PHYSIOLOGY

Hydrocortisone-Induced Enhancement of the Hydroosmotic Effects of Vasopressin and cAMP on the Wall of Frog Urinary Bladder

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There is a number of extracellular and intracellular modulators of vasopressin action [2,6], which appear to provide for the possibility of altering the response to antidiuretic hormone (ADH) and are in some cases responsible for inadequate renal reaction to this hormone [1]. Aldosterone and dexamethasone, a synthetic glucocorticoid analog, enhance vasopressin-induced absorption of water [10]. Aldosterone effect is related to a reduced number of vasopressin receptors [6], inhibited prostaglandin biosynthesis [9] and changed activity of cAMP phosphodiesterase [8]. Several forms of cAMP phosphodiesterase are known [7], therefore under such conditions their ratio and sensitivity to an inhibitor of this enzyme, isobutylmethylxanthine (IBMX), might change, thus promoting cAMP accumulation in the cells and increasing the effect of vasopressin. The present research was aimed at elucidation of the influence of a natural glucocorticoid, hydrocortisone, on the effects of vasopressin and cAMP.

MATERIALS AND METHODS

Experiments were carried out with *Rana temporaria L* frogs. Water transport through the bladder wall was studied by weighing [3]. Ringer solution diluted 1:10 with water was poured into the bladder from the side of the mucous membrane, aerated Ringer's solution being poured from the side of the serous membrane. Vasopressin, hydrocortisone, IBMX (Serva), cAMP (Reanal) were added to solution near the bladder serous membrane.

RESULTS

Vasopressin increased the permeability of the frog bladder wall for water by the scores, water stream attaining the highest values within 10-15 min (Fig. 1). Effects of steroids on antidiuretic hormone were studied with a glucocorticoid, because glucocorticoids were expected to exert a greater influence on the permeability of the bladder wall for water than mineralocorticoids. Effects of steroid hormones, aldosterone among them, on Na^+ transport are associated with genome involvement, and several hours are necessary to realize these effects [4]; that is why experiments with addition of cAMP or vasopressin were studied no sooner than 3 h after addition of hydrocortisone to the solution. Hydrocortisone per se did not change the osmotic permeability of the frog bladder wall, but was conducive to a more effective action of vasopressin (Fig. 1).

This could be caused by a changed state of different components of the system promoting vasopressin-induced increase of permeability for water: the state of vasopressin receptors, the activity

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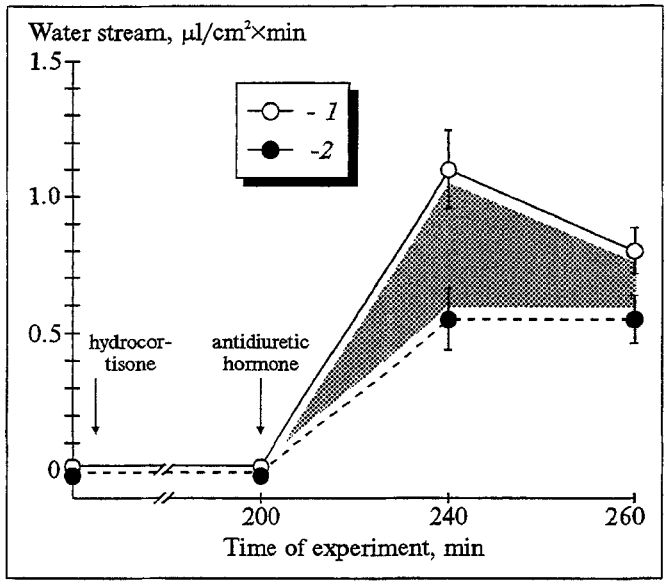

Fig. 1. Effect of hydrocortisone on permeability of frog bladder wall to water during exposure to vasopressin. *1*: addition (shown by arrows) of hydrocortisone (5×10^{-6} M), and of arginine vasopressin (antidiuretic hormone) (5×10^{-9} M) to Ringer's solution near serous membrane; *2*: addition of vasopressin (alone) in the same dose to paired bladder lobe. The zone of differences for hydrocortisone is cross-hatched. Every dot is derived from experiment on 8 species.

of adenylate cyclase and cAMP phosphodiesterase, and the elements of the apical membrane. A previously changed state of the initial part of the intracellular system providing for the effect of antidiuretic hormone was discovered in the presence of steroid hormones [6]. We paid the major attention in this research to the components of intracellular system, which are more distal to the site of cAMP formation. Frog bladders were incubated for 3 h in Ringer's solution with 5×10^{-6} M hydrocortisone. Then, 5×10^{-5} IBMX was added to this solution, and 30 min later, when the inhibitor penetrated into the cell, 2×10^{-3} cAMP was added. When cAMP alone was added, it was inactivated by phosphodiesterase present in the cell, and the osmotic permeability did not grow much (Fig. 2). Addition of cAMP in the presence of blocking of cAMP phosphodiesterase by IBMX markedly raised the permeability of the bladder wall for water. Pretreatment of the bladder tissue with hydrocortisone resulted in a drastic increase of the permeability of the bladder wall and of the water flow.

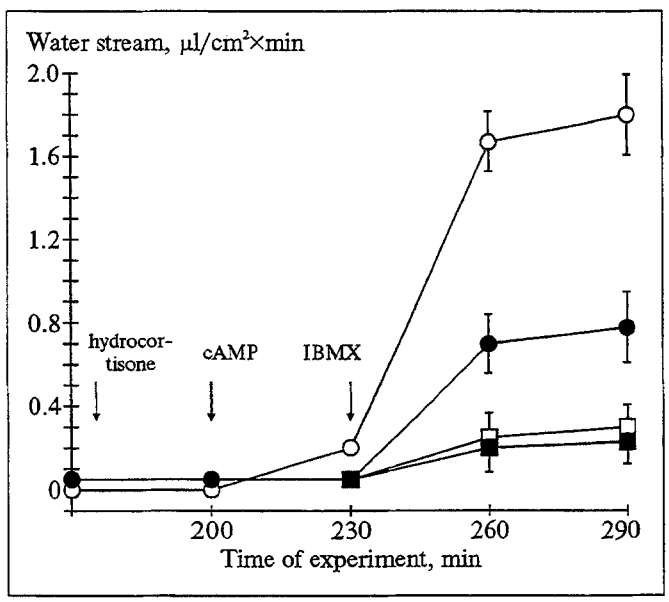

Fig. 2. Effect of hydrocortisone on cAMP-modulated permeability of frog bladder wall for water. The arrow shows addition of hydrocortisone (5×10^{-6} M), cAMP (1×10^{-3}), and IBMX (5×10^{-5} M) to solution near serous membrane. Every dot is derived from experiment on 5 species. Rest notation as in Fig. 1.

Hence, the increased response to vasopressin in the presence of hydrocortisone was caused by changed sensitivity of cAMP phosphodiesterase to IBMX or by a marked decrease of the number of functioning molecules of this enzyme. The greater increase of cAMP after addition of the same dose of IBMX is evidence that the mechanism of action of hydrocortisone largely depends on changes in the intracellular processes located within the system of action of antidiuretic hormone distal to the site of cAMP formation; in particular, this is true for cAMP phosphodiesterase. Recently it was shown that the increased concentration of urea and KCl, but not of saccharose, in the solution inhibited the activity of cAMP phosphodiesterase in the supernatant fraction of renal cells [10]. Regulation of the activity of this enzyme along with other cellular locuses underlies corticosteroid-mediated modulation of the effect of vasopressin, because adrenalectomy resulted in a decrease of the ability of vasopressin (but not of forscolin) to stimulate adenylate-cyclase [5].

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