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Structural and functional changes in the kidneys of rats with toxic nephropathy after a course of drinking mineral water «DONAT Mg»

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Abstract

Kidney disease of various etiologies affects 6-7% of the total population of the globe. Glomerulonephritis and nephropathy of various etiologies make up a significant part of these kidney lesions. Infectious and non-infectious glomerulonephritis and nephropathy are distinguished, the latter are associated with the influence of environmental factors, including toxic substances, heavy metals and even medications.

Magnesium is considered one of the components of the body's stress-limiting system, since all its effects are aimed at reducing the manifestations of stress and normalizing adaptation processes.

A comparative assessment of changes in the kidneys during the simulation of toxic nephropathy and the influence of magnesium-containing agents on the course of the pathology of the experimental model was carried out.

Key words: toxic nephropathy; kidney disease; glomerulonephritis; mineral water «Donat Mg»

Kidney disease of various etiologies affects 6-7% of the total population of the globe [1]. Glomerulonephritis and nephropathy of various etiologies make up a significant part of these kidney lesions. Infectious and non-infectious glomerulonephritis and nephropathy are distinguished, the latter are associated with the influence of environmental factors, including toxic substances, heavy metals and even medications [2, 3].

In addition to damage to the glomeruli, atrophic and dystrophic changes in the epithelium of the convoluted and straight tubules are considered to be an important mechanism of kidney dysfunction. Changes in tubules are associated both with the direct action of nephrotoxics and with hyperfiltration due to damage to part of the glomeruli and the need to preserve the homeostatic parameters of the body (excretion of toxic metabolites). Hyperfiltration causes increased intensity of reabsorption in the tubule epithelium, overloading of epitheliocytes with protein and other substances. Thanks to hyperfiltration, ions that are part of the group of basic elements can be removed from the body, which causes adverse changes in homeostasis and the implementation of metabolic processes. Such rearrangements contribute to the disruption of the activity of regulatory systems and the strengthening of nitrogenous and protein exchanges, which leads to the load and damage to the activity of the body's functional systems, including regulatory ones. As a result, there is further damage to endotheliocytes in the capillaries of the renal corpuscles and intratissue capillaries; structural changes of epitheliocytes and mesangial cells; accumulation of extracellular matrix and deposition of hyaline. Such changes in the kidney tissue determine the progression and increase in damage to kidney function. It is logical to assume that significant changes will occur in the ion-regulating function of the kidneys.

Since metal ions are an important part of the active centers of enzyme molecules, disruption of ion homeostasis leads to changes in enzyme activity. The combination of changes in the activity of enzyme systems in cells and changes in the activity of the vascular system become the basis for further structural and functional damage to the tissue elements of the nephron. Among the ions that are included in the group of basic elements of body tissues, magnesium occupies the fourth position. Its total amount in the human body is from 850 mmol to 1100 mmol. Most of the magnesium is in the muscles, bone marrow, liver and, what is especially important, in the kidneys [4]. The concentration of magnesium in the blood is regulated by the balance between its intestinal absorption and renal excretion [5, 6].

Magnesium performs important functions as an activator of enzymes - cholinesterase, phosphoglucomutase, pyrophosphatase, arginase, carboxylase, dehydrogenase. In addition, magnesium affects the normal functioning of ATP-ases, which ensure the functioning of

transmembrane pumps of ions and substrates. Being in complexes with ATP, magnesium ions ensure the release of energy through the activity of magnesium-dependent ATPases and are necessary for all energy processes in the body. As a cofactor of the pyruvate dehydrogenase complex, magnesium ions ensure the flow of glycolysis products to the Krebs cycle and prevent the accumulation of lactate. Enzymes activated by magnesium are involved in the synthesis and catabolism of proteins, nucleic acids, and mitochondria. Magnesium plays an important role in the energy supply of nerve tissue. It is one of the main elements that maintains the balance of excitation/inhibition processes. Magnesium is considered one of the components of the body's stress-limiting system, since all its effects are aimed at reducing the manifestations of stress and normalizing adaptation processes [7]. It has been proven that magnesium takes an active part in the synthesis of melatonin, which is called the central hormone of adaptation. The effect of magnesium on the regulation of the function of organs and body systems is due to the interaction of magnesium with macro- and microelements. Homeostasis of magnesium in the body is a prerequisite for human health. A decrease in magnesium content in the body is associated with environmental, geographic, nutritional factors, and pathological processes in the body. As a result of the decrease in magnesium content in the body, the concentration of triglycerides in the blood increases, cholesterol esterification decreases, calcium homeostasis and the operation of the magnesium-calcium pump are disturbed. All this contributes to the development of pathological shifts in the contractile activity of smooth muscle fibers. That is, a previous violation of magnesium metabolism can affect the course of kidney pathology, we investigated this in this work [8-10].

A comparative assessment of changes in the kidneys during the simulation of toxic nephropathy and the influence of magnesium-containing agents on the course of the pathology of the experimental model was carried out. It should be noted that the choice of the experimental model was based on the predominant damage to the tubular part of the nephron.

First of all, it should be noted that the use of magnesium-containing products had a unidirectional positive effect on the appearance of the kidneys. They, in contrast to the group of rats with uncorrected toxic nephropathy, acquired sizes corresponding to control animals - 17 mm right and 16 mm left (with uncorrected nephritis, the length of the kidneys was 21-19 mm). The color of the kidney was restored from grayish-brown to brown.

Microscopic studies have determined a moderate positive effect of the applied magnesium-containing products.

The use of magnesium-containing products leads to a significant improvement in the indicators of the functional activity of the central nervous system. At the same time, a 5% bischofite solution has a somewhat greater positive effect. The difference between it and "Donat Mg" is not radical, but has the degree of a stable trend. It should also be noted the greater intensity of motor activity of rats that received a 5% solution of bischofite, which, in our opinion, is connected with the superiority of the excitation processes due to the effect of magnesium directly on the functional state of neurons, the increased supply of Mg^{2+} to the body. The emotional state of rats treated with Mg^{2+} remains close to the data of control animals, although 5% bischofite shows a direct inhibitory effect on this side of the central nervous system. Approaching the number of urinations to control indicators, most likely, indicates the improvement of kidney function, and not the effect of drugs on the state of activity of the central nervous system.

The development of toxic nephropathy leads to a threefold increase in daily diuresis due to a twofold increase in glomerular filtration and a significant decrease in tubular reabsorption (table). Changes in urine production were accompanied by an increase in the excretory function of the kidneys - the content of creatinine in daily urine increased by almost 1.5 times and urea by 2.5 times. The acid-alkaline state of urine became more individual, as its average value remained close to the norm, but the error of the average increased. Violation of the ion exchange function was determined by an increase in the concentration and excretion of Na^+ , K^+ , Cl^- , and a 1.5-fold increase in the concentration and excretion of Mg^{2+} should be noted.

The use of magnesium-containing products in experimental rats did not change the direction of kidney function disorders, but mitigated the degree of these changes. That is, complete recovery did not occur.

The volume of daily diuresis increased, but its rise by 30% - 40% was less than with uncorrected nephropathy. The use of 5% bischofite reduced daily diuresis to a greater extent. Changes in this indicator when using MV "Donat Mg" are associated with a decrease in GFR, and when using 5% bischofite - with an increase in the percentage of tubular reabsorption almost to the norm.

Table - Effect of magnesium-containing products on kidney function in rats with toxic nephropathy

number	Control group (intact rats)	Group with kidney pathology	Group with kidney pathology and «Donat Mg»
Volume of daily diuresis, ml/dm ²	1,03 ± 0,09	3,81 ± 0,12*	2,74 ± 0,05**
GFR, ml/(dm ² ×min)	0,04 ± 0,004	0,08 ± 0,002*	0,07 ± 0,001**
Tubular reabsorption, %	98,16 ± 0,11	88,50 ± 0,04*	95,64±0,075**
Creatinine excretion, µmol	0,004±0,0004	0,006±0,0001*	0,017±0,008**
Excretion of urea, µmol	9,44 ± 0,54	23,47 ± 0,49*	14,6 ± 0,47**
pH of urine, units pH	6,65 ± 0,48	6,39 ± 0,05	7,01 ± 0,09
Mg ²⁺ concentration, mmol/l	3,39 ± 0,02	4,15 ± 0,04*	3,65 ± 0,03
Excretion of Mg ²⁺ , µmol	0,033± 0,0003	0,047± 0,0002*	0,008±0,0004*
Concentration of K ⁺ in urine, µmol/l	172,49 ± 33,1	76,0 ± 1,61*	111,25± 8,12**
Daily excretion of K ⁺ , µmol	0,15 ± 0,02	0,42 ± 0,03*	0,29 ± 0,008**
Na ⁺ concentration, mmol/l	37,13 ± 3,80	122,64 ± 4,55*	81,76 ± 4,17**
Daily excretion of Na ⁺ , mmol	0,30 ± 0,04	0,84 ± 0,09*	0,46 ± 0,02**
Cl ⁻ concentration, mmol/l	290,05±6,47	171,30 ± 0,34*	159,33± 0,19**
Daily excretion of Cl ⁻ , mmol	0,24 ± 0,04	0,64 ± 0,01*	0,53 ± 0,04**

Notes:

* probably relative to the control group (p < 0.05);

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- the data of the control group of animals are taken as 100%.

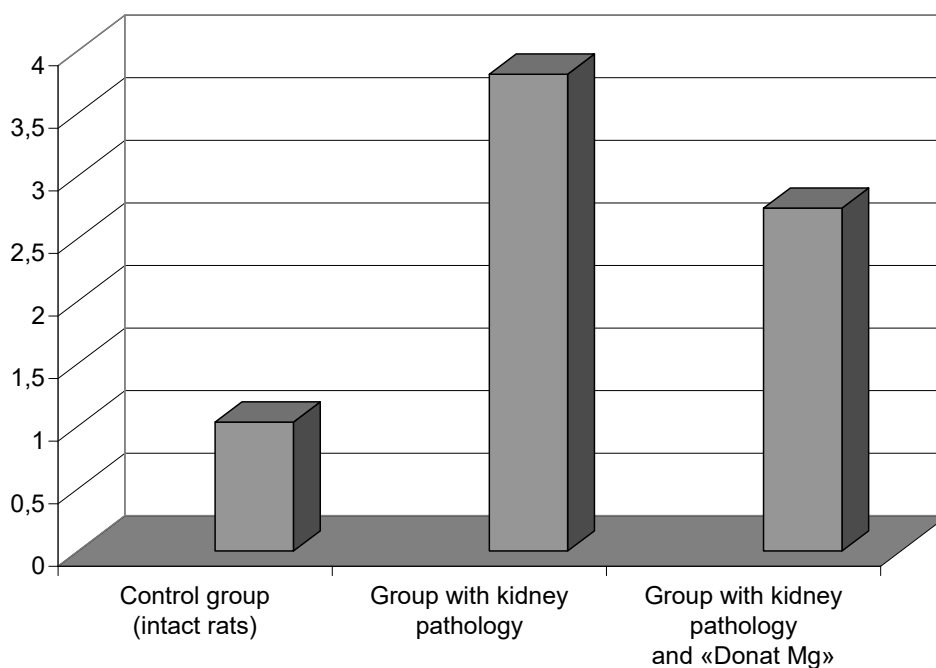


Fig. Volume of daily diuresis, ml/dm²

The excretory function of the kidneys improves significantly, which is evidenced by a decrease in the content of creatinine and urea in the urine. It should be noted that the use of MV "Donat Mg" brings the creatinine content almost to normal, and the urea content decreases, but does not normalize. At the same time, the use of 5% bischofite solution leads to a decrease in the creatinine content below the norm, and the urea content remains significantly higher than the norm. That is, when using magnesium-containing products with different chemical composition, there is an imbalance in the elimination of the final metabolites of nitrogen metabolism. The acid-alkaline state of urine when using 5% bischofite remains at the normal level, and when using "Donat Mg" it shifts to the alkaline side.

As for the ion exchange function of the kidneys, the use of magnesium-containing products leads to a decrease in the concentration and excretion of the studied ions. At the same time, there is a difference in the effect of the studied drugs. When using "Donat Mg", the content of K⁺ increases compared to uncorrected glomerulonephritis by 46%, and when using 5% bischofite - almost twice, approaching the control values. Daily excretion of K⁺ decreases by 30% in the first case and practically does not change under the influence of bischofite.

The concentration of Na⁺ in urine decreases with the use of the studied drugs. At the same time, 5% bischofite almost normalizes this indicator. Urinary excretion of this ion also decreases. It should be noted that this decrease was greater with the use of MV "Donat Mg".

The change in the concentration and excretion of Cl⁻ ions is less significant, but under the influence of bischofite, the excretion of chlorine ions (which was significantly increased in rats with pathology) is restored to the control level.

Exogenous Mg²⁺ contributes to a decrease in the concentration of this ion in urine, but this decrease is insignificant. At the same time, Mg²⁺ excretion significantly decreases under the influence of "Donat Mg" and to a lesser extent - under the influence of 5% bischofite. That is, the additional intake of magnesium reduces its excretion from the body, which can be explained only by the normalization of ion reabsorption in the tubules.

The above data indicate the essential role of magnesium in the normalization of kidney function against the background of incomplete restoration of their structure, but its more effective effect is manifested in the presence of other macroions included in magnesium-containing preparations.

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