EFFECT OF NMDA-RECEPTOR`S ANTAGONIST ON RENAL GLUCOSE REABSORPTION UNDER THE CONDITIONS OF INSULIN RESISTANCE AND CHRONIC RENAL FAILURE

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Introduction. Glucosuria is a common condition in clinical nephrology and dialectology. The nature of this ailment comes to be both renal and extrarenal. Extraenal glucosuria could be detected in patients if the level of blood glucose reaches high values (up to 9.0 mmol/l). On the other hand, renal glucosuria may be accompanied by normal glucose level, but violation of the reabsorption process, for example on the course of chronic glomerulonephritis, nephrotic syndrome or renal failure. Nowadays more than 40% of end-stage renal disease can be attributed to diabetes and these patients have combined renal and extrarenal glucosuria.
N-methyl-D-aspartate receptors are expressed throughout different tissues and organs in human organism, including kidney and seem to be the potential target for treating renal complications under the conditions of diabetes mellitus. NMDA receptors are expressed in the renal cortex and medulla, and appear to play a role in the regulation of renal blood flow, glomerular filtration, proximal tubule reabsorption and urine concentration within medullary collecting ducts. Inhibition of NMDA-receptors may represent a valid therapeutic approach to reduce renal complications of diabetes. One of those agents, memantine, is already in widespread clinical use.

Aim. The study of memantine effect on evidences of the glicosuria and the violation of the renal glucose reabsorption in rats with experimental insulin resistance and chronic renal failure became a focal point of our research.

Materials and methods. The study was carried out on 40 female out-breed rats at the age of 2,5 months, which were divided in 2 groups by 20 animals. To reconstitute toxicant-induced renal injury animals were received a single intravenous dose of 2 mg/kg doxorubicin. During the 6 weeks, all animals are kept on a low sodium, fructose- and fat-enriched diet (to induce persistent insulin resistance). The treatment of animals was carried out by oral administration of memantine in the dose 2.0 mg/kg during last 15 days. After the treatment period animals were given oral glucose load and were kept in metabolic cages for 24-hours diuresis collection. Under the experiment blood and urine glucose was measured by glucose oxidase method.

Results. All experimental animals demonstrated strongly polyuria, glycosuria, high blood glucose level and proteinuria. The use of memantine promoted to decreasing polyuria (in 25.7 ml/24 hours; p less than 0.05) and glycosuria (in 3.6 g/24 hours; p less than 0.05). Also memantine administration caused to better cellular glucose utilization, that was confirmed by decreasing of final blood glucose level in 17.5%. Kinetics studies demonstrated that memantine strikingly increased renal glucose reabsorption.

Conclusions. NMDA-receptor`s antagonist memantine influenced on glucose metabolism and and parameters of glucose excretion. Study of glucosuria and renal glucose reabsorption detected that memantine could be potential drug, used in combined therapy of diabetes mellitus with chronicle renal complications.