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The influence of magnesium preparations on the change in metabolism in the modeling of toxic nephropathy in animals

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Abstract

In an experiment on 39 white Wistar rats of autobred breeding, the authors modeled toxic nephropathy and assessed the possibility of correcting damage using magnesium-containing preparations - 5% Bischofite solution and «Donat Mg». The work was carried out in accordance with the regulatory documents of the European Union and Ukraine.

The results of the studies showed that in addition to damage to the structure of the kidneys: wrinkling of capillary glomeruli, expansion of the Bowman space, destruction of part of the convoluted tubules; there is a violation of metabolic processes in the form of: an increase in the total blood protein, a redistribution of the proportion of different proteins in its composition, a decrease and imbalance of ATPases; increase in fasting amount of glucose; activation of lipid peroxidation and inactivation of AOD (catalase); decrease in magnesium levels in the blood. The use of magnesium-containing preparations by animals - a 5% solution of bischofite or «Donat Mg» had a unidirectional positive effect on the condition of the experimental animals. The structure of the kidneys improved, because. there were fewer wrinkled glomeruli, there were no lymphocytes between the capillaries, visually less damaged

tubules were recorded; the interstitial layers did not differ from the norm; in terms of metabolism, there was a closeness of the total protein and the nomenclature of its components to the control, less changes in the activity of ATPases; LPO/AOZ systems; changes in fasting glucose, similarity of Mg⁺² content to control data.

The authors believe that the intake of exogenous Mg⁺² has a positive effect on the state of redox processes in the cells of the body, which helps to maintain the body's resistance at a higher level and prevents severe kidney damage.

Key words: toxic nephropathy; magnesium; metabolism; bischofite; «Donat Mg».

Kidney diseases of various etiologies are observed in 1.5-2.0% of the human population, which is approximately 6% of the total incidence [1]. Kidney diseases are accompanied by loss of kidney function, the morphological substrate of which is dystrophic and atrophic processes in the epithelium of the tubules, renal corpuscles, and interstitial sclerosis [2]. Since atrophic and dystrophic processes are closely related to disturbances in metabolic processes, it is of interest to participate in the damage to the renal function of the main ions that make up the tissues and body fluids. One of the main cations of the human body is magnesium. In the human body, its content is 25 g, i.e. it ranks fourth among body cations and second among cell cations [3]. A feature of the intake of magnesium in the body is that it is absorbed mainly due to ion diffusion without the participation of cellular ion pumps and membrane transport proteins [4] and is regulated by parathyroid hormone. The excretion of magnesium from the body is about 2 g, more than 100 mg of which are excreted in the secondary urine. At the same time, a significant part of it (60-70%) is reabsorbed in the ascending part of the loop of Henle [5, 6]. Damage to the kidneys during the development of renal pathology causes the excretion of up to 70% of filtered magnesium, which changes the concentration of magnesium in the blood plasma [5, 6], which is the main physiological regulator of its excretion in the urine.

The biological role of magnesium is diverse: it is involved in the regulation of the balance of intracellular potassium, tk. it is magnesium ions that ensure the normal functioning of the Na⁺-K⁺ ATP-membrane pump [8]. Magnesium is actively involved in the activity of the central nervous system, because. is a part of receptor formations, regulates the activity of enzymes of carbohydrate metabolism - the main way of energy production, not only for the nervous system, but also for the tissues of the whole organism [11-14]. First of all, it is the active center of enzymes for the oxidation and phosphorylation of ATPases and enzymes for the metabolism of creatine phosphate (ensuring the activity of the muscular system).

Based on the foregoing, it should be expected that the loss of magnesium in the urine in patients with renal pathology will create difficulties in the activity of the functional systems of the body, which exacerbates the negative consequences of impaired renal function.

However, in the available literature, we did not find data on the specific consequences for the metabolic processes of the body of the loss of magnesium by kidneys damaged in toxic nephritis and the possibility of correcting these disorders with magnesium preparations.

Purpose of the work: to evaluate metabolic disorders in toxic nephritis and the possibility of their correction with magnesium-containing drugs.

Materials and methods of research

The material of this work was the data obtained in the study of 39 white rats of the Wistar line of autobred breeding weighing 200-210 g. The maintenance and work with animals was carried out in accordance with the requirements of the Directive of the European Parliament and Council 2010/63/EU and the Order of the Ministry of Education and Science, Youth and Sports dated March 1, 2012, No. 249 "Approval of the procedure for the implementation by scientific institutions of experiments in experiments on animals.

Animals in accordance with the objectives of the research were ranked into 4 groups:

Group I - 9 animals that were kept in vivarium conditions, were not affected, the results and studies of them were used as controls.

Group II - 10 animals in which toxic nephritis was modeled by a single subcutaneous injection of 1 ml of a mixture of 1 ml of a 50% aqueous solution of glycerol and 1 ml of uranyl acetate.

Group III - 10 animals that received a 5% solution of Poltava bischofite in the free drinking mode against the background of a model of toxic nephritis.

Group IV - 10 animals, which, against the background of toxic nephritis, received «Donat Mg» in the free drinking regimen.

The duration of the experiment was 7 days. At the end of the experiment, the animals were taken out of the experiment by decapitation. During autopsy, a part of the kidneys, a piece of the liver and 5 ml of blood were removed. The removed pieces of kidneys were used for histological studies. The blood taken from animals was used for biochemical studies. The following indicators were evaluated: the content of total protein, albumin and globulins. The activities of Na⁺/K⁺ and Mg⁺²/Ca⁺² ATPases were evaluated on the liver component. The amount of mylonialdehyde (MDA) and catalase activity were also determined in the blood, which showed the state of the LPO/DOZ system; the amount of creatinine and urea, as well as

the amount of magnesium in the blood serum. The data obtained were subjected to standard statistical processing using the Student's coefficient of reliability and tabulated.

Research results

Histological studies of animals of the second group with enlarged kidneys revealed changes characteristic of toxic nephropathy: expansion of the bowline space; paucity of capillary glomeruli; the appearance of vacuoles in the cytoplasm of endotheliocytes; lymphoid infiltration in the glomeruli and around the renal corpuscles; replacement of part of the convoluted tubules with a mixture of a homogeneous eosanophilic substance and epitheliocyte residues; plethora (stagnant) intrarenal vessels; swelling of the epithelial cells of the medulla. Violation of the structure of the tubules was accompanied by changes in the parameters of the studied metabolic processes. The results of their study are shown in Table 1.

Table 1 - Effect of preparations containing magnesium on metabolic parameters in rats with symptoms of toxic nephritis

Groups Indicators	Control	toxic nephritis	toxic nephritis + "Donat Mg +2"	toxic nephritis + 5 % bischofite
Total protein, g/l	67,7 ± 2,74	73,02 ± 1,25	68,66 ± 1,16	70,68 ± 1,36
Albumin, g/l	25,8 ± 1,88	19,90 ± 1,93	23,16 ± 0,78	21,87 ± 1,60
α-1 globulin, g/l	8,28 ± 0,86	14,39 ± 1,63	13,16 ± 0,98	10,14 ± 1,25
α-2 globulin, g/l	10,70 ± 2,20	9,06 ± 0,68	8,01 ± 1,39	9,66 ± 0,49
β-globulin, g/l	11,82 ± 1,79	16,33 ± 1,16	14,08 ± 1,05	17,01 ± 1,57
-globulin, g/l	11,10 ± 0,73	13,34 ± 1,06	12,01 ± 1,09	17,01 ± 1,57
Glucose, mmol/l	4,98 ± 0,22	7,03 ± 0,41	6,05 ± 0,33	5,83 ± 0,30
MDA (POL), mmol/l	5,94 ± 0,21	7,87 ± 0,45	6,43 ± 0,23	6,54 ± 0,33
AOZ (catalase), %	76,7 ± 1,52	60,52 ± 1,46	68,67 ± 1,04	69,6 ± 1,40
Creatinine μmol/l	47,8 ± 0,63	67,10 ± 1,51	57,6 ± 1,20	60,39 ± 0,56
Urea, mmol/l	2,80 ± 0,27	5,80 ± 0,33	4,30 ± 0,30	3,48 ± 0,30
Mg ⁺² /Ca ⁺² - ATPase, mgP/g	9,11 ± 0,93	6,87 ± 0,54	7,85 ± 0,44	7,57 ± 0,70
Na ⁺ /K ⁺ - ATPase, mg P/g	6,40 ± 0,62	3,22 ± 0,45	4,83 ± 0,47	4,65 ± 0,39
serum magnesium, μmol/l	2304 ± 109	1844 ± 175	2083 ± 132	2034 ± 122

According to the data shown in Table 1, the development of toxic nephritis is accompanied by a tendency to increase the protein content in blood plasma. This may be due

to increased fluid loss due to increased diuresis. At the same time, the proportion of different proteins in their nomenclature changes: the proportion of albumins and α -2-globulins decreases and the proportion of other studied proteins increases, which may be due to the presence of auxiliary reactions. Changes also affect carbohydrate metabolism, as evidenced by an increase in blood glucose. There is also a violation of the metabolism of nitrogenous compounds and creatinine with a predominance of catabolism processes, tk. the content of creatinine and urea in plasma increases. Although it is impossible to exclude the connection of changes in these indicators with the state of the excretory function of the kidneys in animals with toxic nephritis. On the part of the LPO/AOZ system, an increase in the content of MDA is observed, i.e. activation of lipid peroxidation, catalase activity significantly decreases, i.e. antioxidant protection of cell membranes weakens. The revealed changes in metabolic parameters are obviously associated with impaired magnesium metabolism. Its content in the blood significantly decreases and simultaneously the activity of both studied ATP-ases decreases, in addition, the ratio of the activity of these enzymes changes. To a greater extent, the activity of $\text{Na}^+ / \text{K}^+ - \text{ATP-ase}$, which provides the Na^+ / K^+ energy pump, is weakened, and, consequently, all vital processes in the cell associated with K^+ are disrupted. The revealed changes in metabolism are systemic in nature and can adversely affect the functional activity of the kidneys.

The use of magnesium-containing preparations (with different content of Mg^{+2}) in animals has a positive effect on the histological picture of the kidneys. At the same time, it should be noted that their influence is unidirectional. First of all, it should be noted the improvement of blood circulation in the kidneys, plasmastasis is not determined, although increased blood supply remains. The appearance of capillary glomeruli improves - most of them retain a rounded shape, and Bowman's spaces are close to slit-like. Also, a large number of renal corpuscles have an outer membrane of the usual type. Also, a significant part of the convoluted tubules in animals that received magnesium-containing drugs had a normal structure. It should be noted that damaged tubules in animals of these groups (received exogenous Mg^{+2}) are preserved: there are tubules protected by eosinophilic masses and accumulations of epitheliocytes; tubules with preserved epithelial lining, in the gaps filled with eosinophilic masses. Visually changed tubules are somewhat less than with uncorrected nephritis. The histological picture of the kidneys is very similar when using «Donat Mg» or 5% bischofite solution.

Positive changes were also revealed when assessing the state of metabolic processes. First of all, it should be noted that the content of magnesium in the blood plasma with the

introduction of exogenous magnesium differed little from the norm. These differences were less significant when using «Donat Mg». The content of total protein also remained close to normal. At the same time, the content of most types of proteins that make up the "total plasma protein" also remained close to normal. The exception was β -globulins, the content of which increased with the use of a 5% solution of bischofite. Preservation of the quantity and nomenclature of proteins is possibly associated with a decrease in the loss of fluid and protein due to the positive effect of magnesium-containing drugs on the structure of the kidneys.

The state of carbohydrate metabolism improved, as evidenced by the normalization of the glucose content when using a 5% solution of bischofite and its significant decrease in comparison with uncorrected toxic nephritis. The revealed difference in the action of the compounds used is most likely due to the difference in the amount of $Mg + 2$ in them and the difference in the components of these drugs. On the part of the LPO/AOZ system, there is a decrease in the content of MDA and the approach of this indicator to the norm, as well as an increase in catalase activity. At the same time, the decrease in the content of MDA is more pronounced with the use of Donat Magnesium, and the activity of catalase is more pronounced with the use of a 5% solution of bischofite.

The activity of ATPases also increased with the use of magnesium preparations. At the same time, the activity of $Na + / K + - ATPase$ increased by 50%, and $Mg + 2 / Ca + 2 ATPase$ - by 15%. Although this indicator did not reach the normal value, its increase obviously contributed to the restoration or increase in the energy supply of trinembrane ion transport, which had a positive effect on intracellular metabolic processes.

Thus, the results of our studies have shown that exogenous magnesium entering the body of an animal with toxic nephritis normalizes its plasma content and positively affects the energy supply of vital processes. This improves the structural and functional characteristics of the renal parenchyma and the course of metabolic processes in the body.

References

1. Pathophysiology. P/r M.N. Zaiko, Yu.V. Biul, M.V. Kreshtal. - 6 types. rework and added. - K. : VSV "Medicine". - 2017. - 736s.
2. Nephrology: national guidelines. P/r N.A. Mukhin. – M.; GEOTAR. Moscow. - 2009. - 720 p.
3. S.A. Golovanov - Can magnesium preparations reduce the risk of recurrence of urolithiasis? / S.A. Golovanov, A.V. Sivkov // Experimental and clinical urology. - 2011. - No. 4. - S. 28-32.

4. Slatopolsky E. – Homiostasis of phosphate and iotheer minerals./ Slatopolsky E., Massry S., Ritz E., Papado A. al. – 1978. - № 9. – Plenum pres. – p. 473-479.
5. Quamme Y.A. – Renal magnesium handling: new insights in understanding old problem // *Kindeg Int.* 1997. – Vol. 52, № 5. – p 1180-1195.
6. al-Ghandi S.M. Magnesium deficiency: pathophysiologic and clinical overview. / S.M. al-Ghandi, E.C. Cameron, R.A. Siutton // *Am. J. Kidney Dis.*, 1994. – Vol. 24. – № 5. – p. 737-752.
7. Whang. R. – Refractory potassium replation. A consequence of magnesium deficiency / R. Whang, D.D. Whang, M.P. Ryan // *Arch. Intern. Med.* – 1992. –Vol. 152 (1) – p. 40-45.
8. Takaya J. – Intracellular magnesium and insulin resistance. / J. Takaya, H. Higashino, Y. Kolayoshi // *Magnes. Res.* – 2004. Vol. 17. – p. 126-136.
9. Instruction 2010/63/EU of European Parliament and Council on animals used research and other purposes protection // *Official Journal.* – 2010. – V. 276. p. 33-79.
10. Order of the Ministry of Education and Science, Youth and Sports of Ukraine No. 249 dated 01.03.2012. – *Official Bulletin of Ukraine* dated 04/06/2012. - 2012, No. 24, p. 82, article 942, act code 60909.
11. Pavliuk N. N., Gushcha S. G., Badiuk N. S. The effect of changes in magnesium metabolism on the structural and functional state of the kidneys during stress-induced endogenous intoxication. / *Actual problems of transport medicine* / 2020;3(61):120-126.
12. Pavlyuk N. M., Badyuk N. S., Vasyuk V. L. Influence of magnesium-containing compounds on the function of kidney rates with the model of toxic glomerulonephritis // *Bulletin of Marine Medicine.* 2020. №4 (89). – P. 116-119
13. Pavlyuk N. M., Badiuk N. S., Gushcha S. G. The state of the functional activity of the central nervous system and peripheral blood and the possibility of correcting their disorders with magnesium preparations // *Actual problems of transport medicine* / 2021;1(63):113-120.
14. Pavlyuk N. M., Badiuk N. S., Gushcha S. G. Comparative evaluation of the effect of magnesium-containing preparations of different chemical composition on kidney function in animals with experimental toxic glomerulonephritis // *Bulletin of Marine Medicine.* 2021. №1 (90)., 68-73.