *AUC* was significantly higher before esomeprazole than before rabeprazole treatment in four of the five time intervals analysed (0–5, 5–11, 11–14 and 0–24 h). When day 0 values were included in the ANCOVA model, the statistical significance of the comparisons did not change (Table 3).

Mean percentage of time with pH > 3 and > 4 on day 1 was significantly greater during rabeprazole than during esomeprazole treatment in the 0–14 h (daytime), 14–24 h (night), and 0–24 h after dosing (Table 2, $P = 0.043$). On day 5, that difference between treatments remained during the night-time interval ($P \leq 0.015$).

On day 0, mean percentage of time with pH > 3 and > 4 in the daytime (0–14 h) and pH > 4 over 24 h were significantly greater before esomeprazole than before rabeprazole treatment (Table 2, $P \leq 0.039$). In contrast, mean percentage of time with pH > 4 in the night (14–24 h) was significantly greater before rabeprazole than before esomeprazole treatment ($P = 0.042$). When day 1 and day 5 values were adjusted for baseline (day 0) in the ANCOVA model, the mean percentage of time with pH > 3 and > 4 on day 1 was still significantly greater during rabeprazole than during esomeprazole treatment in the three intervals analysed ($P \leq 0.011$). In the night on day 5, the differences between treatments in mean pH > 3 and > 4 remained, although they fell short of statistical significance ($P \leq 0.054$).

### *Serum gastrin concentration*

Mean serum gastrin concentrations did not differ between treatments on day 0 (Table 4). Mean gastrin concentrations were higher on day 1 than on day 0, at 3 and 4 h after dosing, but there was no significant difference between treatments in mean $AUC_{0\text{-}4}$ (rabeprazole = 208.6 pg/mL.h and esomeprazole = 213.9 pg/mL.h). On day 5, after the fifth daily dose of medication, the mean serum gastrin concentrations before dosing of both treatments were higher than those at the corresponding time points on days 0 and 1: during rabeprazole treatment, mean pre-dose concentrations increased from 43.4 pg/mL on day 0 to 60.0 pg/mL on day 5; during esomeprazole treatment, mean concentrations increased from 45.8 pg/mL on day 0 to 54.4 pg/mL on day 5. In addition, mean serum gastrin $AUC_{0\text{-}4}$ on day 5 was significantly higher during rabeprazole than during esomeprazole treatment (335.2 vs. 316.0 pg/mL.h, respectively; $P = 0.017$),

Table 1. Mean (s.d.) and median intragastric pH *AUC* at baseline (day 0) and during treatment with rabeprazole or esomeprazole on days 1 and 5

| | | Rabeprazole | | Esomeprazole | | |
|---|---|---|---|---|---|---|
| Day | Interval | Mean | Median | Mean | Median | *P*-value |
| Day 0 | 0–5 h | 48 327 (9513) | 48 073 | 54 267 (9542) | 55 121 | 0.035* |
| | 5–11 h | 47 829 (10 975) | 48 662 | 56 095 (10 496) | 54 887 | 0.011* |
| | 11–14 h | 28 696 (8647) | 28 448 | 36 098 (11 823) | 33 552 | 0.008* |
| | 14–24 h | 71 232 (20 125) | 67 061 | 68 524 (14 942) | 66 328 | 0.421 |
| | 0–24 h | 198 785 (31 510) | 196 937 | 217 174 (33 050) | 214 293 | 0.048* |
| Day 1 | 0–5 h | 60 320 (13 381) | 59 905 | 60 931 (17 606) | 62 656 | 0.860 |
| | 5–11 h | 89 923 (24 225) | 92 770 | 76 607 (21 264) | 75 862 | 0.010* |
| | 11–14 h | 55 744 (9044) | 57 327 | 48 188 (14 076) | 50 327 | 0.028* |
| | 14–24 h | 109 896 (40 996) | 115 285 | 85 770 (23 278) | 79 868 | 0.003* |
| | 0–24 h | 320 687 (60 437) | 317 521 | 274 586 (58 696) | 278 239 | 0.002* |
| Day 5 | 0–5 h | 76 870 (20 367) | 75 285 | 88 059 (12 424) | 87 548 | 0.012* |
| | 5–11 h | 107 766 (13 698) | 111 216 | 97 635 (14 239) | 99 032 | 0.006* |
| | 11–14 h | 61 223 (10 515) | 63 101 | 62 443 (7756) | 61 893 | 0.552 |
| | 14–24 h | 135 922 (34 321) | 137 517 | 108 346 (31 931) | 106 488 | 0.003* |
| | 0–24 h | 385 515 (52 042) | 379 177 | 359 115 (49 404) | 360 625 | 0.045* |

*Significant difference between treatments ($P < 0.05$).

Table 2. Mean (s.d.) and median percentage of time with intragastric pH > 3 and > 4 at baseline (day 0) and during treatment with rabeprazole or esomeprazole on day 1 and day 5

| | | pH > 3 | | | | | pH > 4 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Rabeprazole | | Esomeprazole | | | Rabeprazole | | Esomeprazole | | |
| Day | Interval | Mean | Median | Mean | Median | *P*-value | Mean | Median | Mean | Median | *P*-value |
| Day 0 | 0–14 h | 9.5 (4.0) | 8.4 | 5.3 (3.3) | 6.1 | 0.027* | 5.8 (3.8) | 4.9 | 2.6 (3.0) | 1.0 | 0.006* |
| | 14–24 h | 24.4 (1.7) | 25.4 | 32.9 (2.2) | 33.7 | 0.097 | 13.1 (1.6) | 12.8 | 22.2 (2.1) | 21.1 | 0.042* |
| | 0–24 h | 19.1 (1.4) | 19.1 | 22.3 (1.1) | 24.0 | 0.203 | 11.0 (1.3) | 9.2 | 15.0 (1.1) | 15.8 | 0.039* |
| Day 1 | 0–14 h | 40.8 (7.4) | 42.2 | 16.9 (4.5) | 12.7 | 0.026* | 29.0 (7.4) | 27.5 | 10.8 (4.4) | 8.2 | 0.043* |
| | 14–24 h | 70.3 (3.8) | 70.5 | 59.2 (5.2) | 59.5 | < 0.001* | 59.9 (3.8) | 59.6 | 48.8 (6.0) | 49.0 | 0.001* |
| | 0–24 h | 58.0 (3.0) | 55.1 | 41.7 (2.9) | 40.5 | < 0.001* | 47.8 (2.7) | 46.4 | 33.2 (3.2) | 31.2 | 0.001* |
| Day 5 | 0–14 h | 58.1 (6.5) | 54.7 | 39.6 (6.2) | 40.2 | 0.873 | 43.1 (4.4) | 41.8 | 26.0 (5.5) | 30.1 | 0.979 |
| | 14–24 h | 85.6 (2.9) | 84.1 | 86.1 (2.6) | 83.2 | 0.015* | 78.1 (3.5) | 73.9 | 78.2 (3.2) | 76.2 | 0.007* |
| | 0–24 h | 73.5 (2.6) | 70.8 | 66.8 (2.7) | 65.6 | 0.089 | 62.9 (2.1) | 58.5 | 56.7 (2.2) | 56.8 | 0.087 |

*Significant difference between treatments ($P < 0.05$).

although that difference was less than 6% (95% CI: 1.1–11.0%).

### *Safety and tolerability*

Both drugs were safe and well-tolerated. Consistent with clinical experience, the most common events after both rabeprazole and esomeprazole treatments were gastrointestinal disturbances, including nausea, diarrhoea, constipation and abdominal discomfort.

Overall, the subjects coped well with the discomfort of the pH electrode, with the other study procedures and with the two 6-day stays in the research ward.

## DISCUSSION

Our results show that rabeprazole 20 mg increased intragastric pH more than did esomeprazole 20 mg, after both single and repeated doses. A previous study of the effect of a single dose of several proton pump inhibitors

Table 3. Adjusted means from ANCOVA of pharmacodynamic variables on day 1 and day 5

| Variable | Interval (h) | Day 1 | | | Day 5 | | |
|---|---|---|---|---|---|---|---|
| | | Rabeprazole | Esomeprazole | *P*-value | Rabeprazole | Esomeprazole | *P*-value |
| *AUC* | 0–5 | 62 027 | 59 253 | 0.436 | 76 110 | 88 939 | 0.010* |
| | 5–11 | 90 852 | 75 824 | 0.014* | 108 399 | 97 065 | 0.009* |
| | 11–14 | 57 842 | 46 441 | 0.004* | 62 125 | 61 537 | 0.803 |
| | 14–24 | 108 690 | 86 722 | 0.005* | 134 688 | 109 338 | 0.005* |
| | 0–24 | 330 586 | 266 365 | < 0.001* | 388 005 | 356 810 | 0.033* |
| % time pH > 3 | 0–14 | 72.7 | 56.7 | 0.003* | 85.9 | 85.8 | 0.956 |
| | 14–24 | 39.0 | 18.3 | 0.003* | 56.3 | 41.4 | 0.054 |
| | 0–24 | 59.5 | 40.3 | < 0.001* | 73.7 | 66.6 | 0.091 |
| % time pH > 4 | 0–14 | 63.8 | 44.8 | 0.002* | 78.6 | 77.6 | 0.815 |
| | 14–24 | 26.7 | 12.4 | 0.011* | 40.6 | 28.3 | 0.053 |
| | 0–24 | 50.2 | 31.0 | < 0.001* | 63.3 | 56.4 | 0.092 |

*Significant difference between treatments ($P < 0.05$).

Table 4. Mean (s.d.) pre-dose gastrin concentration and $AUC_{0\text{-}4}$ at baseline (day 0) and during treatment with rabeprazole or esomeprazole on day 1 and day 5

| Day | Treatment | Pre-dose plasma concentration (pg/mL) | $AUC_{0\text{-}4}$ (pg/mL.h) |
|---|---|---|---|
| Day 0 | Rabeprazole | 43.4 (10.5) | 193.3 (51.1) |
| | Esomeprazole | 45.8 (12.8) | 190.8 (46.3) |
| Day 1 | Rabeprazole | 43.8 (11.4) | 208.6 (52.5) |
| | Esomeprazole | 44.0 (12.0) | 213.9 (76.0) |
| Day 5 | Rabeprazole | 60.0 (22.9) | 335.2 (170.7)* |
| | Esomeprazole | 54.4 (17.2) | 316.0 (165.2) |

*Significant difference between treatments ($P < 0.05$). Mean (CI) difference = 6% (1.1–11.0%).

on intragastric pH showed significantly higher median 24 h intragastric pH after rabeprazole 20 mg (pH = 3.4; $P < 0.04$) than after lansoprazole 30 mg (pH = 2.9), pantoprazole 40 mg (pH = 2.2), omeprazole 20 mg (pH = 1.9), and placebo (pH = 1.3).[4] Our results are consistent with those findings, and indicate that rabeprazole 20 mg has greater antisecretory activity than esomeprazole 20 mg after the first dose. Furthermore, although the difference between treatments in mean intragastric pH had decreased after 5 days of dosing, our results suggest that repeated doses of rabeprazole 20 mg may continue to have a greater antisecretory activity than repeated doses of esomeprazole 20 mg, particularly during the night.

We found that rabeprazole increased the percentage of time with pH > 3 and > 4 significantly more than did esomeprazole, on both days 1 and 5. This effect was particularly evident during the night, after both single and repeated doses. A study in patients with GERD is needed to show whether this effect is translated into a greater relief of nocturnal symptoms.

Rabeprazole maintained pH > 4 for 47.9% of the 24-h period on day 1, and 62.3% of that period on day 5. Those values are higher than reported by Röhss *et al.*, in a study of healthy men, who found that rabeprazole 20 mg maintained pH > 4 for only 29.4% of the 24-h period on the first day of dosing; a percentage which rose to 44.5% by day 5.[17] However, Williams *et al.*, in a study of healthy men, showed that rabeprazole 20 mg maintained pH > 4 for 44.1% of the 24-h period on day 1 of dosing, and for 60.3% on day 8.[18] Furthermore, in a study of single doses of rabeprazole 20 mg and esomeprazole 40 mg, Baisley *et al.* found that rabeprazole maintained 24-h pH > 4 for 43.1% of the time on day 1.[19]

Serum gastrin concentrations were higher after both rabeprazole and esomeprazole administration than on day 0 (baseline). After 5 days of dosing, mean serum gastrin $AUC_{0\text{-}4}$ was marginally, but significantly, higher during rabeprazole than during esomeprazole treatment. This result is consistent with the higher intragastric pH found during the rabeprazole treatment.

Our original analysis plan, defined before the start of the study, was to carry out separate ANOVA on intragastric pH data from days 0, 1 and 5. However, we found statistically significant differences between mean pH parameters on day 0 before dosing with rabeprazole and those on day 0 before dosing with

esomeprazole. Given the balanced crossover design of our study, those differences could only have occurred by chance. To account for differences in baseline pH, we did an additional, unplanned ANCOVA in which we adjusted for day 0 values. The results of the unplanned analyses were nearly identical to those of the planned analysis, except that the difference in percentage time pH > 3 and > 4 in the night on day 5 fell just short of significance after we adjusted for baseline pH. Thus, the results of the ANCOVA may be taken as the more 'conservative', but do not alter our overall conclusions.

In summary, in healthy subjects, rabeprazole 20 mg increased intragastric pH more, and maintained pH > 3 and > 4 significantly longer, than did esomeprazole 20 mg. Thus rabeprazole was pharmacologically more potent than esomeprazole by the oral route. Clinical trials are needed to determine whether this difference is important in the treatment of patients with gastric acid-related disease.

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