EFFECT OF CADMIUM ON SOMATOSTATIN INHIBITION OF CHLORIDE SECRETION BY THE RECTAL GLAND OF SQUALUS ACANTHIAS

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Cadmium is known to block calcium channels in certain tissues and to inhibit neurotransmitter release. In previous experiments we found that cadmium blocks the inhibitory effect of neuropeptide Y on forskolin-stimulated chloride secretion and the stimulatory effect of atrial natriuretic peptide. However, cadmium did not alter the inhibitory effect of somatostatin (Fifth annual report of progress, CMTS, MDIBL, Sep. 30, 1990, pp30-31). On the same annual report Forrest et al. report that cadmium, at concentrations as low as 5 and 10 µM, reversed the inhibitory effect of somatostatin (Fifth annual report of progress, CMTS, MDIBL, Sep. 30, 1990, pp20-22). In the present series of experiments we reexplored the issue of the inhibitory effect of cadmium on somatostatin.

Isolated shark rectal glands were perfused using a technique developed in our laboratory. Dogfish were pithed and the rectal glands removed by an abdominal incision. The rectal gland artery, vein and duct were catheterized and the glands placed in a glass perfusion chamber maintained at a temperature of 15° C with running sea water. The glands were perfused by gravity at a pressure of 40 mm Hg. The composition of the perfusate was (in mM): Na, 280; Cl, 280; K, 5; bicarbonate, 8; phosphate, 1; Ca, 2.5; Mg, 1; sulfate, 0.5; urea, 350; glucose, 5; pH, 7.6 when gassed with 99% O_2/ 1% CO_2. Rectal gland secretion was collected in tared 1.5 ml centrifuge tubes over 10 minute intervals. Chloride concentration in the rectal gland secretion was measured by amperometric titration.

The glands were perfused with and without cadmium chloride (250 µM). Three intrarterial 1 µg boluses of vasoactive intestinal peptide (VIP) were given sequentially. Somatostatin (5 x 10^{-7}M) was infused for 40 minutes. The second VIP bolus.was given ten minutes after starting the somatostatin infusion.

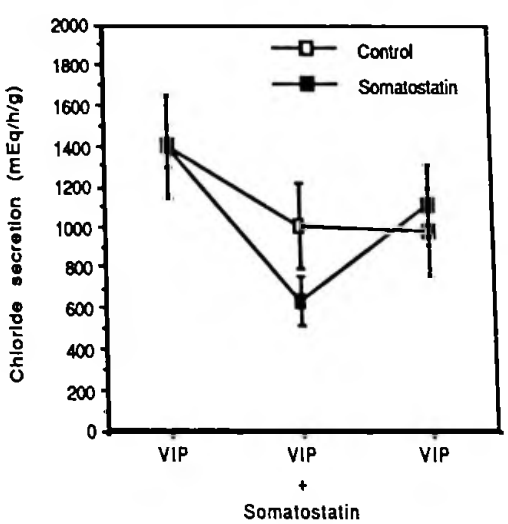
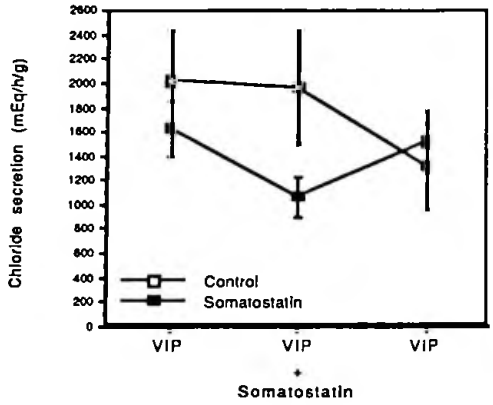


Figure 1. Effect of cadmium chloride on the inhibition by somatostatin of VIP-stimulated chloride secretion. Somatostatin inhibited chloride by 54%, significantly more than the decline in stimulation observed spontaneously in the control group, $p < 0.05$. Control (open squares), n=6, somatostatin (closed squares), n=9. Values are mean ± SEM.

Somatostatin inhibits VIP-stimulated chloride secretion in the presence, Figure 1, or absence, Figure 2, of cadmium 250 µM. The present experiment differs from our previous experiment in that in the latter, after the rate of secretion had stabilized at a basal level, the glands received forskolin and somatostatin simultaneously. Somatostatin prevented the stimulatory effect of

forskolin both in the presence and absence of cadmium. When somatostatin was discontinued secretion rose in response to forskolin. An inhibitory effect of cadmium on chloride secretion was noticed in those experiments as well as in the present ones. Compare the initial rate of secretion in the glands perfused with cadmium, Figure 1 with that of the glands perfused without cadmium, Figure 2.

Figure 2. Somatostatin inhibition of VIP-stimulated chloride secretion. Somatostatin inhibited chloride secretion by 30% an amount not different from that observed in the presence of cadmium. Symbols as in Figure 1. Control, n=6, somatostatin, n=8. Values are mean ± SEM.



In the current experiments cadmium also inhibited the effect of VIP but again did not prevent the inhibitory effect of somatostatin. There is no explanation for the difference between these experiments and those reported by Forrest et al. It is clear from these results that cadmium, that interferes with the inhibitory and stimulatory effect of other peptides, does not interfere with the inhibitory effect of somatostatin. These results suggest that cadmium toxicity is exerted at many different levels.

Cadmium inhibits stimulated chloride secretion and reduces the inhibitory effect of NPY and the stimulatory effect of ANP. Since the effect of ANP is mediated by the release of VIP those findings suggested to us that cadmium interferes with neurotransmitter release and that in addition it has a direct inhibitory effect on the chloride secreting cell. It was important therefore to establish whether cadmium interfered with the inhibitory effect of peptides other than NPY to ascertain whether it blocks a common inhibitory pathway. The above results suggest that it does not. Further studies with other inhibitory peptides are necessary to establish this.

Supported by grants NIH DK 18078, and NIEHS ESO 3828 and the Pew, W.R. Hearst Foundation and Burroughs-Welcome Foundation grants to Heather Brignull, Sonya Hornung, and Douglas Wolff.