УДК: 591.461.2:599.323.4

Slobodyan Ksenia
candidate of medical sciences, assistant of department
Bucovinian state medical university, Chernivtsi, Ukraine

EVALUATION OF THE DISORDERS OF RENAL FUNCTIONS IN SEXUALLY IMMATURE RATS WITH SUBLIMATE NEPHROPATHY UNDER SALT LOAD AND BLOCKADE OF RENAL PROSTAGLANDINS

Summary. *Experiments on 40 white non-linear immature (l-month old) male rats evaluated indices of renal function with sublimate nephropathy at loading by 3% sodium chloride solution in volume of 5% of the body weight under conditions of blockade of renal prostaglandins production with indomethacin and had shown inhibition of diuresis, decrease of sign of the syndrome of sodium ions loss with urine against the background of hypernatremia. Disorders of glomerular-tubular balance were characterized by the loss of positive correlative dependences of relative reabsorption of water with glomerular filtration, filtrative fraction and absolute reabsorption of sodium ions. The defined changes in glomerular-tubular balance in sexually immature rats with sublimate nephropathy under the 3% solution of sodium chloride loading to the extent of 5% of body mass under the condition of blocking the production of kidney prostaglandins by indomethacin with the loss of positive correlation dependence of the relative water reabsorption on glomerular filtration, filtration fraction and absolute reabsorption of sodium ions, confirm the effect of the prostaglandins on the above processes in immature rats. The decrease of the compensatory abilities as to the development of the syndrome of sodium ions loss in immature rats in experiment leads to the disorders of sodium homeostasis and to the development of hypernatraemia.*

Key words: *sublimate nephropathy, loading by 3% sodium chloride solution, indomethacin, immature rats.*

Introduction. It is known that at loading by 3% sodium chloride solution under sublimate nephropathy in sexually immature rats polyuric form of acute renal insufficiency develops [3], due to maximal mobilization of compensatory abilities of prostaglandin E_2 [4, 8] as a vasodilator of efferent kidney arteriole and a factor having natriuretic action as to the state of water diuresis, at which the oliguric form of acute renal insufficiency takes place [2, 7, 10]. Blockade of renal prostaglandins production by indomethacin under such conditions leads to renal vessels' spasm and oliguria development [3]. Coincidently, the analysis of the effect of blockade of renal prostaglandins production by indomethacin on the renal function indices in sexually immature rats with sublimate nephropathy under the 3% solution of sodium chloride loading has practically not been carried out.

Research objective. To determine the effect of blockade of renal prostaglandins production by indomethacin on the renal function indices in sexually immature rats with sublimate nephropathy under the 3% solution of sodium chloride loading.

Materials and methods. Experiments have been carried out on 40 white non-linear sexually immature male rats (month-aged) with the mass 0.06–0.08 kg. The functional state of the kidneys was studied under the condition of 3% solution of sodium chloride loading in 24 h after sublimate nephropathy development (subcutaneous injection of mercuric chloride, 5mg/kg); the studied solution at 37°C and in amount of 5% of body mass was administered through metallic catheter into animal's stomach with the following urine collection during 2 hours. The amount of diuresis (V) was evaluated in ml/2 h/100 g of body mass. Euthanasia of the animals was carried out by decapitation after etherization. Blood was collected into the tubes with heparin. Glomerular filtration (C_{cr}) was evaluated by the endogenic creatine clearance, according to the formula:

$$C_{cr} = U_{cr} \cdot V/P_{cr}$$

where U_{cr} and P_{cr} — concentrations of creatine in urine and blood plasma, respectively.

Filtration fraction of sodium ions (FFNa+) was evaluated by the formula:

$$FFNa+ = C_{cr} \cdot PNa+$$

Excretion of sodium and potassium ions (EFNa+, EFK+) was evaluated by the following formulas:

$$EFNa+ = V \cdot UNa+$$

$$EFK+ = V \cdot UK+$$

Relative water reabsorption ($RH_2O\%$) was estimated as follows:

$$RH_2O\% = (C_{cr} - V) / C_{cr} \cdot 100\%$$

Clearance of sodium ions (CNa+) was estimated as follows:

$$CNa+ = V \cdot UNa+/PNa+$$

Relative reabsorption of sodium ions (RFNa+%) was estimated by the formula:

$$RFNa+\% = (1 - V \cdot UNa+/ C_{cr} \cdot PNa+) \cdot 100\%,$$

where PNa+ — concentration of sodium ions in blood plasma, UNa+ — concentration of sodium ions in urine (estimated by flame photometry method) [1, 6].

Glomerular-tubular balance was studied through correlation analysis between the processes of glomerular filtration, filtration fraction of sodium ions, absolute reabsorption of sodium ions and relative water reabsorption [5].

Indomethacin as a blocker of renal prostaglandins production was administered into the stomach through the catheter in amount 5 mg/kg in 1% solution of gelatin during 3 days [3].

Statistical processing of the received data was performed with the help of computer programs "Statgrafics", "Exel7.0" та "Stattistica".

Research results and their discussion. The analysis of the renal function indices in sexually immature rats with sublimate nephropathy under 3% solution of sodium chloride loading to the extent of 5% of body mass under the condition of blocking the production of kidney prostaglandins by indomethacin showed higher measures of creatinine level in urine, of relative water reabsorption, of sodium ions concentration in blood plasma, of creatinine concentrational index (Table 1). Coincidently, in the condition of blockade of renal prostaglandins production by indomethacin the indices of diuresis, relative diuresis, sodium ions concentration and their excretion, excretion of potassium ions, concentrational index of sodium ions, correlation of concentration of sodium and potassium ions in urine, sodium ions clearance, excretional correlation of sodium and potassium ions to urine creatinine were lower.

The analysis of glomerular-tubular balance in sexually immature rats with sublimate nephropathy under 3% solution of sodium chloride loading to the extent of 5% of body mass under the condition of blocking the production of kidney prostaglandins by indomethacin showed the loss of positive correlational dependencies of relative water reabsorption with glomerular filtration, filtration fraction and absolute reabsorption of sodium ions (Fig. 1, 2).

3% solution of sodium chloride loading under sublimate nephropathy in sexually immature rats does not cause the development of polyuric form of acute renal insufficiency under condition of blockade of kidney prostaglandins production by indomethacin [3], due to elimination of compensatory abilities of prostaglandin E_2 [4] as a vasodilator of efferent kidney arteriole and a factor having natriuretic action. These facts are confirmed by retardation of diuresis, relative diuresis, urinal concentration of sodium ions and their excretion, concentration index of sodium ions, sodium ions clearance, correlation of sodium ions excretion and urine creatinine.

Reduction of compensatory abilities as to the development of sodium ions loss syndrome in experiment on sexually immature rats causes the disorders in sodium ions homeostasis followed by the development of hypernatraemia.

The lower rates of concentration and excretion of sodium ions with urine in experimental sexually immature rats are associated with the less meaningful effect of aldosterone [9] on the above mentioned processes. The higher rate in the experimental relative water reabsorption is defined by the inadequate stage of efficiency of natriuretic mechanisms in animals of junior age group. The same way the higher rates of the relative reabsorption of sodium ions index are explained. There are no diversities as to the concentration and urinal excretion of proteins and this fact is caused by the absence of effect of prostaglandins production blockade on the lesion of proximal tubule in sexually immature rats in the experiment.

The revealed changes in the glomerular-tubular balance in sexually immature rats with sublimate nephropathy in the condition of 3% solution of sodium chloride loading to the extent of 5% of body mass under the blockade of kidneys prostaglandins production by indomethacin, with the loss of positive correlation response of relative water reabsorption on the glomerular filtration, filtration fraction and absolute reabsorption of sodium ions, confirm the effect of prostaglandins on the above mentioned processes in sexually immature rats.

Conclusions

1. In experiments on white non-linear sexually immature (month-aged) male rats with sublimate nephropathy the evaluation of the renal function indices after 3% solution of sodium chloride loading to the extent of 5% of body mass under the blockade of kidneys prostaglandins production by indomethacin revealed the retardation of diuresis, decrease of the syndrome of sodium ions loss with urine manifestation on the background of hypernatremia.

2. Disorders of glomerular-tubular balance in the experimental conditions are characterized by the loss of positive correlation response of relative water reabsorption on the glomerular filtration, filtration fraction and absolute reabsorption of sodium ions.

Perspectives of further investigations. Carrying out the multifactor regressive analysis of the correlation between the indices of renal function in sexually mature and immature rats with sublimate nephropathy at loading by 3% sodium chloride solution in amount of 5% of the body weight under conditions of blockade of kidney prostaglandins production by indomethacin.

Table 1

Renal function indices under sublimate nephropathy and blockade of kidney prostaglandins production by indomethacin in sexually immature rats in the condition of 3% solution of sodium chloride loading to the extent of 5% of body mass with the following urine collection during 2 hours (x±Sx)

Index	Administration of mercuric chloride, 3% solution of sodium chloride loading, sexually immature (n=10)	Administration of mercuric chloride, 3% solution of sodium chloride loading + indomethacin, sexually immature (n=10)
Diuresis, ml/2 h · 100 g	2,78±0,236	0,67±0,083 p<0,001
Relative diuresis, %	55,62±4,725	13,50±1,668 p<0,001
Sodium ions concentration in urine, mmol/l	77,75±8,261	20,62±5,916 p< 0,001
Sodium ions excretion, mkmol/2 h · 100 g	215,86±28,349	10,20±1,217 p<0,001
Potassium ions concentration in urine, mmol/l	21,70±2,051	18,05±1,670
Potassium ions excretion, mkmol/2 h · 100 g	59,97±6,810	11,86±1,811 p<0,001
Creatinine concentration in urine, mmol/l	1,950±0,075	3,75±0,351 p< 0,001
Glomerular filtration, mcl/min ·100 g	553,7±96,36	341,1±49,55
Relative water reabsorption, %	94,80±0,788	98,18±0,267 p<0,001
Blood sodium ions concentration, mmol/l	144,5±1,48	163,5±3,16 p<0,001
Filtration fraction of sodium ions, mcmol/min · 100 g	79,73±13,563	55,26±7,486
Excretion fraction of sodium ions, mcmol/min · 100 g	1,79±0,236	0,085±0,101 p<0,001
Relative reabsorption of sodium ions,%	97,39±0,319	99,80±0,038
Creatinine concentration index, relative value unit (RVU)	23,19±3,068	66,85±9,587 p<0,001
Sodium ions concentration index, RVU	0,540±0,0582	0,129±0,0391 p< 0,001
Correlation of concentration of sodium and potassium ions in urine, RVU	3,584±0,1902	1,163±0,2617 p< 0,001
Sodium ions clearance, ml/2 h · 100 g	1,50±0,203	0,063±0,0082 p<0,001
Urinary protein concentration, mg/ml	0,469±0,2334	0,906±0,3021
Protein excretion, mg/2 h · 100 g	1,434±0,7703	0,476±0,1780
Sodium ions excretion, nmol/100 mcl	44,9±5,45	3,76±0,749 p< 0,001
Protein excretion, mcg/100 mcl	0,242±0,1089	0,142±0,0520
Creatinine excretion, mcmol/2 h · 100 g	5,38±0,443	2,41±0,325 p< 0,001
Correlation of sodium ions and urine creatinine, RVU	40,37±4,289	5,59±1,336 p<0,001
Correlation of potassium ions and urine creatinine, RVU	11,30±1,134	5,31±0,936 p<0,001
Correlation of protein excretion and urine creatinine, RVU	0,251±0,1255	0,220±0,0800

p — odds probability compared with sublimate nephropathy in the condition of 3% solution of sodium chloride loading;

n — number of samples.

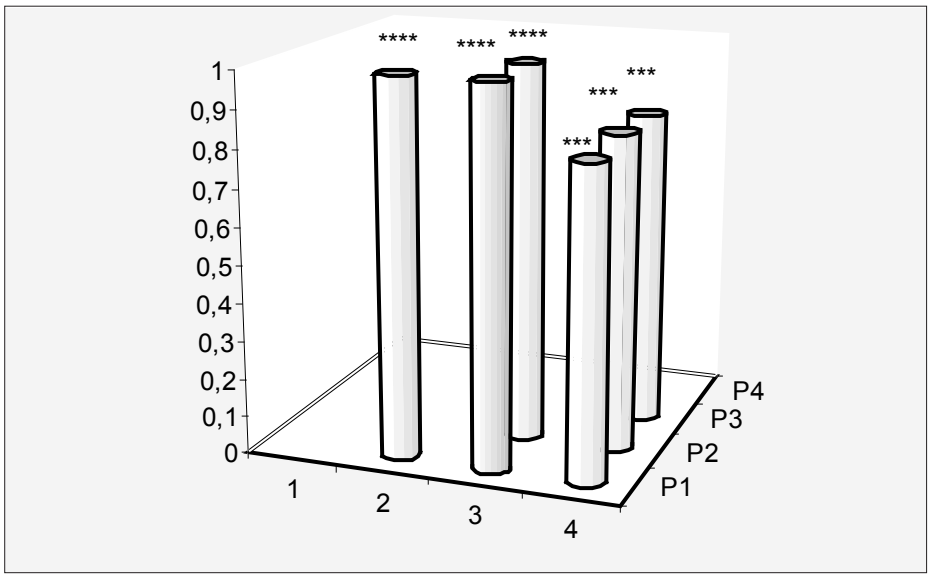

Fig. 1. The state of glomerular-tubular kidneys balance under the sublimate nephropathy in sexually immature rats in the condition of 3% solution of sodium chloride loading

1, P_1 — glomerular filtration (mcl/min/100g);
2, P_2 — filtration fraction of sodium ions (mcmol/min/100 g);
3, P_3 — absolute reabsorption of sodium ions (mcmol/min/100 g);
4, P_4 — relative water reabsorption (%);
probability of correlation relation is defined: *** –p < 0,01; **** –p < 0,001.

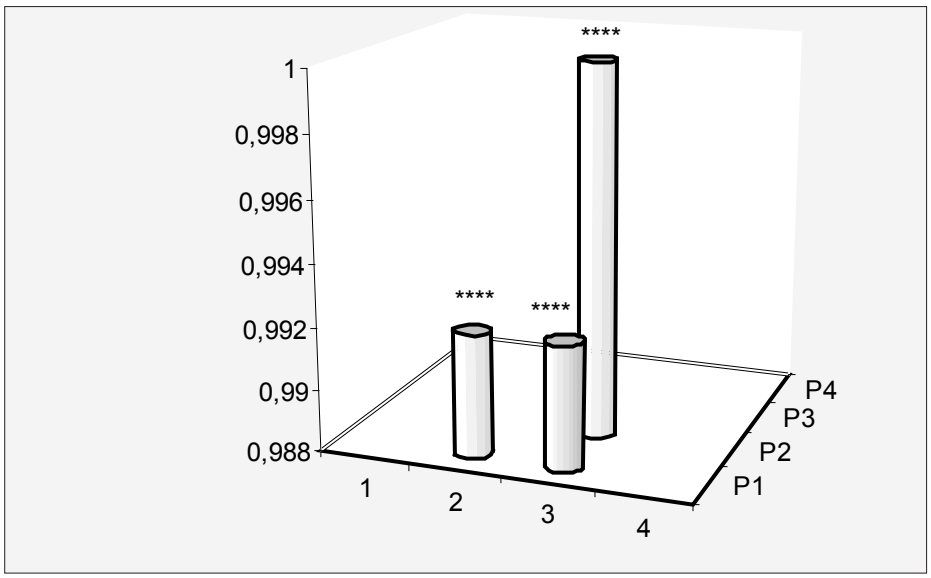

Fig. 2. The state of glomerular-tubular kidneys balance under the sublimate nephropathy in sexually immature rats in the condition of 3% solution of sodium chloride loading on the background of the kidneys prostaglandins production blockade by indomethacin

1, P_1 — glomerular filtration (mcl/min/100 g);
2, P_2 — filtration fraction of sodium ions (mcmol/min/100 g);
3, P_3 — absolute reabsorption of sodium ions (mcmol/min/100 g);
4, P_4 — relative water reabsorption (%);
probability of correlation relation is defined: **** — p < 0,001.

References

1. Boychuk T.M., Rohovyi Yu.Ye., Popovych G.B. Pathological physiology of hepatorenal syndrome under the blood hypoxy. — Chernivtsi: Meduniversytet, 2012. — 192 p.

2. Cogan M.G. Angiotensin II: a powerful controller of sodium transport in the early proximal tubule /M.G. Cogan. // Hypertension. — 1990. — V.15, N5. — P. 451–458.

3. Gozhenko A.I., Dolomatov S.I., Romaniv L.V. Age peculiarities of the liver osmoregulating function in white rats. // Nephrology. — 2003. — V.7, No.2 — P. 82–85.

4. Kukharchuk O.L. Pathogenetic role and methods of correction of integrative disorders in hormonal-messenger systems of sodium homeostasis regulation under the kidneys' pathology: 14.03.05 / Bukovinian State Medical Academy — Odessa, 1996. — 36 p.

5. Kukharchuk O.L. Kidneys' prostaglandins and renal pathology // Prostaglandins. — Chernivtsi: Medinstitut, 1997, — P. 38–42.

6. Rohovyi Yu.Ye., Zlotar O.V., Filipova L.O. Pathophysiology of hepatorenal syndrome on the polyuric stage of sublimate nephropathy. — Chernivtsi: Medical University. 2012. — 197 p.

7. Slobodian K.V. The role of prostaglandin E2 in excretion of osmotically concentrated urine under the 3% solution of sodium chloride loading in intact mature rats. // Bukovinian Medical Herald. — 2008. — V.12. — No.3. — P. 77–80.

8. Glodny B. The vasodepressor function of the kidney: Prostaglandin E2 is not the principal vasodepressor lipid of the renal medulla / B. Glodny // Acta physiol. Scand. —2006. —№ 3. — P. 419–429.

9. Gandhi C. Nebivolol reduces experimentally induced warm renal ischemia reperfusion injury in rats / C. Gandhi, R. Zalawadia, R. Balaraman // Ren. Fail. — 2008. — V.30, N9. — P. 921–930.

10. Gopisetti G. DNA mutilation and apoptosis. / G. Gopisetti, K. Ramachandran, R. Singal // Molecular Immunology. 2006. — V. 43. — P. 1729–1740.

11. Hammerman M.R. Organogenesis of kidney following transplantation of renal progenitor cells / M.R. Hammerman // Transpl. Immunol. — 2004. — V.12, № 4. — P. 229–239.

12. Jucknevicius I. Effect of aldosterone on renal transforming growth factor-beta / I. Jucknevicius, Y. Segal, S. Kren at all // Am. J. Physiol. — 2004. — Vol. 286, N6. — P. 1059–1062.

13. Stevens L.A. Clinical implications of estimating equations for glomerular filtration rate / L.A. Stevens, A.S. Levey // Ann. Intern. Med. — 2004. — V.141, N12. — P. 959–961.

14. Sturgiss S.N. Renal reserve during human pregnancy / S.N. Sturgiss, R.F. Wilkinson, J.M. Davison // Am. Physiol. Regul. Integr. Comp. Physiol. — 2003. — V. 284, N.6. — P.R1521-R1528.

15. Wong P.S.K. The action of angiotensin II on the intracellular sodium content of suspensions of rat proximal tubules / P.S.K Wong, E.J. Johns // J. Physiol. — 1996. — V. 497, N1. — P. 219–227.