PROLACTIN EFFECT ON WATER-SOLUTE BALANCE IN THE RAT MODEL OF CHOLESTASIS OF PREGNANCY IS RENAL AQUAPORIN INDEPENDENT

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Prolactin regulates lactation in mammals, but in fishes and lower vertebrates it controls water-solute balance. Level of this hormone elevates during pregnancy and additionally elevates under condition of cholestasis of pregnancy. Our goal was to determine whether prolactin has any effect on water-solute homeostasis in female rats in the model of cholestasis of pregnancy.

METHODS. For the modeling of pregnancy's prolactin (PRL) level hyperprolactinemia was induced by donor pituitary transplantation under renal capsule of female rat recipient, for the modeling of cholestasis of pregnancy the combination of induced hyperprolactinemia and bile duct ligation was used.

Hyperprolactinemia was confirmed by measure of rat serum prolactin concentration (**Table1**). Surgical procedures were conducted under diethyl ether anesthesia. In these models diurnal diuresis, glomerular filtration rate (GFR) and diurnal sodium excretion were estimated. Aquaporin 1–4 mRNA expression in the renal inner medulla was tested by real-time PCR using 3 housekeeping genes and normalized on GAPDH expression.

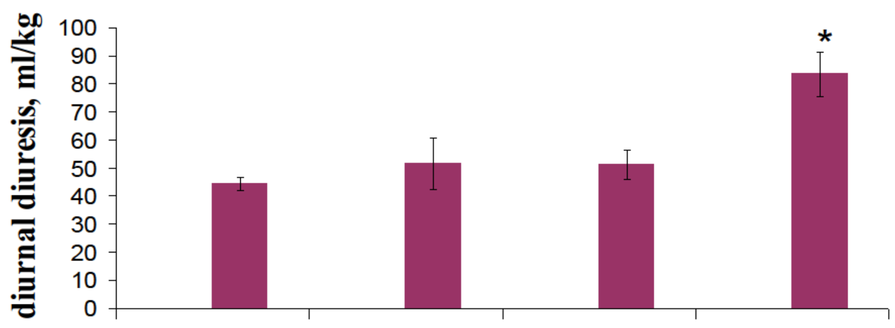
Visual examination of well-vascularized hypophyseal graft

Table 1. The rat serum prolactin concentration in experimental groups. * -p<0,05 compared with normal group

	serum prolactin concentration, ng/ml
Normal	**2,3 0,74 (10)**
Normal+hyperPRL	**12,9 2,93 (6) ***
Cholestasis	**11,8 2,65 (31) ***
Cholestasis+hyperPRL	**48,8 5,78 (17) ***

RESULTS. Persistent hyperprolactinemia combined with obstructive cholestasis led to sharp 2-fold elevation of diurnal diuresis (**Fig.1**) and compensatory water consumption as compared with the control.

Fig 1. The diurnal diuresis in experimental groups.
* -p<0,05 compared with normal group



In spite of this aquaporin 1–4 mRNA expression in the renal inner medulla (**Table 2**) and glomerular filtration rate (**Table 3**) were not changed in this model of cholestasis of pregnancy.

Table 2. The rat aquaporin 1–4 mRNA expression in the renal inner medulla in experimental groups.

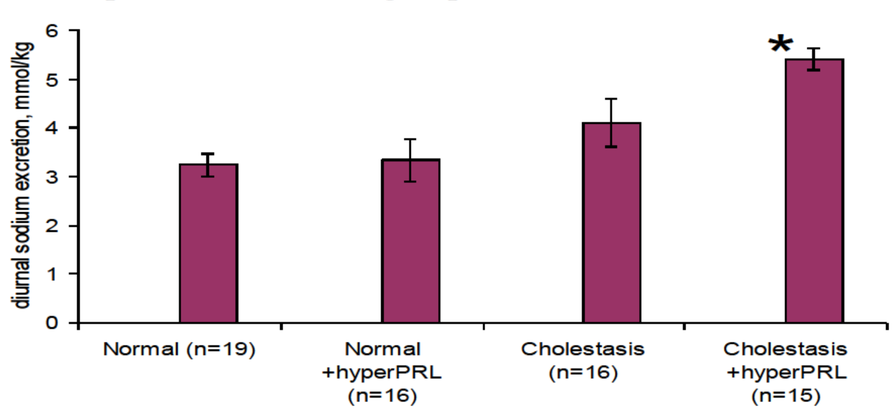
	Aquaporin mRNA expression, % to GAPDH mRNA			
	AQP1	AQP2	AQP3	AQP4
Normal (n=4)	**16,2 2,6**	**49,8 12,1**	**3,2 0,6**	**3,8 0,7**
Normal +hyperPRL (n=6)	**12,9 1,7**	**25,4 6,4**	**3,0 0,6**	**2,3 0,3**
Cholestasis (n=5)	**11,8 1,2**	**42,1 7,4**	**3,9 1,2**	**2,9 0,5**
Cholestasis +hyperPRL (n=6)	**14,4 1,6**	**52,0 5,5**	**3,1 0,4**	**2,7 0,2**

Table 3. The rat diurnal creatinine clearance in experimental groups.

	Diurnal creatinine clearance, ml/kg
Normal	**6800,6 462,5 (13)**
Normal +hyperPRL	**5277,4 454,6 (9)**
Cholestasis	**6076,4 495,3 (7)**
Cholestasis +hyperPRL	**6226,6 399,1 (8)**

In this model sufficient elevation of diurnal sodium excretion as compared with control groups was revealed. Alone bile duct obstruction or hyperprolactinemia had no marked influence on these parameters (**Fig.2**).

Fig 2. The diurnal sodium excretion in experimental groups.
* -p<0,05 compared with normal group



CONCLUSION. The data on diuretic and natriuretic effects of prolactin in the model of cholestasis of pregnancy together with the lack of prolactin influence on GFR and aquaporin 1-4 mRNA expression in renal medulla let us to suggest primary prolactin influence on the sodium transporters in the kidney without substantial modulation of aquaporin expression and vasopressin action.

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