HORMONAL CONTROL OF GLOMERULAR FILTRATION RATE IN A MARINE ELASMOBRANCH (SQUALUS ACANTHIAS)

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The regulation of vertebrate renal function in response to changes in osmoregulatory demands has been the subject of great interest. In fishes that are exposed to changes in salinity, alterations in the rate of glomerular filtration (GFR) is a primary means for regulating the rate of water excretion. These renal adaptive responses appear to be hormonally based but the endocrine mechanisms involved remain elusive. With regard to glomerular function, suggested hormonal mediators include pituitary hormones, arginine vasotocin (AVT) and prolactin; the renin-angiotensin system; and catecholamines (Bentley, 1982 Comparative Vertebrate Endocrinology, 2nd ed., Cambridge). Our previous studies (Yokota and Benyajati, 1986 Bull. MDIBL. 26: 87) have implicated catecholamines in the glomerular response of elasmobranchs in dilute sea water. In the present study, we have further defined the role of catecholamines in the regulation of GFR in marine elasmobranchs by establishing a temporal correlation between the circulating levels of the hormones and renal function. In addition, the possible involvement of peptide hormones (prolactin, atrial natriuretic peptide, AVT, vasoactive intestinal peptide) in the regulation of elasmobranch GFR in a hyposmotic environment as well as in a hyperosmotic environment was investigated.

Methods Female dogfish (Squalus acanthias) were used in all experiments. Fish were placed in a tank with flowing aerated sea water at 13°-15°C and prepared for renal clearance experiments as described previously (Yokota and Benyajati, 1986 Bull. MDIBL. 26: 87). Inulin (5 ml of 15 g% solution in elasmobranch Ringer) was administered as a bolus injection intraarterially for GFR determination. The fish were allowed to recover at least 24 h before experimentation.

Control renal clearance measurements were performed continuously for several hours to ensure steady-state conditions. In experiments with fish undergoing environmental dilution, the water salinity was reduced to 90% sea water (804 ± 28 mosmol/kg, n=6) by the appropriate adjustment of sea water and fresh water delivery rates to the tank. In other experiments, sea water was concentrated by approximately 10% (1055 ± 4 mosmol/kg, n=3), by the addition of sea salts (Instant Ocean) to sea water in a refrigerated-recirculating sea water system (Living Stream). Renal function was continuously monitored before and after salinity changes. Blood samples were obtained in 100% sea water, 90% sea water and 110% sea water for the measurement of circulating hormones.

In animals receiving hormone agonists or antagonists, the renal function was assessed during a control period and during an experimental period while the agents were infused intraarterially at rates from 10 to 50 μl/min for 2 hours. Dorsal aortic pressure was measured directly in cm H_2O from the arterial catheter. Blood and urine samples were frozen for later determinations of inulin and hormones. Catecholamines were assayed by a radioenzymatic method (Cat-a-Kit, Upjohn). Data are expressed as means ± SEM and paired t-test was used to assess statistical significance.

Results and Discussion

Upon exposure of the spiny dogfish to dilute sea water, there was a change in renal function to enhance water excretion, manifested partly by an increase in the rate of glomerular filtration (from 1.29 ± 0.21 to 2.00 ± 0.38 ml/kg.h, n=6, $p<0.05$). On the other hand, placing the fish in a hyperosmotic environment resulted in a significant decrease in water excretion (urine flow rate dropped from 0.22 ± 0.02 to 0.08 ± 0.01 ml/kg.h, n=6, $p<0.001$) as a consequence of a reduction in GFR (from 1.40 ± 0.14 to 0.56 ± 0.05 ml/kg.h, n=6, $p<0.01$). Although there were wide variations in the circulating levels of catecholamines among fish, for individual fish, increased GFR in dilute sea water was associated with increased circulating levels of catecholamines, mainly norepinephrine - the major circulating catecholamine in the dogfish. When GFR was increased from 0.80 ± 0.18 ml/kg.h to 1.14 ± 0.20 ml/kg.h in 90% sea water (n=4), the corresponding plasma concentrations of norepinephrine rose from 309 ± 69 pg/ml to 544 ± 110 pg/ml (n=4) while plasma epinephrine concentrations remained unchanged (343 ± 76 pg/ml in 100% sea water vs. 315 ± 78 pg/ml in 90% sea water). Thus, there appears to be a correlation between the plasma catecholamine concentrations and changes in glomerular function of marine elasmobranchs during environmental dilution.

The concentrations of catecholamines that effectively modulate the rate of glomerular filtration in the dogfish were determined by infusion of three catecholamines, norepinephrine, epinephrine, and dopamine into animals in 100% sea water at four dosages (40, 133, 400, and 1330 ng/min for 2 h). Norepinephrine significantly increased GFR and urine flow rate at 133 and 400 ng/min, probably as the result of increased systemic arterial pressure. Although the pressor response was evident at the highest dose (1330 ng/min), no increase in GFR was observed, perhaps because of afferent glomerular vasoconstriction. Similar dose-response characteristics were observed with epinephrine. However, dopamine had no significant effects on glomerular function at all doses examined. Assuming no degradation, the calculated final concentration range of norepinephrine after infusion (5-160 ng/ml extracellular fluid) encompasses the reported normal physiological concentrations found in the dogfish (Opdyke et al. 1981 Am. J. Physiol. 241: R288).

Peptide hormones have been reported to have significant effects on fish renal function. Prolactin appears to be involved in long-term changes in teleost renal function in response to salinity changes (Foster, Gen. Comp. Endocrinol. 27: 153, 1975). Prolactin level in fresh water-adapted teleost fish is 12 times higher than in sea water-adapted fish (Nicoll et al. 1981 Gen. Comp. Endocr. 44:365). In the dogfish, prolactin infusion (1 µg/animal/2 h) significantly increased GFR (from 0.77 ± 0.26 to 1.81 ± 0.44 ml/kg.h , n=5, $p<0.05$). These results suggest that prolactin may also play a role in the renal response of marine elasmobranchs to environmental dilution.

The possible role of a cardiac natriuretic factor in the renal response of dogfish to salinity changes was also investigated. In our previous studies (Yokota and Benyajati, 1986 Bull. MDIBL. 26: 87), a bolus administration of synthetic atriopeptin II (Peninsula) at the dose of 2 μg/kg in fish in 100% sea water produced a drop in dorsal aortic pressure and decreases in GFR and urine flow rate. In the present study, the constant infusion of atrial natriuretic peptide (Sigma) at a much lower dose (50 ng/animal/2 h) also resulted in a decrease in GFR (from 1.50 ± 0.45 to 0.87 ± 0.26 ml/kg.h, n=5, $p<0.05$) with no significant decrease in dorsal aortic pressure. When the same dose of the atrial natriuretic factor (ANF) was infused into fish in 90% sea water (which had higher levels of circulating catecholamines, see above) GFR increased (from 0.84 to 1.61 ml/kg.h, n=2). The simultaneous infusion of ANF and norepinephrine (133 ng/min for 2 h) resulted in an increase in GFR (from 0.30 ± 0.07 to 1.66 ±0.03 ml/kg.h, n=2) which was quantitatively similar to norepinephrine infusion alone. These observations suggest that the expression of the diuretic or antidiuretic actions of ANF depends upon the volume status of the animal and that plasma catecholamines may be the modulators of its action.

Vasoactive intestinal peptide (VIP), a neurotransmitter, has been found in mammalian renal nerve fibers and in the viscera of the dogfish (Hökfelt et al. 1978 Acta pharmac. tox. 43:78). VIP affects electrolyte and water transport across many epithelia. In the dogfish, VIP is thought to induce rectal gland salt secretion in response to volume expansion (Stoff et al. 1979 Am. J. Physiol. 237: F138). In the present study, infusion of VIP (50 ng/animal/2 h) resulted in a significant increase in GFR (from 1.23 ± 0.30 to 2.31 ± 0.36 ml/kg.h, n=7, $p<0.05$) and urine flow rate, with no significant effect on tubular water reabsorption. This observation suggests the possible involvement of VIP in the regulation of GFR in marine elasmobranchs.

Arginine vasotocin (AVT), the antidiuretic hormone in non-mammalian terrestrial vertebrates, produced no alteration in glomerular filtration at either low or high doses (6ng/animal/2 h and 60 ng/animal/2 h). Our previous studies suggest that AVT does not play a role in the renal response to environmental dilution since plasma AVT concentration did not change under these conditions (Yokota and Benyajati, 1986 Bull. MDIBL. 26: 87). However, AVT may play a role in the regulation of GFR during exposure of the dogfish to 110% sea water. The infusion of an AVT antagonist (D-Et_2-Tyr-(Et)-OVT; Barkowski et al, 1980 Int. J. Pep. n. Prot. Res. 16: 382) in fish in 110% sea water with reduced filtration rate resulted in a marked increase in GFR (from 0.54 ± 0.36 to 2.37 ± 0.18 ml/kg.h, n=2). The infusion of the AVT antagonist into fish in 100% sea water did not change GFR.

In conclusion, we have demonstrated that elasmobranch renal function is regulated by plasma catecholamine concentrations which are responsive to the volume status of the animal. In addition, peptide hormones (prolactin, ANF, VIP, and AVT) appear to play important roles in modulating GFR to meet changing osmoregulatory demands.

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