MECHANISM OF THE INHIBITORY ACTION OF OXYTOCIN ON TRANSPORT OF ISOTONIC FLUID THROUGH THE GALL BLADDER EPITHELIUM

M. S. Yaremenko and O. N. Kharlamova

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The effect of oxytocin on the intensity of absorption of Ringer's solution by the epithelium of the isolated frog gall bladder and on the total Mg-, Na-, K-ATPase activity in its cells was studied. In doses of 0.5-20 m.u/ml, added on the side of the serosal surface of the organ, oxytocin reduced the intensity of isotonic fluid transport and the Na, K-ATPase activity of the epithelial cells of the gall bladder; Mg-ATPase activity was unchanged under these conditions. With an increase in the oxytocin concentration the values of the parameters studied fell exponentially. It is concluded that inhibition of the transport function of the gall bladder epithelium by oxytocin is connected with its inhibitory action on the Na, K-ATPase of the epithelial cells.

KEY WORDS: oxytocin; gall bladder; fluid transport.

Investigations have shown [1, 3, 4] that neurohypophyseal hormones participate in the regulation of water and electrolyte absorption by the gall bladder epithelium. Under the influence of these hormones the intensity of absorption falls significantly in the gall bladder. Oxytocin [1, 3] has a particularly strong inhibitory action. The gall bladder epithelium transports NaCl actively into the lateral intercellular spaces, and this is followed by the migration of water through the epithelium along the osmotic gradient [4, 7, 10]. The enzyme Na, K-ATPase has a role in NaCl transport by the epithelium [9].

It is therefore important to determine whether oxytocin acts on the ATPase system of the gall bladder epithelial cells.

EXPERIMENTAL METHOD

The frog gall bladder, which is highly sensitive to the action of oxytocin [1], was used. The gall bladder, freed from traces of bile, was fixed to a thin polyethylene cannula and filled with isotonic Ringer's solution. This preparation was weighed on torsion scales and immersed in aerated Ringer's solution at 18-20°C for 3 h. The preparation was weighed periodically and the rate of absorption of isotonic fluid from the interior of the gall bladder was estimated from the decrease in its weight. In some experiments the fluid contained in the lumen of the gall bladder was periodically withdrawn and its Na ion concentration determined by flame photometry. At the end of the experiment a homogenate was prepared from the mucous membrane of the gall bladder and the total Mg- and Na, K-ATPase activity in it was determined [2, 8]; the result was expressed as the number of micromoles inorganic phosphorus (P_{in}) set free from ATP during incubation with 1 mg protein of the homogenate for 1 h. The rate of transport of water (in μl) and Na (in μeq) was calculated per 100 mg weight of the gall bladder wall over periods of 15 or 60 min. Oxytocin was added to the solution from the side of the serosal surface of the gall bladder in doses of 0.5-20 m.u./ml.

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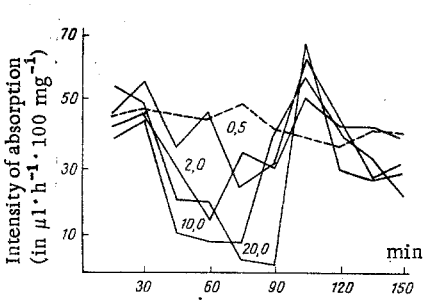

Fig. 1

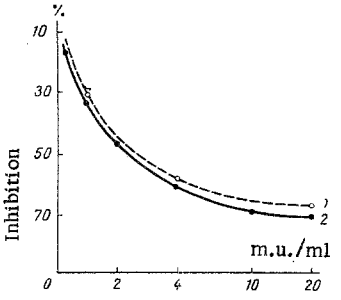

Fig. 2

Fig. 1. Effect of different doses of oxytocin on intensity of absorption of isotonic Ringer's solution from gall bladder lumen. Broken line – control; continuous lines – different experiments. Numbers above lines give doses of oxytocin (in m.u./ml).

Fig. 2. Decrease (in % of control) in rate of absorption of isotonic fluid (1) and Na, K-ATPase activity (2) during the action of various doses of oxytocin on the gall bladder.

TABLE 1. Rate of Absorption of Water and Na and ATPase Activity of Frog Gall Bladder Epithelial Cells in the Control and under the Influence of Various Doses of Oxytocin (M ± m)

Experimental conditions		No. of determinations	Q_{H_2O}	Q_{Na}	ATPase activity		
					Mg, Na, K-($n=8$)	Mg-($n=8$)	Na, K-($n=8$)
Control		51	46,5±2,2	5,18±0,24	15,1±0,6	11,4±1,4	3,5±0,4
Oxytocin (in m.u./ml)							
1		10	28,6±4,6	3,14±0,51	14,1±2,7	11,6±2,8	2,5±0,4
	P		<0,01	<0,001	<0,01	<0,5	<0,02
4		10	19,5±5,4	2,14±0,49	13,3±2,3	12,1±3,0	1,2±0,3
	P		<0,001	<0,001	<0,001	<0,5	<0,001
20		6	15,0±2,5	1,65±0,038	12,4±2,1	11,5±2,3	0,9±0,2
	P		<0,001	<0,001	<0,02	<0,5	<0,01

Legend. Q_{H_2O}, Q_{NA}) quantity of H_2O (in μl) and Na (in μeq) transported through the gall bladder wall in 1 h per 100 mg weight of tissue. ATPase activity expressed in μmoles P_{in} liberated in 1 h per mg protein.

TABLE 2. Percentage of Decrease in Rate of Absorption of Isotonic Fluid and of Na, K-ATPase Activity of Epithelial Cells during the Action of Oxytocin on the Gall Bladder

Dose of hormone (in m.u./ml)	No. of determinations	Rate of absorption		Na, K-ATPase activity	
		$M \pm m$	P	$M \pm m$	P
1	4	–38,4±1,9	<0,02	–33,0±6,3	<0,02
4	6	–58,0±4,1	<0,001	–66,0±3,8	<0,001
20	4	–67,5±3,7	<0,001	–70,7±6,9	<0,001

EXPERIMENTAL RESULTS

The addition of oxytocin reduced the rate of transfer of isotonic fluid through the gall bladder wall (Fig. 1). The effect increased with an increase in the hormone concentration in the medium. The level of absorption fell exponentially (Fig. 2).

The presence of oxytocin in the medium led to a marked decrease in activity of total and Na, K-ATPase of the epithelial cells. In this case also, with an increase in the acting dose of hormone the ATPase activity of the epithelial cells fell exponentially (Fig. 2). Only the Na, K-ATPase activity fell under the influence of the hormone, and this led to a decrease in the total ATPase activity; Mg-ATPase activity was unchanged (Table 1).

Analysis of these results shows that the rate of absorption of isotonic fluid and the Na, K-ATPase activity were reduced about equally by the same doses of oxytocin (Table 2). A high degree of correlation ($r = 0.99$) was found between these changes.

It can be concluded from these results that oxytocin, through its action on the tissue of the frog gall bladder, inhibits the activity of the enzyme systems responsible for the transport of isotonic fluid through the epithelial barrier of the gall bladder; this is evidently the mechanism whereby oxytocin exerts its effect on the absorptive function of the gall bladder.

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