Short communications

Effect of propranolol on gastric acid secretion in rats

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The effect of propranolol, a β-adrenoceptor blocking agent, has been investigated on gastric acid secretion in pylorus and cardiac-ligated rats. Compared to the control group, propranolol significantly diminished the gastric acid secretion, and inhibited the formation of gastric ulceration.

Considerable controversy surrounds the action of β-adrenoceptor antagonists on gastric acid secretion. β-Adrenoceptor blocking agents have been reported to produce stimulation (Konturek & Oleksy, 1969; Evan & Lin, 1970), inhibition (Bass & Patterson, 1967; Pradhan & Wingate, 1966; Okabe, Saziki & Takagi, 1970; Geumei, Issa & Abd-El-Samie, 1972a; Geumei, Issa, El-Gendi & Abd-El-Samie, 1969, 1972b) or no effect (Haigh & Steredman, 1968; Misher, Pendleton & Staples, 1969) on gastric secretion. The discrepancy may be attributed to difference in species, drug dosage, route of administration, physiological states of the stomach and the technique used.

Recently, we have shown that propranolol inhibited both basal and histamine-stimulated gastric secretion in man (Geumei *et al.*, 1969, 1972b) and histamine-stimulated gastric secretion in pigeons (Geumei *et al.*, 1972a). In this study an attempt was made to investigate the effect of propranolol on gastric acid secretion and incidence of gastric ulceration in rats.

Methods.—Male Sprague-Dawley rats with body weights ranging from 215–263 g were used. The animals, housed in individual cages, were deprived of food for 24 h prior to the experiments but were allowed water *ad libitum*. All operative procedures were performed under ether anaesthesia and all collections of gastric juice were 5 h in duration. Pylorus ligation, with care not to occlude any blood vessels, and cardiac ligation, with sparing of vagi, were performed (Skoryna & Webster, 1960). At the end of the surgical procedure, 1 mg/kg (±)-propranolol hydrochloride in a volume of 1 ml normal saline (0·9% NaCl w/v) was injected in the tail vein (20 rats); in the control group (15 rats) 1 ml saline was injected intravenously. The animals were caged separately and had no access to food or water for 5 h, after which each was killed by decapitation. The stomach was removed. Gastric contents were collected in a graduated test tube and the total acidity was determined by titration with N/10 NaOH using phenolphthalein as an indicator. The pH was determined with a glass electrode. The stomach was cut open along the greater curvature and examined for mucosal ulcers in the glandular portion. The ulcer index was measured on a graduated score from 0 (no ulcer) to 5 (linear ulcer >3·0 mm in length). Preventive ratio is calculated as follows,

$$\text{Preventive ratio (\%)} = \frac{\text{Ulcer index (control)} - \text{Ulcer index (drug)}}{\text{Ulcer index (control)}} \times 100$$

Level of significance was calculated using Student's *t* test.

Results.—The effect of propranolol on gastric secretion collected 5 h after ligation of pylorus and cardia is summarized in Table 1. Propranolol (1 mg/kg i.v.) produced a significant ($P<0·01$) reduction of gastric acid secretion and protected the rats against mucosal lesions.

Discussion.—In the present study propranolol significantly inhibited the gastric acid secretions in rats. This confirms the antisecretory effects of propranolol described previously in man and pigeons (Geumei *et al.*, 1969, 1972a, 1972b). Thus, a species difference is unlikely. Our results are in close agreement with those reported by Okabe *et al.* (1970) after subcutaneous administration of propranolol in pyloric-ligated rats. However, our data do not confirm the observation of Misher *et al.* (1969) that gastric secretion in conscious fistula rats was not reduced after orally administered propranolol. We also obtained an inhibitory effect of propranolol on gastric ulceration. Previous authors seem, however, to disagree concerning the effect of propranolol on the incidence of gastric ulceration. Thus Rosoff & Goldman (1968) demonstrated an increase in the incidence of ulceration in immobilized rats after propranolol (0·5 mg/kg i.p.), whereas significant inhibition of ulceration was observed

TABLE 1. *Effect of propranolol on the gastric acid secretion in rats*

Treatment	No. of rats	Body wt. (g)	Secretory volume (ml)	pH	Total acid output (μequiv)	Ulcer index	Preventive ulcer ratio (%)
Control (0·9% saline) i.v.	15	235·1±2·6	1·31±0·33	2·17±0·47	85±18	13·9±1·1	—
Propranolol (1 mg/kg) i.v.	20	233·6±2·4	0·63±0·14	3·52±0·31	38±5*	4·0±0·7	71·2*

The results are means ± S.E.M. * Statistically significant as compared to control ($P<0·01$).

by Okabe *et al.* (1970) after subcutaneous injection of 20–50 mg/kg propranolol.

Gastric antisecretory effects of other β-adrenoceptor blocking agents, dichloroisoproterenol and pronethalol, have also been reported in experimental animals (Pradhan & Wingate, 1966; Bass & Patterson, 1967). Potentiation of atropine action on basal gastric secretion by β-adrenoceptor antagonists was recorded in patients with duodenal ulcer (Anshelvich, 1969).

We conclude that propranolol depresses gastric acid secretion and inhibits gastric ulceration.

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