The New Histamine H₂-Receptor Antagonist Ranitidine

Duration of Action

H. G. Dammann¹, P. Müller², H. Kather², and B. Simon²

¹ Medizinische Universitätsklinik Hamburg, Martinistraße 52, D-2000 Hamburg, Federal Republic of Germany
² Medizinische Universitätsklinik Heidelberg, Bergheimerstraße 58, D-6900 Heidelberg, Federal Republic of Germany

Summary. The antisecretory effects of a new histamine H₂-receptor antagonist, ranitidine hydrochloride, have been investigated on basal and pentagastrin-stimulated acid secretion in healthy volunteers 5 and 10 h after oral administration of 150 mg. In addition, the 24-h intragastric pH-profiles have been measured in patients undergoing parenteral nutrition after three doses of 150 mg ranitidine per day.

A 40% inhibition of basal acid output has been noted even 10 h after drug intake. The intragastric pH-values were raised above 5 for at least 24 h.

The new H₂-antagonist ranitidine has been proven to be a potent and long-acting antisecretory compound.

Key words: Gastric acid secretion – H₂-receptor antagonists – Pentagastrin – Ranitidine

Introduction

In vitro studies had shown that the aminomethylfuran derivative, ranitidine hydrochloride, is a competitive histamine H₂-antagonist without significant activity at histamine H₁- or at cholinergic receptor sites [1, 3]. On a molar basis ranitidine has been reported to be four to seven times as potent as cimetidine as an antisecretory agent when tested in various experimental animal models [1, 3].

First clinical studies also underline the activity of ranitidine as an inhibitor of gastric acid secretion resulting from a variety of stimuli [2, 5–9]. The duration of action of an histamine H₂-receptor antagonist is of particular interest in the treatment of peptic ulcer disease. Therefore, basal and pentagastrin-stimulated acid secretion has been measured 5 and 10 h after oral ranitidine. In addition, the 24-h intragastric pH-profiles have been examined after oral ingestion of this new receptor antagonist.
Material and Methods

Six healthy male volunteers with the mean age of 24 years (range 21–26 years) were studied. Informed consent was obtained from each volunteer.

In one experimental series basal and pentagastrin-stimulated (2 μg/kg × h) acid secretion was measured before and 5 h after 150 mg oral ranitidine. In another series the effects of 150 mg oral ranitidine on both parameters were determined in the same subjects before and 10 h after drug administration. The H₂-antagonist was given at 10 p.m. and gastric acid analyses were performed after an overnight fast at 8 a.m.

Basal and pentagastrin-stimulated acid secretion were determined from the four 15 min collection periods, as described in detail elsewhere [9]. The statistical calculation of the results was carried out by the Wilcoxon-test for paired samples.

The intragastric 24-h pH-profile was measured in six patients between 52 and 71 years of age with an increased risk of GI-bleeding undergoing strict parenteral nutrition. The patients suffered from respiratory insufficiency (n=4) and drug intoxication (n=2). The basic therapeutic handling of the patients was not altered during the control as well as the test period.

The intragastric pH was assessed by measuring the pH in 3–5 ml samples of gastric contents aspirated hourly by a naso-gastric tube whose position in the antrum was controlled by means of X-ray. The aspirated juice was clear and free of hematin. These patients served as their own controls: In a randomized fashion the 24-h control period was followed by another 24-h test period or vice versa. In the test period three doses of 150 mg ranitidine per 24 h (at 10 a.m., 4 p.m., and 10 p.m.) were given. Two hours after ingestion of the drug pH-measurements were carried out as described above.

The described protocols were approved by the Clinical Human Studies Committee.

Pentagastrin (Gastro-Diagnost) was obtained from Merck, Darmstadt (FRG). Ranitidine-hydrochloride was kindly supplied by Glaxo Group Research Ltd. Ware, Hertfordshire (UK).

Clinical Laboratory Tests

The following tests were carried out before drug administration and during the period of gastric analyses studies as well as pH-measurements: Blood count (including differential counts), determination of creatinine, urea, electrolytes, transaminases, bilirubin, alkaline phosphatase, prothrombin time, and urine analysis.

Results

Table 1 summarizes the effects of orally administered ranitidine on basal and pentagastrin-stimulated gastric acid secretion in six healthy volunteers. Before drug administration basal acid output averaged 1.4–1.6 mmol/h and pentagastrin-stimulated secretion 20.5–21.5 mmol/h, respectively.

Five hours after taking 150 mg ranitidine a marked inhibition of both parameters was observed. Basal acid output decreased by 70%, whereas hormone-stimulated gastric acid secretion was suppressed by about 40% (P < 0.05). Even 10 h after 150 mg ranitidine the basal acid output was still depressed by about 38% (P < 0.05). However, no significant effect on pentagastrin-stimulated acid secretion has been noted at this time.

In a second series of experiments the influence of three oral doses of 150 mg ranitidine on the 24-h intragastric pH-profiles in patients undergoing strict parenteral nutrition has been tested (Fig. 1). During the 24-h control period which preceded or followed the ranitidine test period in a randomized fashion, the intragastric pH was constantly around 2 or less. Following ranitidine, intragastric...