Compared actions of secretin (S), cholecystokinin (CK) and caerulein (C) on dog choleresis

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The aim of this study was to ascertain whether a close similarity exists in the choleretic actions of these polypeptides as one would expect from the work of Jones & Grossman (1970).

The experiments were carried out on 14 dogs anaesthetized with a phenobarbital/pentobarbital mixture. The dogs were cholecystectomized and fasted for 24 h before the acute experiment. Experiments were made with and without exogenous taurocholate support (836 (nEq/kg) min). When individually given by a 2 h i.v. infusion, the polypeptides did not show marked difference sufficient to denote substantially different capacities of affecting bile secretion, and the choleretic effect consisted of an increase in flow accompanied by an increase in HCO_3^- concentration; the latter showed some irregularity in the case of CK (20 ng kg^{-1} min^{-1}). No increase in the output of bile salts or other solid components of bile was observed. However, a significant ($P < 0.001$) increase in Na^+ and K^+ concentrations was constantly observed with S (0.05 u.c. kg^{-1} min^{-1}). In the case of C (20 ng kg^{-1} min^{-1}), stimulation of flow was regularly preceded by an inhibition during the first 20 min of infusion.

Surprisingly, the results were different when an 80 min C infusion was superimposed on a S or CK infusion started 60 min before: no early inhibition was apparent, a marked increase in flow was promptly produced, but the C effect very soon vanished although C infusion was continued. The increase in flow during the first 20 min of C infusion was constantly higher than what one would have expected if a mere summation of effects had taken place. Contrary to what was found with the infusion of individual polypeptides, the concentration of HCO_3^- decreased and, slightly but constantly, so did that of Na^+ and K^+; bile salt concentration remained constant or increased, whereas that of cholesterol and bilirubin decreased. Consequently, bile salt output increased remarkably. Combined infusions of S and CK showed a purely summative effect.

These results suggest that C, at least when combined with gastrointestinal hormones, has a mechanism of action which does not exactly overlap that of S (to which it is not structurally related), as happens at the pancreatic secretion level, or that of CK (with which it shares the C-terminal octapeptide): other sites in the biliary secretory system could be involved.

Reference

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Effects on salivary glands of the chronic administration of eledoisin and physalaemin to rats

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Eledoisin (EL) and physalaemin (PH) are active endecapeptides of natural origin which resemble Substance P in their biological activity and chemical structure (Erspamer & Anastasi, 1962; Bertaccini, Cei & Erspamer, 1965; Erspamer, 1971).

EL and PH are the only substances so far known which are able to ameliorate and sometimes to cure salivary and lacrimal insufficiency of Sjoegren's syndrome (de Caro, Cordella & Miani, 1969; Bietti, de Caro & Capra, 1974).

It would be of interest to elucidate the mechanism of this therapeutic effect which is still completely unknown. Thus, the purpose of this paper was to check whether chronic administration of EL or PH to rats produced: (1) morphological alterations of salivary glands; (2) modified sensitivity of salivary glands to single

injections of either EL or PH themselves; (3) alterations in the chemical composition of saliva.

Our experiments showed that: (1) chronic administration of PH, but not of EL, produced enlargement of the main salivary glands; (2) chronic treatment with EL did not modify, whilst chronic treatment with PH reduced, glandular sensitivity to single injections of EL; (3) amylase activity of saliva from chronically EL-treated rats exceeded amylase activity of saliva obtained from controls or chronically PH-treated rats, regardless of the inducer employed; (4) in our experimental conditions not only was PH a stronger agonist than EL on a molar basis, but it also produced a saliva chemically different from the one evoked by EL.

The possible role of these modifications in determining the therapeutic effect of PH and EL was discussed.

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Effects of salbutamol on gastric acid secretion and gastrin liberation after feeding in conscious Heidenhain pouch dogs

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The main finding to be presented is that salbutamol decreases gastric acid secretion in response to feeding in conscious dogs with Heidenhain pouches. This result was to be expected since this drug has been shown to decrease acid secretion in response to pentagastrin (Curwain, Holton & Spencer, 1972). Since the response of the Heidenhain pouch to feeding is due to endogenous gastrin, there remained the possibility that secretory inhibition was partly due to interference with gastrin release. For this reason we have measured plasma gastrin concentrations during the response to food and during administration of salbutamol.

Six healthy bitches with well-established Heidenhain pouches were used. After an overnight fast, a standard meal of cooked, minced ox liver (20 gm/kg) plus 5-10 gm NaCl was given. Venous blood samples were taken every 15 min and plasma gastrin concentration was measured by radioimmunoassay. Gastric secretion was collected and acid measured by titration. Salbutamol sulphate (0.2 $\mu g\ kg^{-1}\ min^{-1}$ i.v.) was given for 30 min beginning 60 min after feeding during the secretory plateau. The acid secretory rate and plasma gastrin concentrations were compared with those in control experiments in which no salbutamol was given.

Acid secretory rate was significantly reduced during the two 15 min periods following the end of salbutamol infusion. The mean reductions were 58% and 51% respectively, $P < 0.05$ (t test for paired data). A mean reduction of 26% ($0.05 > P < 0.1$) was seen in the second 15 min period during the infusion of salbutamol. There were no significant changes in plasma gastrin concentration during the acid secretory inhibition.

In another series of experiments salbutamol (0.2 or 0.4 $\mu g\ kg^{-1}\ min^{-1}$) was given for 10 min before feeding and for 30 min afterwards. Acid secretion was significantly reduced in the first hour after the meal (mean reduction = 43.9% ± 12.4% s.e., $P < 0.05$). Total gastrin output during the first 60 min after feeding was not significantly altered by salbutamol. However, the pattern of gastrin liberation was different. In the control experiments peak plasma gastrin concentration occurred in the first 15 min after feeding after which it fell to a plateau maintained for the next 30 minutes. In the salbutamol experiments the peak was absent and the plateau of gastrin concentration was higher than but not significantly different from that in the control experiments.

We conclude that salbutamol decreases the gastric acid secretory response to feeding in the conscious Heidenhain pouch dog. The mechanism by which the initial gastrin response is altered during salbutamol remains to be elucidated.