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INVESTIGATION OF THE EFFECT OF NATURAL CHLORIDE-MAGNESIUM SOLUTION ON THE FUNCTIONAL STATE OF KIDNEYS WITH EXPERIMENTAL ARTHROSIS

Abstract. *Arthrosis was simulated by means of dexamethasone injection into the knee joint of albino Wistar outbred rats. Urine secreting and excretory function of the kidneys against the ground of development of pathological process was examined in rats of the 1st group, in the 2nd group it was studied against underlying arthrosis and transdermal use of balneological remedy "Magnesium oil" (containing 95% of Magnesium chloride). Healthy rats constituted the 3rd control group. Diurnal urine exertion was found to be 17% less as much in rats with arthrosis at the expense of 43% decrease of glomerular filtration rate, 30% decrease of potassium, sodium and chlorine excretion and 10% decrease of creatinine excretion. Transdermal application of chloride-magnesium solution with general mineralization of 15 g/L resulted in practically complete restoration of urine secreting kidney function with a partial restoration of their excretory function – excretion of potassium and creatinine did not differ from the level of that of the 3rd group, and secretion of sodium and chlorine increased as compared to the 1st group but did not reach the level of that of control. Analysis of the data obtained enables to suggest that functional kidney state is disturbed in case of arthrosis development. Even partial restoration of the kidney function under the influence of magnesium-containing remedy results in stabilization of homeostasis and promotes elimination of degenerative changes in joints.*
Key words: *experimental arthrosis, albino rats, functional kidney state, chloride-magnesium solution.*

Introduction. Nowadays arthrosis (osteoarthrosis) is considered to be a serious issue of public health in the whole world afflicting approximately 15% of the Earth population. The risk of occurrence of arthrosis is increasing considerably with age [1-3]. In Ukraine functional disorders of the muscular-skeletal system are the most spread phenomenon among social-active and capable of functioning part of the population [4]. Pharmacotherapy of arthrosis assumes the use of corticosteroids and pain-killers. Due to their administration exhausting and painful syndrome is eliminated, and reparative processes in cartilages are renewed. To influence on all the main links of pathological processes and correct systemic disorders a spectrum of indicated pharmacological agents should be considerably wider, and it results in steady increase of undesirable accumulation of side effects in the form of toxic lesions, allergic reactions etc.

Indication of bigger amount of pharmacological agents leads to addiction, occurrence of toxemia in patients, metabolic disorders of vitamins, macro- and trace elements, and reduces adaptive resources of the body [5]. At the same time, the kidneys must eliminate not only waste products from the patient's body promoting arthrosis development, but the products of pharmacological agent metabolism as well. The kidneys eliminate the most toxic metabolic waste products from the body. In case excretory kidney function is not appropriate or decreased due to earlier experienced diseases and intake of medicines, the products of protein metabolism are accumulated in certain organs and cause specific pathology [6, 7]. In addition, there is a certain correlation between disorders of kidney function and pathology of the connective and osseous tissues [8, 9]. Magnesium deficiency in the body is reported to promote disorders of the structural-functional state of the osseous tissue and development of arthrosis, osteoarthrosis, osteoporosis etc. [10, 11]. It is stipulated by its participation in important nutritious requirements of the bone, that is, magnesium is an element regulating mineralization, growth, elasticity and strength of the osseous tissue, and what is the most important – it enhances reparative potential of bones. Among different tissues of the body it is the osseous tissue that is the main depot of magnesium [12]. Magnesium balance in the body depends on dynamic interaction between its absorption in the intestine, metabolism in the osseous tissue and its further kidney excretion [13]. Magnesium homeostasis is regulated by means of transient receptor potential (TRP) proteins— TRPM6 and TRPM7. TRPM6 is responsible for magnesium homeostasis on the organic level, and TRPM7 — on the cellular level.TRPM6 is predominantly expressed in the kidneys, lungs, intestine; TRPM7 — in all the organs and tissues [14]. The kidneys are able to reabsorb up to 99% of magnesium filtrated through the glomerular membrane. In case of reduced intake of magnesium by the body with food its excretion by the kidneys decreases, and in case of excessive intake – it increases. Magnesium reabsorption in the kidneys occurs mainly in the proximal portion of the tubules and in the thick ascending portion of Henle's loop. But in case of a long deficiency of magnesium the latter will be taken from the osseous depot. Primary disorders of kidney function can cause hypomagnesemia as a result of reduced tubular reabsorption of magnesium by damaged kidneys [15].

The data presented above substantiate the possibility to administer magnesium-containing remedies to correct functional kidney state in case of degenerative diseases of the joints.

Objective: to determine participation of kidney functional changes in pathogenesis of experimental arthrosis and substantiate the possibility of effect of the balneological remedy "Magnesium oil" solution in case of its transdermal application on functional kidney changes of rats with experimental arthrosis.

Materials and methods. The study was conducted on 40 albino male Wistar rats with the body weight of 180 – 200 g. The rats were divided into three groups: the first group (20 rats) included intact animals as the control group; the second group (10 animals) – rats with simulated arthrosis, and the third group (10 rats) of animals receiving the course of applications with "Magnesium oil" on the afflicted joint since the 7th day of the experiment against the development of pathologic model. The course included 6 procedures 20 minutes each every other day. During the experiment the animals were kept on constant food and water regimen under vivarium conditions at the State Institution «Ukrainian Scientific-Research Institute and the Ministry of Public Health of Ukraine». The experiment on animals was carried out according to the existing legal documents [16]. The model of arthrosis was simulated by means of injecting 0,1 ml of dexamethasone into the knee joint in the dose of 0,4 mg per 100 g of the body weight. Dexamethasone solution was injected once a day during three days. The functional kidney state was assessed by the effect on the urine secreting and excretory kidney function. The following indices were examined: glomerular filtration rate, tubular reabsorption, diurnal diuresis, diurnal urine exertion, creatinine and urea excretion, concentration and excretion of sodium, potassium and chloride ions with daily urine. The methods suggested in the manual were used in the study [17]. The data obtained were statistically

processed in a number of experiments using th programs for medical-biological studies Statistica and the software Microsoft Excel 2007. The changes within the ranges of Student tables < 0,05 were considered to be reliable [18]. The balneological remedy "Magnesium oil" was used in the experiment — Poltava bischofite (Ukraine) purified from the compounds of iron and heavy metals and dissolved in distilled water in the ratio 1 per 22 with mineralization 15,0 g/dm3. The obtained solution is bromine, chloride, magnesium containing of a high mineralization. The content of chloride ions in the solution is — 10,638 g/l, sulfate ions — 0,7012 g/l, hydrocarbonate ions — 0,1037 g/l, magnesium ions — 3,6480 g/l, calcium ions — 0,0400 g/l, sodium and potassium ions — 0,3288 g/l та bromine — 0,127 g/l.

Results and discussion. Against the ground of development of experimental arthrosis a reliable 17% decrease of diurnal urine exertion was determined ($p < 0,01$), which is stipulated by a considerable (43 % in case of $p < 0,001$) decrease of glomerular filtration rate (GFR) of primary urine (Table 1). Even reliable decrease of the percentage of fluid reabsorption in the tubules (0,5 % with $p < 0,001$) did not promote increase of diuresis.

Table 1.

Functional kidney state of rats with arthrosis under the influence of "Magnesium oil" solution with the course external application

Indices	I group	II group	III group
	%	%	%
Diurnal urine exertion, ml/dm2 of the body surface	100	83**	92*
Glomerular filtration rate, ml/(dm2·×min)	100	57 ***	100
Tubular reabsorption, percentage before filtration, %	100	99,53***	100,13***
Creatinine excretion, mmol	100	90***	110***
Urea excretion, mmol	100	100	100
pH of daily urine, units of pH	100	98,6	96
Potassium ion concentration in daily urine, mmol/l	100	80*	120*
Daily excretion of potassium ions, mmol	100	65**	100
Concentration of sodium ions in daily urine, mmol/l	100	68 *	80 *
Daily excretion of potassium ions, mmol	100	67***	70 ***
Concentration of chloride ions in daily urine, mmol/l	100	75*	82*
Daily excretion of chloride ions, mmol	100	60 ***	68 ***

*Notes: the data of the experimental groups are presented in per cents to the data of the first control group of rats assumed as 100 %; * — P < 0,05 — reliability of comparison; ** P < 0,01 — reliability of comparison; *** P < 0,001 — reliability of comparison.*

Excretory and ion-regulating kidney function was inhibited which was demonstrated in reliable 10% decrease of creatinine excretion ($p < 0,001$) and decreased concentration and excretion of potassium ions with daily urine (20 and 35 % less with $p < 0,01$), sodium and chloride ions in an average 30 % ($p < 0,001$). Therefore, development of experimental arthrosis can be suggested to be associated with disorders of urine secreting and ion regulating kidney functions. Application of "Magnesium oil" produces a positive effect on the kidney function of rats disturbed by arthrosis development (Table 1). GFR renewed to the control data, but simultaneous activation of the second (other) process of urine formation - increased volume of tubular reabsorption of water in the kidney tubules does not enable diurnal urine exertion to reach the control level,

although diuresis increases as compared to the group of animals with arthrosis. Creatinine excretion renewed to the level of the control data and increased them 10% as much ($p < 0,001$). In comparison with the group of animals with experimental arthrosis in rats with pathology under the influence of "Magnesium oil" the concentration of potassium and chloride ions increased 12 and 7% as much ($p < 0,05$), and their excretion 3 and 18 % as much ($p < 0,01$), but these indices do not reach the control values and remain inconsiderably lower. Excretion of potassium ions renews completely and their concentration is not only renewed but increases the control index on 20% ($p < 0,01$). It should be noted that GFR is a leading parameter determining excretion of sodium by the kidneys, since the amount of sodium filtrating through the tubules is directly proportional to the volume of glomerular filtration. In this case inconsiderable changes of GFR are sufficient to provoke considerable changes of sodium filtration. That is, considerable decrease of GFR against the ground of development of arthrosis stipulates reduced concentration and excretion of sodium, and application of "Magnesium oil" solution during restoration of GFR produces a positive effect on sodium metabolism as well. Incomplete restoration of the concentration and excretion of sodium and chlorine ions can be explained by increased volume of tubular reabsorption. The obtained data correspond to the information contained in the literature concerning a regulating effect of magnesium on the condition of water-electrolytic metabolism in the body [19]. Creatinine excretion increases 27% as much as well ($p < 0,001$). In daily urine the concentration of potassium and chloride ions decreases (34 and 27 % respectively with $p < 0,001$)), but their excretion does not change ($p > 0,5$ and $p > 0,5$). At the same time, concentration of sodium ions increases on 105 % ($p < 0,001$), and their excretion – on 218 % ($p < 0,001$).

Conclusions: 1. In rats with experimental arthrosis inhibited urine secreting and excretory kidney function were determined: diurnal urine exertion becomes 17% less at the expense of 43% decrease of glomerular filtration rate; creatinine excretion decreases 10% as much, and excretion with daily urine of potassium, sodium and chlorine ions in an average 30%. Thus, these functions can be suggested to participate in the formation of pathological process.

2. Application of balneological remedy "Magnesium oil" solution in case of its external use results in restoration and reconstruction of functional kidney state, disturbed by pathological process development, stipulating stability of homeostasis and promoting elimination of degenerative changes in joints of rats with experimental arthrosis.

Prospects of further studies. The obtained experimental data improve the opinion concerning the participation of kidneys in pathogenesis of arthrosis which is a scientific basis to perform further clinical tests of "Magnesium oil" solution in patients with this pathology.

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