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INFLUENCE OF QUERTINE ON THE FREE RADICAL LIPID PEROXIDATION IN PATIENTS WITH URONEPHROLITHIASIS COMORBID WITH METABOLIC SYNDROM

Abstract.

The pathogenesis of urolithiasis is partially determined by oxidative stress, whose main cause is an imbalance in the oxidant-antioxidant system, which is manifested by excessive formation of reactive oxygen species and weakening of the effectiveness of antioxidant protection.

The research aims to study the effect of quertine on the processes of lipid peroxidation (LPO) in patients with UN comorbid with MS. Patients with UN of Group 1 (control) (n = 38) received traditional therapy. Group 2 (comparison) patients with UN comorbid with MS (n = 42) received, in addition to traditional therapy, conventional drugs that correct metabolic disorders. Group 3 (main) patients with UN comorbid with MS (n = 38) received quertine on the background of traditional therapy and drugs that correct metabolic disorders. During treatment, patients with UN demonstrated an accumulation of TBA-AP for the entire period of treatment with traditional therapy. The level of LPO intermediate products, namely of DC and TC, increased significantly after 14 days and after 1.5-2 months of follow-up, respectively. The content of endogenous α-tocopherol (α-TF) and glutathione reductase (GR) activity also decreased moderately after 14 days and after 1.5-2 months of treatment, respectively. In patients with UN comorbid with MS, inhibition of the intensity of LPO processes was observed, which was manifested in a moderate decrease in the pool of TBA-AP final product after 3-6 months to 0.82 ± 0.02 μmol / ml ($p<0.05$). Thus, the use of quertine in combination with traditional therapy, drugs that affect metabolic processes, and differentiated uricostatic and uricolytic drugs contributed to the LPO processes normalization and the AOS restoration.

Keywords: *quertine, lipid peroxidation, urate nephrolithiasis, metabolic syndrome.*

Kidney stone disease (KSD) is one of the most common urological diseases. In recent years, the incidence of urate nephrolithiasis (UN) has increased from 5-10% in the 1950s to 20-30% at present. The term "urolithiasis" refers to a metabolic disease associated with various endogenous and/or exogenous causes (including a composite nature) and characterized by the presence of stones in the kidneys and urinary tract, which are prone to recurrence and often determine a severe course of the disease [1]. Although "unmodified" factors such as gender, geographical location, genetic and ethnic characteristics, are important in the etiology of KSD, the interest of researchers is attracted by "modified" KSD risk factors such as obesity, diabetes mellitus and metabolic syndrome [2]. The danger of MS is connected with its long and asymptomatic course with the onset in childhood and adolescence, which gives prerequisites for the further development of diabetes, cardiovascular disease (arterial hypertension (AH) and atherosclerotic lesions) resulting in early disability and premature mortality [3]. Hyperuricemia associated with impaired glucose tolerance, dyslipidemia and hypertension in patients with abdominal obesity is considered as a component of insulin resistance syndrome [4]. Patients with MS have an increased risk of KSD development, which indicates that it should be viewed as a systemic disorder. Taking into account the components of MS, including obesity, the presence of diabetes or hypertension, the possibility of developing urinary stones appears with the presence of hypercholesterolemia, hypertriglyceridemia, and a high level of low-density lipoprotein [5].

It is well known that any pathological process takes place against the background of the formation of reactive oxygen species (ROS) and the intensification of free radical oxidation of biosubstrates. Thus, an important role in the pathogenesis of the vast majority of the urinary system diseases, including KSD, is played by oxidative stress (OS), whose main cause is an imbalance in the oxidant-antioxidant system, which is manifested by excessive ROS formation and weakening of antioxidant protection (AOP) [6, 7]. This peculiarity of some urological pathologies is due to the fact that the kidneys are constantly exposed to exogenous oxidants (xenobiotics), which can be found in the environment and invade organism in many different ways; unsaturated fatty acids serve as a substrate for the LPO reaction; microorganisms cause activation of phagocytes, which produce a significant amount of ROS [6].

Dysfunction of AOP leads to the formation of a large number of ROS. Having high reactivity, ROS can irreversibly damage biologically important molecules, causing inflammation due to the activation of phagocytes accumulated in the kidneys, resulting in OS [7].

The use of drugs with a high content of bioflavonoids can be considered promising [8]. Bioflavonoids are exogenous natural low-molecular antioxidants with the ability to prevent and neutralize bioreactive oxygen species (BOS) by preventing lipids peroxidation and the formation of chelated complexes with metals. Flavonoids inhibit the active forms in the cycle of arachidonic acid, reduce the formation of BOS, synergistically interact with antioxidant vitamins (A, E, beta-carotene), enhancing their antioxidant potential. The phenolic structure of flavonoids allows the molecule to interact with free radicals, reducing the intensity of the LPO. This inhibits the formation of the main negative factor – malonic dialdehyde [9, 8].

Flavonoids regulate the functional state of the capillary walls, reducing their fragility, which is important for the restoration of microcirculation in the organs. They also have anti-inflammatory, antibacterial, antispasmodic, antihypertensive, antiproteinuric, antihematuric action. Flavonoids are characterized by a membrane-stabilizing effect. They also inhibit platelet aggregation and their adhesion to vascular endothelium, improve the rheological properties of blood, protect microvessels and tissues from destruction, and act as hepatoprotectors. The metabolic action of flavonoids is associated with stimulation of protein synthesis and acceleration of cell regeneration after damage. Flavonoids also have anti-allergic and diuretic effects. Finally, another positive property of flavonoids is the potentiation of the ascorbic acid action and the possibility of co-administration with physiologically active plant substances (alkaloids, saponins, peptins, etc.) [9, 8].

To treat UN comorbid with MS, it is important to use drugs with antioxidant, membrane stabilizing, antidiabetic, anti-atherosclerotic, nephroprotective, cardioprotective, antispasmodic properties. One of the important drugs with above-mentioned properties is quertine, which is an aglycone of many plant flavonoid glycosides. At the same time, flavonoids differ from synthetic means in terms of safety, and the possibility of their long-term use without complications. However, these a priori safe means are hardly used by the official medicine due to the lack of objective data on their therapeutic action effectiveness. In this regard, the diagnosis and treatment of UN comorbid with MS is an urgent problem in urology, a necessary condition and an important part of the algorithm for KSD metaphylaxis.

This research aims to study the effect of quertine on the processes of LPO in patients with UN comorbid with MS.

Materials and methods. The research was conducted based on the urology department of the Zaporizhzhia Central District Hospital. Groups of patients were divided into control, comparison and main ones, depending on the presence of a comorbid pathology accompanied by UN and on the nature of drug treatment. A total of 118 people were included in the study. Indicators obtained from healthy individuals (donors) were taken as normal.

Group 1 (control) (n = 38) included 19 men and 19 women aged between 22 and 73 years (average age was 45.27 ± 1.93 years). The circumference of the abdomen before treatment in men was 89.17 ± 0.88 (cm), in women 78.42 ± 0.41 cm, total 84.80 ± 0.88 cm. The weight of patients with UN reached 72.36 ± 0, 96 kg; the height was 172 ± 10 cm; body mass index (BMI) was 24.34 ± 0.14 kg / m2. Patients with UN received traditional therapy: anticholinergic drug riabal 1 tablet (30 mg) 3 times a day or antispasmodic no-spa 1 tablet (40 mg) 3 times a day, nonsteroidal anti-inflammatory drug dexalgin 2 ml (50 mg) for intramuscular pain, granulated Uralit-U – 1 teaspoonful (2.5 g) 2-3 times a day depending on the pH of fresh urine (6.2-6.8), water blast.

In Group 2 (comparison) (n = 42), there were 16 men and 26 women aged between 30 and 80 years (average age was 59.14 ± 1.67 years) with UN comorbid with MS. Abdominal circumference before treatment in men was 109.48 ± 1.59 cm, in women 110.73 ± 1.34 cm, total - 110.30 ± 1.01 cm. The weight of patients with UN comorbid with MS was 96.62 ± 1.13 kg; the height was – 169 ± 10 cm and BMI was 33.90 ± 0.38 kg / m2. Patients with UN comorbid with MS were treated with traditional therapy and conventional drugs that correct metabolic disorders: atorvastatin 1 tablet (20 mg) per day in the evening, metformin 1 tablet (1000 mg) 1-2 times a day, allopurinol 1 tablet (100 mg) 3 times a day, liprazid ½-1 tablet (20 mg) per day in the morning, vitamin B_6 1 tablet (50 mg) 2 times a day, magnesium oxide 1 tablet (0.5 g) 2 times a day.

Group 3 (main) comprised patients (n = 38) with UN comorbid with MS, who received traditional therapy and conventional drugs that correct metabolic disorders, on the background of bioflavonoids were 10 men and 28 women aged between 40 and 78 years 59.89 ± 1.34 years). The weight of patients in this group was 99.18 ± 1.15 kg, height - 168 ± 10 cm, BMI was 35.02 ± 0.45 kg / m2. The circumference of the abdomen before treatment in men was 110.50 ± 1.82 cm, in women - 112.32 ± 1.37 cm, total - 110.50 ± 1.82 cm. Patients of the main group received traditional therapy and conventional drugs, which correct metabolic disorders, on the background of quertine 1 tablet (40 mg) 3 times a day.

In the group of healthy individuals (n = 30), there were 13 males and 17 females aged between 21 and 68 years (average age was 34.83 ± 2.04 years).

The study of the condition of patients with UN and UN comorbid with MS was conducted studies by anamnestic, objective, clinical and laboratory, radiological, ultrasound, radioisotope, biochemical methods, according to the protocol approved by the Order of the Ministry of Health of Ukraine № 1-1/152 (item 2) "Urolithiasis, kidney stones" dated March 6, 2003.

MS was diagnosed according to the 2005 International Diabetes Federation recommendations and was based on the presence of central obesity (waist circumference in men over 94 cm and over 80 cm in women, BMI ≥25) and two additional MS criteria, found in patients with urate nephrolithiasis

All patients were examined after obtaining their informed consent in accordance with GCP IHC requirements.

Enrollment criteria included the following: confirmed urate nephrolithiasis or urate nephrolithiasis

comorbid with MS; age between 18-80 years; a patient's informed consent to the study and pharmacotherapy.

Exclusion criteria were the following: the presence of concomitant oncological, psychoneurological, pulmonary and other somatic diseases (e.g. gout); refusal from the proposed treatment and re-examination; intake of drugs absent from the standards of urate nephrolithiasis and MS treatment; alcoholism and drug addiction; for women – pregnancy and lactation.

According to the protocol, the participants underwent several laboratory and instrumental studies: general blood and urine test, urine pH test; measurement of abdominal circumference, body weight, and body mass index; kidneys ultrasonography, Doppler imaging, X-ray examination of the kidneys (plain and excretory urography), radioisotope renography, electrocardiography, blood pressure control.

Indicators of the processes of LPO and antioxidant system (AOS) were evaluated by the content of TBA (thiobarbituric acid) active products (AP) and analyzed by the reaction with TBA according to the method of A.I. Andreieva [10]. The content of diene (DC) [11] and triene conjugates (TC) [12] of higher fatty acids was studied spectrophotometrically in heptane extract. The content of α-tocopherol (α-TF) was investigated spectrophotometrically in heptane extract according to the method of Y. Biery, A. Feels [13]. The activity of glutathione reductase (GR) was studied spectrophotometrically by reducing NADP H_2 [14].

The study of LPO and AOS in the blood serum was performed and followed up before treatment; 7 days, 14 days, 1.5-2 months, 3-6 months after. The results were statistically processed with Statistica 13.0 software.

Results and discussion

The research of indicators of LPO and AOS processes demonstrated that in the course of treatment in control, main, and comparison groups, there were ambiguous changes in the levels of intermediate and final products of free radical lipid peroxidation, as well as in GR activity and in the content of endogenous antioxidant α-TF. The presence of OS is evidenced by an increase in the level of TBA-AP in the group of patients with UN before treatment in contrast to the group of healthy individuals (by 108.3%) (Fig. 1). Comorbidity of KSD with MS contributed to an increase in this indicator in patients of the main comparison groups by 2.52 times and 2.83 times, respectively. The level of LPO intermediates increased intensively in these groups: DC - 3.72 times and 3.64 times, respectively; TC - 2.90 times and 2.97 times, respectively. In the control group, the increase in DC and TC was also significant - 3.70 times and 2.07 times, respectively.

In contrast to the group of healthy individuals, the pool of endogenous α-TF decreased in the control, comparison, and main groups by 55.94%, 56.47% and 62.14%, respectively. At the same time, GR activity in these groups also decreased by 19.28%, 37.39% and 33.72%, respectively.

Thus, before treatment, patients with UN demonstrated the activation of LPO, as well as pronounced changes in the biological membranes' condition, which induces the depletion of protective mechanisms. The presence of MS in patients with UN exacerbated the processes of OS, which was accompanied by a weakening of AOS and activation of free radical lipid oxidation.

The data presented in Fig. 1 indicate a significant progression of the content of LPO products and inhibition of AOS in the control group patients with UN during the observation. Thus, the level of final LPO products - TBA-AP increased significantly after 7 and 14 days of follow-up by 15.78% and 29.05%, respectively. A significant increase in this indicator was observed 1.5-2 months (by 42.45%) and 3-6 months (by 50.83%) later. A less significant increase in the level of DC intermediate product was observed after 14 days, 1.5-2 months and 3-6 months (by 23.86%; 28.88% and 47.15%, respectively). At the same time, the content of TC intermediate products significantly increased after 3-6 months of follow-up (by 49.31%). At that time, the content of endogenous α-TF decreased slightly by 9.44% after 7 days and significantly by 33.75%; 40.62% and 46.6%, respectively, after 14 days, 1.5-2 months and 3-6 months of follow-up. Similarly, there was a moderate decrease in GR activity after 1.5-2 months (by 23.74%) and a pronounced one 3-6 months (by 34.6%) later.

Data from the study of LPO and AOS in groups of patients who received traditional therapy and conventional drugs that correct metabolic disorders are presented in Fig. 1. Based on this, it is obvious that the severity and directivity of changes in indicators were ambiguous.

The level of TBA-AP end products in patients with UN comorbid with MS (comparison group) after 1.5-2 months of treatment was not significantly inhibited (11.22%) and it became more pronounced after 3-6 months (19.73%) of follow-up. Treatment with drugs that correct metabolic disorders, contributed to a moderate reduction of LPO intermediate products, namely of DC and TC after 7 days of follow-up (16.12% and 22.83%, respectively), after 14 days (18.89% and 17, 04%, respectively), after 1.5-2 months (by 17.95% and 18.38%, respectively) and after 3-6 months (by 16.81% and 19.05%, respectively). At the same time, there was an increase in the pool of endogenous α-TF (by 16.64%; 18.67% and 20.93%, respectively, after 14 days, 1.5-2 months and 3-6 months of treatment). Besides, the activity of the enzyme anti-peroxide protection of GR was moderately restored by 16.79%; 17.17% and 18.65%, respectively, in the same follow-up period.

In the group of patients with UN comorbid with MS (main group) who received traditional therapy and conventional drugs for metabolic processes improvement on the background of quertine, there was a moderate decrease in TBA-AP after 7 days and a significant one after 14 days, 1.5 -2 months and 3-6 months (by 16.18%; 31.50%; 48.66% and 56.31%, respectively).

The level of LPO intermediate products, namely DC and TC also decreased moderately after 7 and 14 days of treatment (by 22.30%; 26.96%, respectively and by 38.51% and 29.35%, respectively). A significant decrease in these indicators was observed after 1.5-

2 months (by 46.86% and 37.33%, respectively) and after 3-6 months (by 57.26% and 42.86%, respectively). Restoration of the endogenous antioxidant α-TF content in the blood was observed in patients of the main group significantly after 7 days of treatment (37.03%), after 14 days (53.37%), after 1.5-2 months (89, 08%) and in 3-6 months (by 103.87%). At the same time, the activity of the anti-peroxide enzyme GR was restored by 34.09%; 53.70%; 86.39% and 95.31%, respectively, after 7 days, 14 days, 1.5-2 months and 3-6 months of treatment.

Assessing the results of the study as a whole, it is possible to conclude that the disturbances of OS processes in patients before treatment contributed to the progression of LPO and inhibition of AOS. The level of the LPO final products – TBA-AP and intermediate products – DC and TC – increased significantly before treatment in patients of the control, comparison, and main groups. During treatment, patients with UN demonstrated accumulation of TBA-AP for the entire course of the traditional therapy. Simultaneously, the level of LPO intermediate products – DC and TC –increased significantly after 14 days and after 1.5-2 months of the follow-up, respectively. Endogenous α-TF content and GR activity also decreased moderately after 14 days and after 1.5-2 months of treatment, respectively, which indicates AOS inhibition.

Activation of OS in patients with UN along with DNA degradation and progression of LPO processes caused damage to fibroblasts, stimulated thromboxane formation, reduced local defence activity, increased epithelial and endothelial permeability, increased mucus secretion. Such mechanisms are the basis of OS processes; besides, they determine one of the links in the UN pathogenesis, caused by oxidative damage, inhibition of membrane enzyme activity, deepening changes in physicochemical properties of lipid metabolism [15, 16].

Positive results of treatment in patients with UN comorbid with MS (comparison group) were achieved due to complex treatment with diet, water regimen and pharmacotherapeutic agents such as Uralit-U, allopurinol, atorvastatin, metformin, liprazid, vitamin B_6, MgO. This was confirmed by inhibition of the intensity of LPO processes, which was manifested in a moderate decrease in the pool of the final product of TBA-AP after 3-6 months to 0.82 ± 0.02 μmol / ml. The inclusion of quertine in the treatment of patients with UN comorbid with MS contributed to an even greater reduction in the level of TBA-AP after 3-6 months to 0.38 ± 0.04 μmol / ml, which was close to healthy individuals. In patients of the comparison group during the course of treatment, there was a moderate decrease in the intermediate LPO products such as DC and TC. In the main group patients, the level of DC and TC decreased more intensely compared to the other group of patients who received only traditional therapy and drugs for metabolic processes improvement. In patients of the comparison group, there was a recovery of α-TF – endogenous antioxidant, which was employed for the inhibition of free radicals and the stabilization of the phospholipid layer of biomembranes after 14 days, 1.5-2 months and 3-6 months of treatment. There was also a moderate progressive recovery of the activity of the anti-peroxide enzyme GR within the same period of treatment. Simultaneously, the recovery of endogenous α-TF and GR activity was significant in the main group patients. Thus, the level of α-TF increased after 3-6 months of treatment to 11.56 ± 0.34 μmol / ml (in healthy individuals 14.98 ± 0.41 μmol / ml). The activity of GR was significantly restored after 3-6 months to 26.45 ± 0.99 μmol / ml, which exceeded the level of this indicator in healthy individuals (up to 20.43 ± 0.76 μmol / ml).

After treatment with quertine, patients with UN comorbid with MS demonstrated an improvement in general condition and increased vitality. In most patients, lumbar pain, headaches, tinnitus, and dizziness decreased, and blood pressure returned to normal.

The experiments performed are consistent with other studies that have discovered that changes in renal function are associated with the processes of LPO and AOSin patients with urate nephrolithiasis [15]. Disorders of purine, carbohydrate and lipid metabolism exacerbate disorders of the functional state of the kidneys and the processes of free radical lipid oxidation [15].

The study of the effect of quertine on MS, induced by a high-fructose diet, in laboratory rats found that the development of insulin resistance and carbohydrate intolerance is inhibited [17]. The nephroprotective effect of quertine was confirmed in experimental studies under conditions of kidney damage of various etiologies, where quertine had a positive effect on the structural and functional state of the kidneys, normalized renal excretory function and nitrogen metabolism, and caused antioxidant effects [18].

In experimental ovarioectomized animals with MS caused by a high-sucrose diet, the use of the drug "Quertine D" results in a decrease in the secretion of albumin in the urine (albuminuria) and the level of LPO products – DC [4]. In the experiment with modelled streptozotocin diabetes mellitus, "Quertine D" reduced basal hyperglycemia and the levels of higher fatty acids in the blood serum, and of LPO products; superoxide dismutase activity increased, and glucose-6-phosphatase activity in the liver and kidneys decreased. ADP-induced platelet aggregation and morphostructural changes in the kidneys and the progression of microalbuminuria decreased as well [19].

Thus, quertine, having a powerful antioxidant effect based on the neutralization of the free radicals, stabilizes cell membranes, which has a pronounced activating effect on the enzyme system of the body's own AOS system [16].

Conclusions

1. In patients with UN comorbid with MS, the development of OS was observed, which was manifested by the activation of free radical lipid oxidation and AOS inhibition.

2. The use of quertine in conjunction with traditional therapy, drugs that affect metabolic disorders, and differentiated uricostatic and uricolytic drugs contributed to the normalization of the LPO processes and the AOS restoration.

3. Further studies of treating UN comorbid with MS patients with quertine, traditional drugs, conventional drugs that correct metabolic disorders, and differentiated uricolytic and uricostatic therapy, will allow, based on the results, to correct the condition and also indicators of kidneys functional state, carbohydrate, lipid, purine and electrolyte metabolism, to improve patients' health and quality of life.

Keywords: quertine, lipid peroxidation, urate nephrolithiasis, metabolic syndrome.

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Figure 1

Dynamics of changes in lipid peroxidation and antioxidant system in patients with urate nephrolithiasis (UN) (control group), urate nephrolithiasis comorbid with metabolic syndrome (UN + MS) (comparison group), and patients with urate nephrolithiasis comorbid with metabolic syndrome who received quertine (main group)

Indicator	Groups of patients	Before treatment	After 7 days	After 14 days	After 1,5-2 months	After 3-6 months
TBA-AP, μmol/ml	healthy individuals	0.36±0.03				
	control	0.75±0.04*	0.86±0.02* p<0.05	0.95±0.03* p<0.05	1.06±0.03* p<0.05	1.12±0.03* p<0.05
	UN+MS, comparison	1.02±0.03*/§	0.94±0.04* p>0.05	0.96±0.03* p>0.05	0.91±0.04* p<0.05	0.82±0.02*/§ p<0.05
	main	0.91±0.05*	0.76±0.04*/+ p<0.05	0.62±0.06*/§/+ p<0.05	0.47±0.07*/§/+ p<0.05	0.38±0.04 §/+ p<0.05
DC, μmol/ml	healthy individuals	0.51±0.01				
	control	1.89±0.17*	2.18±0.15* p>0.05	2.35±0.08* p<0.05	2.44±0.06* p<0.05	2.79±0.05* p<0.05
	UN+MS, comparison	1.90±0.12*	1.59±0.09*/§ p<0.05	1.54±0.09*/§ p<0.05	1.56±0.06*/§ p<0.05	1.58±0.05*/§ p<0.05
	main	1.86±0.20*	1.45±0.05*/§ p<0.05	1.15±0.07*/§ p<0.05	0.99±0.04*/§/+ p<0.05	0.80±0.06*/§/+ p<0.05
TC, μmol/ml	healthy individuals	0.040±0.003				
	control	0.083±0.006*	0.085±0.007* p>0.05	0.093±0.006* p>0.05	0.114±0.004* p>0.05	0.124±0.004* p<0.05
	UN+MS, comparison	0.116±0.006*	0.085±0.004* p<0.05	0.097±0.005* p<0.05	0.095±0.003* p<0.05	0.094±0.003*/§ p<0.05
	main	0.119±0.013*/§	0.087±0.005* p<0.05	0.084±0.005* p<0.05	0.074±0.004*/§/+ p<0.05	0.68±0.004*/§/+ p<0.05
α-TF, μmol/ml	healthy individuals	14.98±0.41				
	control	6.60±0.27*	5.98±0.19* p<0.05	4.37±0.24* p<0.05	3.92±0.14* p<0.05	3.52±0.13* p<0.05
	UN+MS, comparison	6.52±0.48*	7.34±0.39* p>0.05	7.63±0.18*/§ p<0.05	7.74±0.19*/§ p<0.05	7.89±0.35*/§ p<0.05
	main	5.67±0.30*/§	6.71±0.35* p<0.05	8.69±0.63* p<0.05	10.72±0.33*/§/+ p<0.05	11.56±0.34 */§/+ p<0.05
GR, μmol/lh	healthy individuals	20.43±0.76				
	control	16.49±0.86*	14.65±0.83* p>0.05	14.84±0.72* p>0.05	12.58±0.61* p<0.05	10.78±0.37* p<0.05
	UN+MS, comparison	12.79±0.81*/§	14.39±0.42* p>0.05	14.93±1.27* p<0.05	14.98±0.51* p<0.05	15.17±0.42*/§ p<0.05
	main	13.54±0.36*/§	18.16±0.59 §/+ p<0.05	20.82±0.85 §/+ p<0.05	25.24±1.69 */§/+ p<0.05	26.45±0.99 */§/+ p<0.05

Note: * – reliability in relation to a group of healthy people; § – reliability in relation to the group of patients with urate nephrolithiasis; + – reliability in relation to the group of patients with urate nephrolithiasis comorbid with metabolic syndrome on the background of quertine intake; p<0.05 – reliability in relation to treatment and the process of observation during the treatment of patients.