Comparative study with ranitidine and cimetidine on gastric secretion in normal volunteers*

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SUMMARY The inhibitory effect of ranitidine and cimetidine on pentagastrin stimulated volume, acid and pepsin secretion has been studied in eight healthy volunteers. Both compounds inhibit all measured components of gastric secretion in a dose dependent manner. On a molar basis ranitidine is on average 11·14 times for volume, 13·04 times for acid, and 9·74 times for pepsin secretion more potent than cimetidine as measured by the ID₅₀-values.

Ranitidine has been shown to be a specific and effective histamine H₂-receptor antagonist in the standard systems. It has also been shown to be a potent inhibitor of gastric acid secretion in man. Therefore ranitidine, like cimetidine, is a potential therapeutic agent in peptic ulcer disease; however, its therapeutically effective dose compared with that of cimetidine is not known. It was the purpose of the present investigation to study the dose response relationship of ranitidine and cimetidine in inhibiting gastric acid and pepsin secretion in man.

Methods

The experiments were done in eight healthy male volunteers aged 26·3±1·4 years (range 20–31 years) and weighing 67·4±2·2 kg (range 61–79 kg). The protocol was approved by the ethical committee of the medical faculty of the University of Tübingen, and written informed consent was obtained from each individual. The protocol was as follows: after an overnight fast a nasogastric tube was placed into the stomach and the correct position was tested by repeated suction. Gastric secretion was collected in 15 minute periods for 240 minutes by an automatic suction device (Gastrovac, Fa. Hirtz). Volume was measured to the nearest millilitre, acidity was determined by automatic titration against 0·1 N sodium hydroxide (Autoburette Radiometer, Copenhagen), and pepsin content by Berstad's method using bovine pepsin as standard. Acid output is given as mmol H⁺/15 min and pepsin output as mg pepsin/15 min if not otherwise stated. After a basal 60 minute period gastric secretion was stimulated by an intravenous infusion of 6 µg/kg/h pentagastrin for three hours. After one hour of pentagastrin infusion cimetidine (25, 50, 100, or 200 mg) or ranitidine (2·5, 5·0, 10·0, or 20·0 mg) was injected intravenously. Thus, the secretory tests were repeated nine times in each subject in a randomised order, one test serving as a control without injection of either cimetidine or ranitidine. Between each test at least three days elapsed. The dose response curves in each individual subject were constructed from the second and third period after injection of the inhibitor normalised as percentage of the corresponding periods of the experiment in which no inhibitor was injected. Each point represents the mean±SEM of one experiment in each subject. From these dose response curves the ID₅₀S with their confidential limits were calculated. The dose response curves were tested for parallelism by the method of Cavalli-Sforza. Blood samples were drawn before the first and last secretory test for haematology and blood chemistry in order to detect adverse reactions.

REAGENTS

Pentagastrin (Gastrodiagnost, Merck, Darmstadt) 500 µg/2 ml; cimetidine (Tagamet, Smith Kline & Dauelsberg, Göttingen) 200 mg/2 ml; ranitidine-HCl (kindly supplied by Glaxo Group Research Ltd., Ware) 10 mg/ml. Pepsin 100 units/g (Merck,

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Ranitidine vs cimetidine on gastric secretion

Fig. 1 Mean values of acid secretion of eight healthy volunteers in response to pentagastrin (PG) and after inhibition by different doses of cimetidine (C) and ranitidine (R).

Darmstadt). Haemoglobin was prepared in our own laboratory according to the prescription given by Berstad (1970).

Results

Basal secretion of all secretory tests as calculated by adding all four periods and dividing them by two was: volume: 16.4±3.2 ml/30 min; acid: 0.6±0.2 mmol H⁺/30 min; pepsin: 13.7±3.4 mg/30 min. Pentagastrin-stimulated secretion reached a plateau after 30 minutes of stimulation. Therefore only the

Fig. 2 Dose response curves of ranitidine (R) and cimetidine (C) for inhibition of pentagastrin stimulated gastric volume secretion in eight healthy volunteers. Values: mean ± SE. The horizontal bars represent the calculated ID₉₀, ± 95% confidential limit.

Fig. 3 The same as in Fig. 2 for acid secretion.

Fig. 4 The same as in Fig. 2 for pepsin secretion.
last 30 minutes of the first pentagastrin hour were 
evaluated: volume: 98.1 ± 4.7 ml/30 min; acid: 
12.6 ± 0.6 mmol H+/30 min; pepsin: 63.2 ± 3.7 
mg/30 min. There was a slight fading in secretion 
during the following two hours in most of the 
subjects; this is a well-known phenomenon.

Both histamine H₂-receptor antagonists caused a 
dose dependent inhibition of volume, acid and 
pepsin secretion in the range of the doses tested. 
Acid response to pentagastrin and its inhibition by 
rantidine and cimetidine is representative for the 
secretory pattern of the other two variables (volume 
and pepsin secretion). Therefore the mean values of 
acid secretion in response to pentagastrin and to the 
doses of rantidine and cimetidine tested are shown 
in Fig. 1. The dose response curves (Figs. 2-4) as 
calculated for each individual subject did not differ 
significantly from being parallel. The ID₅₀s with 
their 95% confident limits on a weight basis are 
as follows for rantidine: volume 6-68 ± 2-32 mg, 
acid 4-24 ± 2-04 mg, and pepsin 4-40 ± 1-86 mg; for 
cimetidine: volume 53-63 ± 25-16 mg and 39-60 ± 
30-68 mg, pepsin 30-70 ± 23-82 mg. From the data 
the following molar ratios of potency for the three 
variables can be calculated: volume 11:14 (range 
1:41-14-70), acid 13:09 (range 1:78-19:19), pepsin 
9:74 (range 0:71-11:61). From the recovery time 
there was no indication for a difference in the 
duration of action between the two drugs.

At the beginning and at the end of the study 
laboratory data were within the normal range.

Discussion

The results have shown that rantidine and cimetidine 
both effectively inhibit pentagastrin-stimulated 
volume, acid and pepsin secretion in normal 
volunteers. From the normalised data a parallel 
dose response relationship for all three secretion 
variables is evident. The relative potencies of both 
drugs as calculated from ID₅₀s differ from those published 
so far. This is probably because in none of the 
studies dealing with dose comparison was a dose 
response relationship over a wide submaximal range 
of both drugs established. All secretory components 
(fluid, acid, and pepsin) were almost equally affected 
by both drugs in their effective dose range. From 
the present study no conclusions can be drawn as to 
whether the two drugs differ in the extent of maximal 
inhibition they can produce: that is worth another 
study. From the time that has to elapse between 
maximal inhibition and recovery it looks as if there 
is no difference between the two drugs. That would 
reflect the almost identical half lives of both drugs. 
It has to be emphasised that, in this study, both 
compounds were given intravenously as a bolus 
injection. If the drugs differ in their bioavailability it 
might be necessary to correct the dose of rantidine 
for oral administration according to these 
differences.

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References

1 Glaxo-Allenburys Research (Ware) Ltd. AH-19065, 
histamine-H₂ receptor antagonist. Clinical investigators 
2 Domschke W, Lux G, Domschke S. Gastric inhibitory 
action of H₂-antagonists rantidine and cimetidine 
3 Hagenmüller F, Zeitler-Abu-Ishira A, Classen M. 
Hemmung der Magensäuresekretion durch den His-
tamin H₂-Rezeptorantagonisten AH-19065 (Ranitidine) 
im Vergleich zu Cimetidine—eine Doppelblindstudie 
(abstract). Z Gastroenterol 1979; 17: 583
4 Peden NR, Saunders JHB, Wormsley KG. Inhibition of 
peptagastrin-stimulated and nocturnal gastric secretion 
5 Simon B, Göttling E, and Kather H. Ranitidin: Ein 
potenter oral wirksamer Hemmer der menschlichen 
Säuresekretion (abstract). Z Gastroenterol 1979; 17: 
582.
6 Berstad A. A modified hemoglobin substrate method 
for the estimation of pepsin in gastric juice. Scand J 
7 Cavalli-Sforza L. Biometrie, Grundzüge biologisch-
medizinischer Statistik. Stuttgart: Gustav Fisher 
Verlag, 1969.
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