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## **Influence of mineral water on the structural and functional state of the rats kidneys with metabolic syndrome**

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### **Abstract**

In white rats in the setting of development of metabolic syndrome inhibition of the urinary and excretory functions of the kidney, with impaired water-ion balance (the kidneys excrete slightly hyperosmotic urine in a small amount) on the background of structural signs of dystrophies. Daily diuresis is reduced by 37% due to a decrease in glomerular filtration rate (GFR) by 22% and an increase in the percentage of tubular reabsorption ( $p < 0.001$ ), excretion of creatinine, urea and chloride decreased by 22%, 15% and 56%. The excretion of

potassium and sodium ions increases by 14% and 38%, respectively. The daily urine is greatly delayed. Two-week internal course administration of low-mineralized sodium chloride water has a positive effect on impaired renal function: the volume of diuresis is increased by 15% by accelerating GFR by 20% and restoring the value of tubular reabsorption. Creatinine excretion is increased by 20% and urea by 32%. The excretion of potassium and sodium ions is increased by 50% and 166%, respectively.

Excretion of chloride ions and urine pH is fully restored. Microscopically determined residual manifestations of dystrophic processes in the kidneys, which against the background of the recovery of processes of urination and stimulation of ion-regulating and excretory functions of the kidneys, indicates the ability of the applied sodium chloride MW to correct the structural and functional disorders of the metabolic syndrome.

**Key words: mineral water, metabolic syndrome, structural and functional state of the kidneys, white rats.**

**Introduction.** The prevalence of metabolic syndrome (MS) in modern society has progressively increased in recent years, which takes on the nature of the epidemic, it occurs on average in every fifth adult in the population of developed countries [1]. An alarming signal is the spread of MS incidence among children and adolescents [2]. According to the Ministry of Health statistics for 2011, 26% of adults in Ukraine suffer in MS [3]. The World Health Organization characterizes MS as a “pandemic of the 21st century” [4].

According to NCEP-ATPIII (National Cholesterol Education Program-Adult Treatment Panel III), the criteria for MS are the presence of three or more of the following disorders: abdominal obesity, fasting hyperglycemia, hypertriglyceridemia, hypertension, low-density lipoprotein cholesterol [5]. The most widespread and accepted view is the role of insulin resistance as a mechanism that triggers the entire cascade of metabolic related disorders that lead to MS [6].

One of the main reasons for the spread of insulin resistance, which in turn leads to the development of obesity and metabolic syndrome, is the spread of the modern high-calorie diet [7].

The relationship of caloric diet with the development of MS allows in experimental studies to simulate MS in animals using diet. Such studies allow us to understand the causes of the development and progression of MS, as well as to identify potential methods for its prevention and treatment [8].

Features of pathogenesis of MS suggest that effective for correction is restorative medicine with the use of non-medication, that is, the correction of the constituent mechanisms of MS with the help of natural healing resources, which include MW [9, 10, 11].

MW influence carbohydrate metabolism by increasing the activity of glycolytic processes and normalizing the breakdown of carbohydrates to the end products of metabolism. This is due to the influence of MW on the synthesis and accumulation in tissues of adenosine triphosphoric acid. In addition, the intake of MW in violation of glucose tolerance, increasing the activity of carboxylase, normalizes the decarboxylation of pyruvic acid, which contributes to the complete combustion of intermediate products metabolism. MW have an inhibitory effect on the processes of gluconeogenesis by suppressing the action of glucocorticoid hormones [12].

The authors show that some MW stimulate the secretion of gastrointestinal hormones, including insulin [13]. Under the influence of MW, there is an increase in the sensitivity (sensory) of insulin receptors, which ensures optimization of the course of metabolic processes and, as a consequence, prevention of the formation of diabetes, atherosclerosis, coronary heart disease, obesity, hypertension, etc. [14, 15].

Experimental studies have shown that MW of low mineralization have a powerful diuretic effect, which ensures the rapid elimination of the body from toxic metabolites that accumulate upon disruption of carbohydrate metabolism [16, 17]. In the available literature, no evidence was found regarding the effect of sodium chloride mineral waters on kidney function in laboratory animals against the background of metabolic syndrome development.

Based on the above, the purpose of the work is to evaluate the effect of the internal use of low-mineralized sodium chloride mineral water on the impairment of the functional state of the rat kidney with a model of metabolic syndrome.

**Materials and methods of research.** Experimental studies were conducted on 34 white male Wistar rats of a self-bred breeding body with a weight of 280.0-320.0 g. Animals were handled in accordance with existing legal documents [18].

Animals were ranked in three groups. And the group consisted of 10 intact animals. Group II - 12 animals with MS model; Group II - 12 animals, which in the background of the development of the MS model internally received a course of loading with CF. The MS model in animals was reproduced for 72 days. Rats received an additional 30 g of white rusks per animal per standard diet and consumed only 10% distilled water fructose solution in free-range drinking mode. CF of the animal was obtained against the development of MS (from the 60th to the 72nd experiment). The CF was injected into the esophagus

by a soft probe with olive once a day, at a dose of 1% by weight of the animal in the evening, taking into account features of daily rhythm of rats.

In the study, mineral water was used which by its physicochemical composition was classified as slightly mineralized sodium chloride without specific components and properties, slightly alkaline. The total mineralization is 2.20g/l, the content of chloride ions is 950.3mg/l, the content of ions of sodium and potassium is 732.0 mg/l.

The functional state of the kidneys was evaluated by the influence on the function of the urinary tract (glomerular filtration rate, tubular reabsorption, diuresis), excretory function (by the excretion of creatinine, urea and chlorides). Ion-regulating function (by concentration and daily excretion of sodium, potassium and chloride ions) was investigated. Determined the acid-alkaline reaction of daily urine in terms of the concentration of hydrogen ions.

Morphological studies have determined changes in the structure of kidney tissues before and after CF. To do this, after removing the animals from the experiment under ether anesthesia, the kidney pieces were removed, which were fixed with 4% paraformaldehyde, carried out with high strength alcohol and poured into the celloidin. From the blocks made sections, which were stained by review methods hematoxylin-eosin. The data obtained were compared with similar indicators of intact rats (control group).

Methods and techniques used in the research are published in the "Guide" and guidelines [19, 20]. Statistical processing of the data obtained in the series of experiments was performed using the programs of biomedical studies Statistica and Exel. With all means of processing statistical material, those within the range of the Student's tables were considered to be significant shifts less than  $<0.05$ .

## Results and discussion

Studies have shown that MS is accompanied by changes in kidney function. Table 1 shows the data on the functional status of the kidneys of rats with MS model and rats with MS model, who received a course in CF.

Table 1. Functional state of the kidneys with the MS model and the MS model rat and the CF course

Indicators	Group control	Group of model MS	Group of MS model and CF course
Daily diuresis, ml/dm <sup>2</sup> of body surface	100	63*	115*
Speed glomerular filtration, ml/(dm <sup>2</sup> × min)	100	78*	120*
Tubular reabsorption, percentage to filter, %	100	100,16*	100
Creatinine excretion, mmol	100	78*	120*
Urea excretion, mmol	100	85*	132*
pH of daily urine, unit	100	133*	99
The concentration of potassium ions daily urine, mmol	100	211*	125*
Daily excretion of potassium ions, mmol	100	114*	150*
Concentration of sodium ions daily urine, mmol/l	100	234*	418*
Daily excretion of sodium ions, mmol	100	138*	266*
Concentration of chloride ions per day, mmol/l	100	88*	64*
Daily excretion of chloride ions, mmol	100	44*	90

**Notes:** For 100% accepted data control group animals; \* - the significance of the changes calculated from the control group ( $p < 0.05$ ).

The development of MS in rats is accompanied by a decrease in the activity of urinary processes. Daily diuresis volume decreased by 37% ( $p < 0.001$ ) due to

a decrease in glomerular filtration rate (GFR) - by 22% ( $p < 0.01$ ) and an increase in the percentage of tubular reabsorption by 0.16% ( $p < 0.001$ ). A decrease in the daily excretion of nitrogen metabolites has been established: creatine excretion is decreased by 22% ( $p < 0.001$ ) and urea excretion is decreased by 15% ( $p < 0.001$ ). The pH of the daily urine is compounded (its value increases by 33%). The concentration of potassium and sodium ions in the urine increases by 111% and 134%, respectively, and their excretion increases by 14% and 38%, respectively. However, the concentration of chloride ions is reduced by 12%, and their excretion - by 56%. It can be considered that a delay in the body of rats with the MS model of chloride ions contributes to the retention of water in the body and reduce the volume of diuresis daily.

That is, the kidneys excrete a somewhat hyperosmotic urine in a small amount. The use of sodium chloride MV in animals with MS leads to stimulation of urinary and excretory function of the kidneys: the volume of diuresis increases by 15% ( $p < 0,05$ ) due to the acceleration of GFR - by 20% ( $p < 0,01$ ) and decrease to the level of control of the value of tubular reabsorption ( $p > 0,5$ ). A significant increase in creatinine excretion by -20% ( $p < 0.01$ ) and urea by 32% was found. The excretion of potassium and sodium ions increases by 50% and 166%, respectively. The excretion of chloride ions and urine pH is restored and does not differ from that of the control group ( $p > 0.5$ ).

Microscopic studies of the rat kidney with a model of metabolic syndrome have established: kidney calves are characterized by the presence of vacuoles and edema in the cytoplasm of endothelial cells, the nuclei are medium, homogeneous dark colored. Bowman's space of the renal corpuscles punctate, the interstitium between the tubules swollen with the presence of lymphocytes; hyaline cylinders are observed in the inferior tubules, and some of them have a significant (up to lacuna) extension, some tubules with disordered epithelium. That is, there were signs of kidney dystrophy with impaired water-ion balance.

In rats that received CF in the background of MS development, microscopically determined positive changes, namely: part of the vast majority of nephrons without visual changes, in the epithelium part of the glomeruli - vacuoles. Irregular tubules without visual changes, interstitial layers with edema and the presence of single histocytes. Therefore, residual manifestations of dystrophic processes in kidney tissues and incomplete restoration of the water-ion balance are observed.

## **CONCLUSIONS**

Thus, the internal course use of low-mineralized sodium chloride water in rats with a model of metabolic syndrome has a restorative effect on the urinary function of the kidneys (the daily diuresis volume and tubular reabsorption on the background of GFR stimulation are fully restored). The excretory and ion-regulating functions of the kidneys are restored and stimulated in the form of increased excretion of creatinine, urea, potassium ions, sodium and decreased excretion of chloride ions. The established changes are caused by positive changes in the kidney parenchyma, which according to microscopic studies, consist of normalization of the structure of capillary bodies and most of the tortuous tubules.

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