EFFECT OF ACETAZOLAMIDE ON INTRAOCULAR PRESSURE IN ALEWIFE (Alosa pseudohasengus)

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Past studies have shown that the intraocular pressure (IOP) in marine fish and bullfrog can be measured non-invasively with a pneumotonograph (PTG). These studies have shown the IOP for dogfish (8.5 ± 0.37 mmHg), alewife (14.8 ± 0.5 mmHg), sculpin (6.6 ± 0.36 mmHg), and bullfrog (29.0 ± 0.35 mmHg) (Bull MDIBL 24:38-39, 1984). Preliminary studies in this report indicate that intraperitoneal acetazolamide at 5 and 7 mg/100 g in alewives lowered the IOP by 4 to 7 mmHg at 24 hours, similar to the decrease reported in lake trout by Hoffert (Comp Biochem Physiol 17:104-114, 1966). It was therefore the purpose of this study to establish a dose response for the effect of acetazolamide on IOP in the alewife.

The alewives were taken from the Union River at Ellsworth, Maine, and were kept at the laboratory in running seawater. The weight of the alewives ranged from 110 to 264 g with the mean of 165 g. The PTG was calibrated to measure IOP by preparing a standard curve and comparing the measured PTG pressure to the IOP measured by direct cannulation over a range of 0 to 30 mmHg. The pressure in the eye was varied by the height of a reservoir connected to a needle in the anterior chamber. Subsequent PTG pressure measurements were obtained from MS-222 anesthetized alewife and the actual ssure was determined from the standard curve. Acetazolamide was prepared in sterile water and concentrations of 0.1, 1.0, and 5.0 mg/100 g were injected intraperitoneally, and the IOP was measured at 4, 12, and 24 hours. The IOP showed no change during the first 12 hours and by 24 hours there were measured decreases. The IOP data following acetazolamide has been expressed as delta IOP from the initial pretreatment value. Twenty-four hours after the acetazolamide injection, profound physiological changes occurred in the alewives. The fish exhibited labored respiratory movement, a general lack of body movement, loss of both buoyancy and equilibrium, and loss of ability to color adapt by just turning black. Between 13 to 36% of the fish were near death at 24 hours after injection and these were not used in the experiment.

The results of our study have shown that an intraperitoneal injection of saline as a control does not change the IOP in 24 hours from the normal IOP in the MS-222 anesthetized alewife from a control value of 15.0 ± 0.23 mmHg (n=190) (Fig. 1). Following a dose of 0.1 mg/100 g, the IOP decreased by 1.48 ± 1.2 mmHg. At 1.0 and 5.0 mg/100 g of acetazolamide, the IOP decreased by 3.34 ± 0.82 and 5.42 ± 0.99 mmHg, both significantly lower than the control values (Figure).

Measurement of carbonic anhydrase* in the iris-ciliary body of alewives was 100 enzyme units per gram using the hydration of CO_2 at 0°C with a barbital buffer (4 to 10 mM) and Bromthymol Blue indicator (Maren et al, Comp Biochem Physiol 67B:69-74, 1980).

This study shows that inhibition of carbonic anhydrase in the alewife by acetazolamide will decrease the IOP. A similar decrease of 6 mmHg was reported by Hoffert (Comp Biochem Physiol 17:104-114, 1966) for the lake trout with a dose of 7 mg/100 g of acetazolamide. This decrease in IOP could be attributed to a marked decrease in HCO_3^- in the aqueous humor following acetazolamide injection (Hoffert and Fromm, Comp Biochem Physiol 198:333-340, 1966). The dose response also indicates that a concentration of acetazolamide of 0.1 mg/100 g does not decrease IOP significantly, but there is a 10% and 22.3% decrease in IOP with 1 and 5 mg/100 g, respectively, which compares with the previously reported data on rabbit by Wistrand et al (Acta Pharmacol Toxicol 17:337-355, 1960) who reported a 30.3% decrease in IOP following IV 1.0 mg/100 g and no significant decrease with 0.1 mg/100 g. These studies suggest that the carbonic anhydrase in the ciliary body of teleosts may be inhibited by the above acetazolamide treatment and could account for the decrease in IOP. (This research was supported in part by NIH grants R01 EY00933, T32 EY07016, and P30 ES01985).

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Figure. Intraocular Pressure Change Following Acetazolamide.
Number in circle represents sample number.