EFFECT OF DIAZEPAM ON CHLORIDE SECRETION AND CELL VOLUME IN THE RECTAL GLAND OF THE SHARK (SQUALUS ACANTHIAS)

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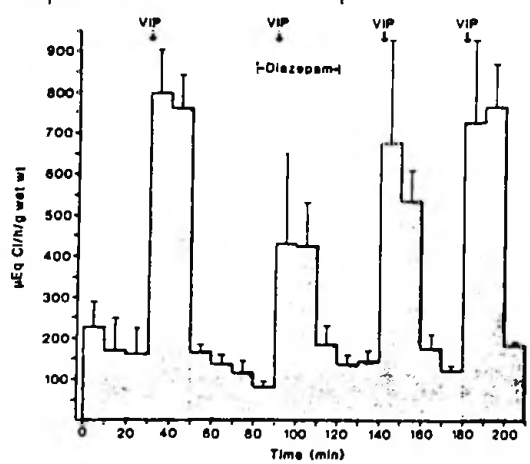
The novel "peripheral" benzodiazepine (BZD) receptor is distributed in several non-neuronal tissues of a variety of species (Haefely, et al., Adv. Drug Res. 14:166, 1985) including the mammalian kidney where it is mostly localized to the thick ascending limb (TAL) (Beaumont, et al., Am. J. Physiol. 247:F718, 1984). It is postulated that putative endogenous ligands interact with this receptor to modulate cell function. BZDs inhibit ouabain-sensitive oxygen consumption in rabbit medullary TAL (Ziyadeh, et al., Clin. Res. 35:639, 1987), suggesting inhibition of NaCl transport in this nephron segment. Because the shark rectal gland secretes Cl^- in a manner analogous to Cl^- absorption in TAL, we evaluated the effect of diazepam (a non-selective BZD agonist) on the transport function of the rectal gland.

Cell water and ion distribution were examined using slices of rectal gland as previously described (Kleinzeller and Goldstein, J. Comp. Physiol. B154:561, 1984). Compared with control, incubation of slices in 10 or 100 µM diazepam for 30-180 min did not result in any significant alteration in total tissue water, cell volume and the apparent intracellular concentrations of Na^+, K^+, and Cl^-.

The isolated perfused gland was studied as previously described (Silva, et al., Am. J. Physiol. 233:F298, 1977; Ziyadeh, et al., Bull. MDIBL 25:163, 1985). In the resting state, perfusion with diazepam (100 µM) did not alter Cl^- secretory rate (n=4). We next evaluated the effect of diazepam on the response to vasoactive intestinal peptide (VIP), the major Cl^-- secretagogue hormone of the rectal gland (Stoff, et al., Am. J. Physiol. 237:F138, 1979). Each gland (n=3) was stimulated with 4 boluses of 0.5 µg VIP (Figure). Ten min before the second bolus, diazepam (100 µM) was infused for a total of 40 min. For 20 min following the first bolus, Cl^- secretion was 783 ± 93 µEq/h/g wet weight (mean ± SE); following the second VIP bolus, the 20-min secretory rate was significantly attenuated to 431 ± 152 during diazepam infusion ($p<0.05$; reduction by 48 ± 13%). The Figure also shows that the effect of diazepam is reversible; secretion gradually recovers during the third and fourth VIP bolus. There was no significant difference in Cl^- secretion for 20 min following the fourth bolus (750 ± 133 µEq/h/g) compared with the response to the first bolus.



In summary, diazepam reversibly reduces VIP-induced Cl^- secretion in the isolated perfused shark rectal gland. Intracellular ion distribution and cell volume are not altered by diazepam, excluding a cytotoxic effect. Further studies are required to evaluate whether BZD receptors are present in the rectal gland and to dissect the mechanism of action of diazepam in the cascade of events leading to stimulation of Cl^- secretion by VIP.