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Pathogenetic and Sanogenetic Mechanisms of the Influence of Mineral Waters (Siliconed and with Increased Organic Substances) of Different Osmularity on the Exposure of Toxic Nephritis

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ABSTRACT

In white rats, on the background of the development of toxic kidney damage, polyuria was established, an increase in daily excretion of creatinine and urea, a significant loss of chloride ions. In order to correct the development of pathology were used 3 weakly mineralized mineral waters (MW) with the content of biologically active substances: 2 silicon MW and 1 MW with high content of organic substances. Investigation of the functional state of the kidneys (volume of diuretic daily, glomerular filtration rate, tubular reabsorption percentage, creatinine excretion, urea and chloride ions) was performed at the 8th day of the experiment. MW with a higher osmolality and the content of metasilicic acid has a more pronounced restorative effect on the urine-forming function of the kidneys and the removal of chloride ions. MW with high content of organic substances has a slow corrective effect on renal dysfunction.

Keywords: *rats, experimental nephritis, functional state of the kidneys, mineral water;*

INTRODUCTION

At the present stage of the development of medicine for the complex treatment of kidney diseases, along with medicaments, non-medicated methods of treatment are increasingly being used, in particular, natural medical resources - mineral waters (MW), peloids, clays, etc. It was the MW that became widely used in medical practice due to the possibility of their long-term use, the combination of their general non-specific action on the processes of sanogenesis of the organism with an effect on local pathogenetic mechanisms [1]. Improvement of the effectiveness of the development of treatment methods is achieved by conducting preclinical studies in experimental animals with reproduction of the appropriate pathological model in them, which allows us to determine the presence or absence of therapeutic properties of the applied MW. A special place among the MWs used in nephrology is a group of weakly mineralized waters with high content of biologically active components and compounds, which include silicon, organic matter, hydrogen sulfide, and others. The MW of weak mineralization (up to 1 g / l) in some cases is effective to a greater extent than water of high mineralization. Under the influence of such MW, the metabolism of tissues were stimulated, components of the MW are included in the composition of hormones, enzymes, vitamins, and metabolites [2, 3].

It should be noted that, in spite of some success, so far, many questions regarding the biological role of such active components remain unexplored [4]. For example, silicon is an important (essential) for life microelement. Taking into account the prevalence and number of silicon in nature and human body, it is recognized that it should play an important role in the health of humans and animals [5]. In this aspect, attention is drawn to the experimental data of authors, which are established when rats are kept on a diet depleted on silicon. It has been determined that a decrease in the concentration of silicon in the blood correlates with a decrease in its urinary excretion, indicating the active involvement of the kidneys in regulating the balance of silicon in the body (presumably due to its renal reabsorption) [6]. In addition,

experimental work on the study of the influence of weakly mineralized MW with a different concentration of metasilicate acid has been shown to have a significant stimulating effect on the urinary processes in the body of healthy white rats, which was determined by an increase in daily diuresis on average by 300-550%, to a large extent, due to acceleration the velocity of glomerular filtration (VGF), and to a lesser extent - by reducing the percentage of tubular reabsorption [7]. In other works was investigated the effect of weakly mineralized waters with high content of organic on the functional state of the kidneys of healthy animals and it is determined that under their influence the volume of daily diuresis increases by an average of 180 - 220% [8]. Experimental and clinical trials have shown the diuretic action of this type of MW and therapeutic properties in urological diseases [3]. High biological activity of the MW of this type is associated with organic substances, which include low molecular weight fatty acids, amino-like substances, organic acids and phenolic acids, phenols, bitumen and humic substances. Recently, there has been a growing interest among many specialists in various fields regarding the study of water-soluble humic substances, as safe, biologically active and promising substances in the context of green chemistry and biotechnology [9]. Attention is also drawn to the definite role of autochthonous microflora (microbiota) in both the creation and assimilation of organic components in MW, which also affects the biological activity of MW [10, 11].

Taking into account the above, the purpose of the work is to study the correction of toxic changes in the functional state of kidneys of rats with experimental jade when internal application of silicon MW and MW with high content of organic substances.

PROPOSED METHODOLOGY AND DISCUSSION

The experiment was conducted on 50 white male rats of the Vistar line of outbred breeding, obtained from the private enterprise "Biomodelservice", Kyiv, Ukraine. Experimental studies were conducted in accordance with the rules established by the Directive of the European Parliament and the Council (2010/63 / EU), by the order of the Ministry of Education and Science, Youth and Sports of Ukraine No. 249 of March 1, 2012 "On Approval of the Procedure for conducting scientific experiments, experiments on animals by scientific institutions " and methodical recommendations [12, 13, 14]. During the experiment, the animals were in the experimental biological clinic (vivarium) of the State Institution «Institute Research of Medical Rehabilitation and Balneology of the Ministry of Health of Ukraine» in the conditions of free access to food and water. The animals were kept in standard laboratory conditions: photoperiod - light / darkness 12:12; air temperature - 20 ± 2 ° C; Humidity - 55 ± 10%. The rats were kept (contained) in cages of food plastic (400 × 550 × 250 mm) with soft wood chips as bedding. All animals were divided into 5 groups. Group 1 - intact rats (control comparison group). Group 2 - animals with jade. Groups 3rd, 4th and 5th - animals with jade, who received the course on the second day after the reproduction of the pathology; during the course of 7 days, in the mode of free access to drinking, they received MW – "Barvinok", "Regina" and "Lotus" respectively. The model of toxic kidney damage in white rats was reproduced by single-dose subcutaneous administration of 0.5 mg uranyl acetate dissolved in 0.5 ml of a 50% aqueous solution of glycerol per 100 g of rat body mass [15]. Reproduction of the model of nephritis in rats was accompanied by a sharp reduction in the duration of life (5-7) days. Investigation of the functional state of the kidneys was carried out at the 8th day of the experiment. Determine the volume of diuretic daily, for which the animals were placed and special cages for collecting daily urine. The functional status of the kidneys was evaluated according to the state of the function of urine formation (glomerular filtration rate, tubular reabsorption, daily diuresis), excitatory function (by excretion of creatinine, urea and chlorides), in addition, the acid-alkaline reaction of daily urine was determined on the basis of the concentration of hydrogen ions. Concentration of creatinine in urine was carried out using Popper's method. Determination of urea in daily urine was carried out by urease method with a Nessler reagent. Determination of chlorides in urine was performed by the Mora method.

The methodical method and method, which was used in the research, was published in the manual and approved by the order of the Ministry of Health of Ukraine dated 09/28/2009 № 692 [16]. Statistical processing of the data in the series of experiments was carried out with the involvement of programs for medical and biological researches Statistica and Exel. For all

means of processing the statistical material, reliable shifts were those that were within the probability of the Student tables <0.05.

The following MW were used in the study:

- "Barvinok" - silicon mineralized hydrocarbonate sodium water. The content of hydrocarbonates - 1,8544 g / l; chloride-ion content - 0,2165 g / l; sulfate content - 0,0177 g / l; the content of sodium ions and potassium ions - 0,07051 g / l; content of calcium ions 0,0580 g / l; the content of magnesium ions - 0,0401 g / l. Contains orthoboric acid at concentrations of 33.0 - 52.0 mg / l. Total mineralization is 2.89 g / l. The content of meta-silicic acid is 190 - 240 mg / l. Osmolality is - 50,6 mosm / l.
- "Regina" is a weakly mineralized hydrocarbonate sodium-magnesium-calcium hydrocarbon. The content of hydrocarbonates - 0,3904 g / l; chloride-ion content - 0,0107 g / l; sulfate content - 0,0193 g / l; the content of ions of sodium and potassium - 0,0207 g / l; the content of calcium ions is 0.0820 g / l; the content of magnesium ions - 0,0255 g / l. Total mineralization is 0,55 g / l. The content of meta-silicic acid is 36.0 mg / l. Osmolality is - 10.2 mosm / l.
- "Lotus" (Zbruchanska 77) - with a high content of organic substances, weakly mineralized hydrocarbonate magnesium-calcium water. The content of hydrocarbonates is 0.4453 g / l, the content of chloride ions is 0.0572 g / l, the content of sulfates is 0.0282 g / l, the content of sodium and potassium ions - 0,1568 g / l, the content of calcium ions 0,0320 g / l, the content of magnesium ions - 0,0268 g / l, the total mineralization is 0,80 g / l. The content of metasilicate acid - 16,24 mg / l Organic matter content in the form of organic carbon - 0,016 g / l. The osmolality is - 17,8 mosm / l.

Experimental Results

The development of nephritis in rats leads to a significant increase in the volume of diuretic daily - by 266% (p <0.001) due to an increase in the velocity of glomerular filtration (VGF) by 42% (p <0.001), while a significant decrease of 10.03% reverse suction of the liquid (Table 1). Daily excretion of nitrogenous exchange products on the background of nephrite development in rats is increasing: withdrawal of creatinine increases by 42%, and urea - by 120% (p <0.001). The removal of chlorides increases by 147%. In addition, previous studies in the development of experimental nephritis in rats revealed a violation of the metabolism of electrolytes: the daily excretion of potassium, sodium, and chloride ions increases by 180, 45 and 120% [17].

Table1. *Indicators of the functional state of kidney of rats with nephritis and rats, who received the course of MW "Barvinok", "Regina" and "Lotus" on the background of the development of nephritis.*

Indexes	2nd group with nephritis	3rd group nephritis with a rate of MW "Barvynok"	4th group nephritis with a rate of MW "Regina"	5th group nephritis with a rate of MW «Lotus»
Daily diuresis, ml / dm2 of the body surface	367*	187*	210*	294*
Glomerular filtration rate, ml / (dm 2 · min)	142*	106	108	166*
Tubular reabsorption, filtration rate,%	90*	99,42*	96,98*	88.21*
Creatinine withdrawal, mmol	142*	116*	108	166*
Urea removal, mmol	220*	186*	156*	185*
pH of daily urine, c.u.	95	104	102	90*
Daily excretion of chlorides, mmol	247*	50*	342*	130*

Notes:

1. *100% of the data is taken from the control group of animals;*
2. ** - reliable changes are calculated in relation to control (p <0,05).*

The use of rats with nephritis MW "Barvinok" leads to positive changes in the functional state of the kidneys. The volume of diuresis is reduced by 180% (but exceeds the control data by 187%) due to complete recovery of VGF (p> 0.5) and almost complete recovery of the percentage of

back absorption of the fluid in the renal tubules (from 90% in animals with nephritis - 99 , 42% after the completion of the MW course). Creatinine excretion declines from 142% to 116% (26%), urea 220% to 186% (34%), and chloride withdrawal decreases from 247 to 50% (even lower than the control group).

The use of rats with nephritis MW "Regina" also leads to positive changes in the functional state of the kidneys. The volume of diuretic diuresis decreases from 367 to 210% due to the complete restoration of VGF (p> 0.5). At the same time, the full recovery of the percentage of reverse suction of the fluid in the renal tubules is not determined (although the reabsorption value is recovered from 90% to 96.98%, but remains reduced by 3,02%.) Excretion of creatinine is fully restored, excretion of urea decreases from 220 to 156%, and the chloride output decreases from 247 to 182%.

Consequently, both MW "Barvinok" and MW ”Regina“ have a significant restoring effect (but with some differences) on the urinary and the excretory function of the kidneys in rats with experimental nephritis. Under the influence of MW “Regina”, the volume of daily diuresis is insignificant (by - 23%) higher than the corresponding index of rats consuming MW “Barvinok”, which is caused by incomplete restoration of tubular reabsorption process. But under the influence of the MW “Regina”, creatinine clearance is restored to the level of control, the urea removal exceeds the control group rats by 56%, whereas under the influence of MW “Barvinok” the yield of creatinine and urea exceeds the control data by 16% and 86%. In addition, attention is drawn to the differences in the excretion of chlorides which are of opposite nature: from a decrease in their excretion under the influence of MW “Barvinok” by 50% to an increase of 242% under the influence of MW “Regina”.

It can be assumed that the differences in the action of silicon MW are due to the difference in their osmolality and the ratio of their macrocomponents and the bioactive component, which is metasilic acid. MW "Barvinok" has a greater osmolality (50.6 mosm / l versus 10.2 mosm / l of MW "Regina".

In addition, MW "Barvinok" contains much more sodium ions and chloride ions than hypotonic MW “Regina”, resulting in a more powerful restorative effect on the functional state of kidney of animals with jade, causing a different nature and direction of redistribution of water between the inside - and extracellular spaces, which is determined by the almost complete restoration of the tubal reabsorption process and the reduction of excretion of chlorides.

MW "Lotus" does the same in a direction, but has less restorative effect than silicon MW. Volume of diuretic daily decreases from 367% to only 294% (which exceeds the data of the control group of healthy animals by 194%). On the one hand, this is due to a significant acceleration of the VGF by 66% compared with the control group, and by 24% compared with the group of rats with pathology. On the other hand, this effect is due to a significant decrease in tubal reabsorption - by 11.79% against the group of healthy animals, and by 1.79% against the group of rats with nephritis. The removal of urea and creatinine did not differ significantly from that of the second group of rats with pathology, that is, it remains elevated compared to the control group. In this case, the excretion of chlorides is significantly reduced compared to the second group of animals, and exceeds the data of healthy animal groups by only 30%. It should be noted that the silicon MW "Regina" and MW with high content of organic substances "Lotus" have almost the same osmolarity (10,2 and 17,8 mosm / l versus 50,6 mosm / l, which has MW "Barvinok"), and the difference in their corrective action when used in rats with toxic lesion of the kidneys can be explained by the peculiarities of the chemical composition of the MW, that is, the presence of biologically active substances.

Despite the fact that MW is considered relatively weak bioactive agents, positive effects from the use of silicon MW against the background of the development of an experimental pathology model (which is characterized by high mortality) have been shown to have a supportive effect on the state of functional activity of the kidneys in the modeling of nephritis.

CONCLUSIONS

- The development of experimental nephritis in rats is accompanied by the phenomenon of polyuria with an associated increase in the daily excretion of nitrogen exchange products and a significant loss of chlorides.
- The use of both silicic MW has a unidirectional character corrective effect on the functional state of kidney of rats with nephritis. MW "Barvinok" with greater

osmolality y and the content of metasilic acid has a more pronounced restorative effect on the urine-forming function of the kidneys and the removal of chlorides than MW "Regina".

- With high content of organic substances MW "Lotus" has a slow corrective effect on renal dysfunction due to their toxic lesion.

Thus, it can be considered that an important place in the implementation of the biological effect of MW is the presence in their composition of certain biologically active substances (acting in microdoses) and their relationship with osmolality.

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