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Hyperprolactinemia in cholestasis of pregnancy is associated with decreased renal outer medulla Na+/K+-??Pase activity and elevation of pSTAT5

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Context. Pregnant women demonstrate an increased blood prolactin (Prl) concentration. Prl level additionally increases (pathological hyperprolactinemia) during the cholestasis of pregnancy (CP), - pathology connected with the disturbance of a bile secretion or outflow and pathological changes of water-salt balance. Kidney functional failure in the CP is connected with a natriuretic effect of Prl. The renal Prl receptor signaling under condition of CP is not investigated. There are long and short isoforms of Prl receptors. Prl receptors are also expressed in kidneys. STAT5s (Signal Transducers 5 and Activators of Transcription) are the key proteins of Prl receptor long isoform (LR) signaling. Prl binding with LR induces STAT5 phosphorylation, its translocation to the nucleus and the modulation of target genes expression. One of such molecular target of Prl may be renal Na+/?+-???ase.
Objective. Revealing of the role of Na+/?+-???ase as a potential target of Prl and the involvement of LR tested by STAT5 phosphorilation in Prl renal effects in the CP model.
Methods - Main Outcome Measure(s) - Patient(s). Surgical operations in outbred mature female rats divided into 4 experimental groups: intact, with condition of pseudopregnancy (hyperprolactinemia), with cholestasis and with cholestasis and hyperprolactinemia (CP model); Na+/?+-???ase activity assay (method of Rathbun and Betlach); western blotting of STAT5 and its phosphorylated form (pSTAT5) in the renal cortex and outer medulla (rabbit polyclonal anti-STAT5 antibody and rabbit polyclonal ?nti-STAT5 (phospho Y694) antibody (Abcam, Kanada) were used).
Intervention(s). Modeling of CP in rats by induction of pseudopregnancy and obstruction of the bile duct.
Results. In renal outer medulla Na+/?+-???ase activity declines in the model of CP as compared with intact rats ($p<0,05$). In the renal cortex Na+/?+-???ase activity does not change in all groups as compared with intact rats. In the CP pSTAT5 expression significantly increases in comparison with intact rats only in outer medulla of kidney ($p<0,05$). The level of protein expression of STAT5 does not change in all groups as compared with intact rats neither in the cortex nor in outer medulla of kidney.
Conclusion. Under condition of hyperprolactinemia in CP Na+/?+-???ase takes part in the realization of the natriuretic Prl effect in the renal outer medulla, which may realize through LR and pSTAT5.

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