Effects of prostaglandin E_2 on rat gastric mucosal blood flow, as determined by ^{14}C-aniline clearance

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Prostaglandins inhibit gastric acid secretion in the rat, dog and man. Wilson & Levine (1969), using the aminopyrine clearance technique in the dog, suggested that prostaglandin E_1 (PGE_1) acts by reducing gastric mucosal blood flow. However, Jacobson (1970) concluded that this reduction was secondary to the inhibition of acid secretion.

In the present investigation on the rat, changes in gastric mucosal blood flow during PGE_2 inhibition of acid secretion have been studied using a ^{14}C-aniline clearance technique. It was considered that this method, which in the dog gives similar results to those obtained using aminopyrine (Curwain & Holton, 1971) was the more suitable for studies in small animals such as the rat.

The gastric lumen of the urethane-anaesthetized rat was perfused with 0·9% saline and blood samples were taken from a carotid artery. ^{14}C-aniline was injected intravenously in a loading dose of 2 μCi/kg followed by a continuous infusion of 2 (μCi/kg)/h to maintain a steady plasma concentration. At regular intervals the ^{14}C-aniline content of the gastric perfusate and arterial plasma was determined by liquid scintillation counting following extraction into benzene. The amount of aniline infused was either 6 (μg/kg)/h or 10 (mg/kg)/h, the latter dose being similar to that used in dogs. Comparable percentage changes in clearance were seen with both dose concentrations, though with the low dose, clearance values (ratio of gastric output to plasma concentration) were smaller, implying that not all the extractable ^{14}C-aniline in the plasma was available for diffusion into the stomach.

A direct relationship between clearance and acid secretion was observed during pentagastrin-(20(μg/kg)/h) and histamine-(2(mg/kg)/h base) stimulated gastric secretion. This suggests that an increase in acid secretion is accompanied by a corresponding increase in mucosal blood flow.

PGE_2 (2 (μg/kg)/min) infused intravenously caused almost complete inhibition of acid secretion within 30 minutes. With high levels of acid secretion, inhibition was accompanied by a decrease in clearance. However, the ratio of clearance to acid output rose, suggesting that the reduction in acid preceded the fall in clearance. In some experiments, where acid secretion was low, clearance rose at a time when acid secretion was being inhibited. Further, when PGE_2 was infused during basal secretion, an initial increase in clearance values was also observed, indicating a direct vasodilator effect on the mucosa.

These results in the rat support the conclusions that prostaglandins do not inhibit gastric acid secretion primarily by a reduction in mucosal blood flow.

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Effects of isoprenaline on gastric acid secretion and mucosal blood flow during stimulation by pentagastrin or feeding

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Histamine-induced gastric acid secretion in dogs may be either increased or decreased by infusions of isoprenaline. In conscious dogs small doses (about (0·2 μg/kg)/min) increased and large doses (about (2 μg/kg)/min) decreased secretion; whereas in acute experiments in anaesthetized dogs the only effect observed was an increase of histamine-induced secretion (Curwain, Endersby & Holton, 1971). Since acid secretion is more readily depressed when it is induced by means other than histamine (Harries, 1957) we have investigated the effect of isoprenaline on secretion stimulated by infusions of pentagastrin and by feeding (that is by endogenous gastrin).

In eleven experiments on four conscious dogs with Heidenhain pouches, infusion of isoprenaline (0·05–2 μg/kg)/min decreased acid secretion induced by pentagastrin (5 μg/kg)/hour. In three experiments in acute anaesthetized dogs isoprenaline (0·2 μg/kg)/min also decreased pentagastrin-stimulated secretion. Isoprenaline (0·06–0·25 μg/kg)/min also decreased the (gastrin induced) secretion in response to feeding in seven experiments in the four Heidenhain pouch dogs. On no occasion was an increase of acid secretion observed when secretion was induced by these means.

The effects of isoprenaline on mucosal blood flow was studied in five experiments on two of the Heidenhain pouch dogs using the aniline clearance method (Curwain & Holton, 1971). Mucosal blood flow decreased when acid secretion (induced by pentagastrin) fell in response to isoprenaline but the ratio of blood flow to secretion increased. When noradrenaline (0·1–0·5 μg/kg)/min was used to decrease mucosal blood flow and acid secretion induced by pentagastrin or feeding, the ratio of blood flow to secretion remained unchanged (five experiments in two dogs).

We can conclude from these experiments that the inhibitory effect of isoprenaline on pentagastrin (or gastrin) induced secretion is not secondary to a fall in mucosal blood flow and is probably due to a direct antagonism between isoprenaline and the secretory mechanism initiated by gastrin. We cannot exclude the possibility that the inhibitory action of noradrenaline is secondary to mucosal vasoconstriction.

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