Salmefamol: inhibitor or stimulant of gastric acid secretion?

S.P. CANFIELD, B.P. CURWAIN, J.A. KING & CAROLYN PRICE

Department of Physiology, St Mary's Hospital Medical School, London W2 1PG

β_2-Adrenoceptor agonists have been shown to inhibit pentagastrin-induced gastric acid secretion in both dog (Curwain, Holton & Spencer, 1972; Daly & Stables, 1977) and rat (Lundell & Svensson, 1974). We have investigated the action of a drug of this type, salmefamol, on gastric acid secretion and mucosal blood flow (MBF) in 4 conscious dogs with well-established Heidenhain pouches and also in a rat isolated stomach preparation. The results showed the expected inhibition of secretion in the dog but there was a stimulation of acid output by salmefamol in the *in vitro* preparation.

Submaximal doses of either pentagastrin (2μg kg^{-1} h^{-1}) or bethanechol chloride (1μg kg^{-1} min^{-1}) were infused i.v. in saline (1 ml/min) in the dogs until a plateau of acid secretion was obtained. MBF was estimated by radioactive aniline clearance (Curwain & Holton, 1973). Salmefamol (0.2 or 0.8 μg kg^{-1} min^{-1} i.v. for 30 min) was tested against each secretagogue in each of the 4 dogs. The control rates of acid secretion and MBF were taken as the mean values for the 4 successive 15 min periods immediately before giving salmefamol. The means of the 2 successive 15 min samples giving the lowest rate of acid secretion were used as test values. Secretory rate was profoundly decreased (between 33 and 98%, mean 76%) in each of the 8 experiments. Changes in MBF were variable but in each experiment the ratio of blood flow to secretion increased.

The isolated stomachs from rats (35–50 g) were set up as described for the guinea pig by Holton & Spencer (1976) and were stimulated with either bethanechol chloride (1.7×10^{-5}M) or pentagastrin (2×10^{-5}M). The acid output was measured over four 15 min periods. The drug was then washed out and the tissues incubated for 1 h with salmefamol (10^{-5}M) before a second dose of the same stimulant was added in the presence of salmefamol. The results are expressed as the percentage increase above the spontaneous secretory rate in the absence of drugs.

The mean increase in acid output due to the pentagastrin alone was 185 ± 4.7% and 299 ± 15.6% in the presence of pentagastrin and salmefamol (s.e., $n = 3$). The values for bethanechol were 276 ± 88% and 356 ± 72% ($n = 3$) respectively. The results do not show any evidence of inhibition of the secretory response. Paired t tests indicated that the increase in the response in the presence of salmefamol was significant both for bethanechol ($P<0.05$) and pentagastrin ($P<0.02$). Salmefamol alone (10^{-5}M) increased the rate of acid secretion by 231 ± 19% ($n = 6$).

The concentration dependence of this salmefamol-stimulated acid secretion and the action upon it of various established inhibitors of acid output is being investigated.

References

CURWAIN, B.P. & HOLTON, P. (1973). The measurement of dog gastric mucosal blood flow by radioactive aniline clearance compared with amidopyrine clearance. *J. Physiol. Lond.*, **229**, 115–131.

CURWAIN, B.P., HOLTON, P. & SPENCER, J. (1972). The effect of β_2-adrenoceptor stimulants, salbutamol and terbutaline on gastric acid secretion and mucosal blood flow in conscious dogs with Heidenhain pouches. *Br. J. Pharmac.*, **46**, 566–567P.

DALY, M.J. & STABLES, R. (1977). The effect of (−)-isoprenaline and (±)-salbutamol on pepsinogen and acid secretion in the dog. *Br. J. Pharmac.*, **59**, 323–325.

HOLTON, P. & SPENCER, J. (1976). Acid secretion by guinea-pig isolated stomach. *J. Physiol., Lond.*, **255**, 465–479P.

LUNDELL, L. & SVENSSON, S.E. (1974). Implication of gastric mucosal histamine in inhibition by isoprenaline of pentagastrin-induced gastric secretion. *Br. J. Pharmac.* **52**, 69–75.

Comparative assay of histamine H_2-receptor antagonists using the isolated mouse stomach

J.A. ANGUS*, J.W. BLACK & M. STONE

Departments of Pharmacology, and Statistics & Computer Science, University College London

There is still insufficient evidence about the nature of the interaction between H_2-receptor antagonists and histamine on gastric acid secretion to argue that the inhibition of physiologically-induced acid secretion is due to blockade of histamine receptors. Bunce & Parsons (1976), using isolated rat stomachs, found a pA_2 value for metiamide equivalent to that measured in atrial and uterine tissues but the slope of the Schild plot of 0.73 was significantly different from unity. Apparently the necessary conditions for simple competitive inhibition were not met. To assess the significance of this finding we have assayed the activity of burimamide, metiamide and cimetidine on the isolated, lumen-perfused whole mouse stomach preparation (Angus & Black, 1978).

Each preparation was equilibrated with a single