

**The Republic of Kazakhstan
Ministry of Health
B.U. Jarbusynov Urology Research Center**

**REPORT
OF
CLINIC TRIAL RESULTS OF
RENALOF
IN UROLITHIASIS PATIENTS**

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Relevancy

Urolithiasis is one of the frequent urologic diseases, the second disease in the world after non-specific inflammatory kidney and urinary tract diseases and not less than 3% of population suffer from it (F.C Delvecchio, G.M Preminger, 2003).

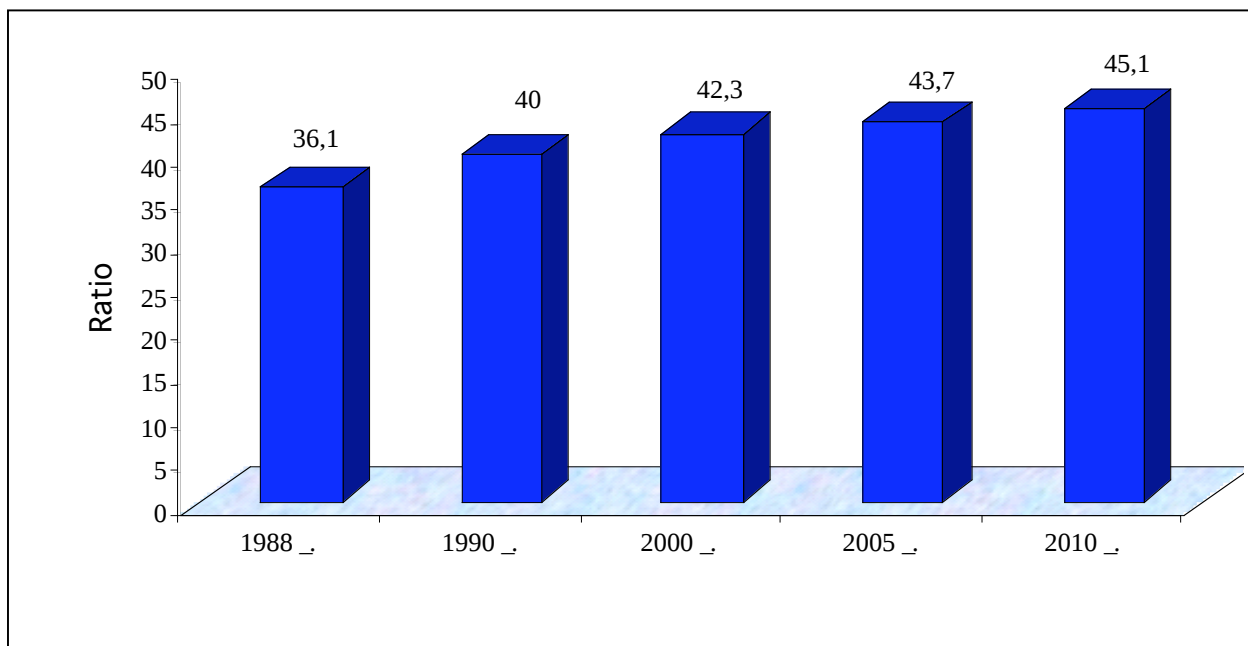
The frequency of urolithiasis is progressively growing which is evidenced by the urolithiasis patients. The growth in the incidence of urolithiasis is related to the impact of a series unfavorable exogenic and endogenic factors of human body. The exogenic factors include climatic, geographic, housing conditions, occupation. Due to prevalence and complexity of therapeutic/diagnostic guidebooks, the urolithiasis problem draws the attention of scientists and practitioners and remains relevant for a series of reasons.

The urolithiasis patients constitute the major part of patients in daily urologic practice. Optimal management of these patients requires knowledge of diagnostics, rational treatment of acute renal colic, calculus removing therapy and modern calculus removing methods. Beside this, all practicing urologists must have basic knowledge of etiologic factors of calculi formation and be able to assess the metabolic risk to prevent the backset of calculi formation.

In the last decade, owing to rapid development of new technologies, potentials of treatment of urolithiasis have considerable grown, deep mechanisms of calculi formation discovered and important successes achieved in medicinal treatment of various aspects of urolithiasis.

In Kazakhstan also the world tendency is noticed towards incidence of urolithiasis among the population. This is linked to a series of factors: The Republic of Kazakhstan is located in the region with dry and hot climate, unsettled status and lack of sources of drinking water, there are areas with unfavorable environment where concentrations of various highly active toxicants in water, soil, air are high which alter the urine physical and chemical properties resulting in its lithogenic properties.

According to the data provided by M.K.Alchinbayev and co-authors(2004), the urolithiasis average incidence in the Republic of Kazakhstan made in 1988 36.1 per 100,000 individuals, in 1990 40.0, in 2000 42.3, in 2005 43.7 per 100,000 individuals. According to the forecast data, this indicator in 2010 will make 45.1 per 100,000 individuals. The steady growth in urolithiasis incidence in the last years is linked to urbanization, deterioration of environment, expansion of the infrastructure resulting in prevalence of urban style of life of the RK residents and leading to disorders of various metabolism in human body resulting in numerous pathologies one of which is calculi formation in the urinoexcretory system.



Picture 1. Urolithiasis incidence growth variation in Kazakhstan

The complexity and diversity of the etiologic factors result in numerous cascading disorders of various human body metabolisms.

These metabolic disorders specify the complexity of choice of pathogenetic treatment of urolithiasis. According to the data provided by V.P.Alexandrov, Y.G.Alyayev, M.M.Gazymov, the metabolic disorders included imbalance of calcium, xanthine, oxalate, purines, hormones of parathyroid glands in human body.

But more significant causes resulting in the urolithiasis incidence growth are the endogenic factors: hypodynamia, nutrition habits, metabolic disorders in human body (A. Erbargci, 1999).

At present, removal of calculus is the main phase of treatment of patients suffering from urolithiasis. However, removal of calculus can only improve the urodynamics and correct the inflammation process in urinary tracts. Especially, as removal of calculus may affect the metabolic processes occurring in the body of each patient. It is for this reason that the assessment of the outpatient treatment effectiveness and post operational setback metaphylactics of urolithiasis are equally important (O.L.Tiktinsky, 2000; H.-G. Tiselius, 2002; N.K.Dzeranov, 2004). According to the data provided by Strohmaier W.L. (2006), 60,000 cases of urolthiasis result in 5.8 ml lost days and the losses amount to about euro 500 ml. Effective metaphylactic measures save euro 170 ml.

The current objective of urolithiasis researchers is not only removal of calculus from the urinary tracts, but also prophylaxis and elimination of the causes that result in its formation (S.H.Al-Shukri, 1999; O.V.Konstantinova, 1999; Y.G. Alyayev, 2002).

The modern literature does not contain enough data of the status of the problem of metabolic disorders remedy which play direct role in calculi formation in patients suffering from urolithiasis. The diagnostics of metabolic disorders in patients suffering from urolithiasis and making up the differentiated process that allows to remedy the revealed disorders are an important step forward in the urolithiasis metaphylactics. This allows, in a series of cases after removal of concretion, to carry out effective therapy in accordance with the type of revealed changes and in this manner to reduce the incidence of relapse into calculi formation (M. Menon, 2003; D.A.Beshliyev, 2005).

The objective of the research is assessment of the effectiveness of treatment of urolithiasis with Renalof.

pharmacologic properties of the medicine. This new medicine contains activated extract of couch grass (*Agropyron Repens*), the natural diuretic effect of which makes it an ideal medicine for treatment of any urinal tract infections. Moreover, it can stimulate urine flow and facilitate removal of renal calculus. The tranquilizing effect of this herb reduces irritation and inflammation. It also produces an antimicrobial effect as destroys the pathogens and prevents their growth.

ENERGY VALUE (per 100 g)

Energy value	318 kcal (1,330 kJ)
Proteins.....	0.6g
Carbohydrates.....	78.0g
Fats.....	0.3g

AVERAGE VALUE PER CAPSULE

Content	g/capsule
Agropyron Repens extract (couch grass)...	12g
Mannitol	88g
Maize starch.....	200g
Magnesium silicate	25g

Proceeding from the composition of this medicine, painless or less painful removal of calculus, good epithelial regeneration after excretion of calculus and anti-inflammatory effect on the urinary system can be expected.

The clinical researches showed that Renalof produces a pronounced anti-inflammatory, spasmolytic and litholytic effect on patients suffering from urolithiasis and secures complete painless removal of small concretions through the urinary tract. Whereas, in none of the cases, renal colic was observed.

The data of international clinic observations show that monthly treatment with Renalof results in normalization of clinic urine test indicators.

For instance, most patients' urine, prior to treatment with Renalof, contained high concentrations of erythrocytes and leucocytes, while albumen, mucus and salts were not determined.

Renalof can be effectively used in complex treatment of patients suffering from urinary system diseases: in patients with urolithiasis, pyelonephritis as well as to improve the renal function and to improve the life quality of patients with urolithiasis who are contraindicated surgical and other vigorous treatment methods. Renalof is recommended for painless removal of small concrements and sand from kidneys and gall bladder(urate, oxalate, mixed calculi), for prevention of inflammations, treatment of renal colic.

Material and methods

This work is based on the analysis of clinical/laboratory and instrumental examination of 78 patients diagnosed to have urolithiasis. All patients were medically examined and treated in B.U.Jarbusynov Urology Research center clinic. The breakdown of urolithiasis patients by sex is provided in Table No 1.

Table 1. Breakdown of urolithiasis patients by sex.

Sex of patients	Number	%
Males	41	52.5
Females	38	48.7
Total	78	100

The average age of patients, males: 49.7 ± 9.7 , females: 51.4 ± 6.2 .

The patients with concrements in the urinary system were analyzed for the nature of operative interventions.

According to the data of Table 2, 35.8% of patients did not undergo surgical treatment. 15 patients received open surgical treatment of which: 11 (14.1%) were subjected to pyelolithotomy, 3 (3.8%) to ureterolithotomy, 1 (1.2%) to nephrectomy. The percentage of remote lithotripsy constituted 23 (29.4%), ureterolithoextraction 12 (15.3%).

Table 3. The nature of operative intervention in urolithiasis patients

Type of operative intervention	Quantity	%
Open: pyelolithotomy	11	14.1

Nephrectomy	1	1.2
Ureterolithotomy	3	3,8
Remote lithotripsy	23	29.4
Ureterolithoextraction	12	15.3
W/O operative intervention	28	35.8
Total	78	100

All the patients were subjected to clinic examination as per generally accepted method. The obtained results were comprehensively assessed taking into account the diagnostic methods.

All the patients who participated in the research were subjected to mandatory overall clinic/laboratory research aimed at finding out the causes of presence of activity in the inflammatory process (general urine and blood tests (Zimnitski test, Roberg test, determination of the urine saturation factor, glomerular filtration rate calculation), detection of metabolic disorders (blood biochemical test, assessment of uric acid concentration in blood and urine, urine citrate), as wells as urine chemical composition test. Instrumental examination: ultrasound examination of urogenital system has been carried out for all patients who participated in the research, plain excretory urography and computerized tomography of urogenital system. The concrement average size was 0.6 ± 0.2 mm.

All patients were divided into two groups:

Group 1: 41 patients received combination therapy that included anti-bacterial, spasmolytic treatment and treatment with Renalof.

Group 2: 37 patients received similar treatment without litholytic medicine.

Table 4. Characteristics of major indicators of researched groups.

Indicator	Researched group (n-41)	Control group (n-37)
Age, years	48.1±7.2	49.4±5.9
Duration of disease, years	6.6±3.9	6.9±3.6
Concrement spotting	kidneys	kidneys
Concrement size, mm	0.7±0.2	0.6±0.3
Concrement denssity, units	787±16.8	792±17.5

Group 1 patients received 2 Renalof capsules twice a day. During the research, blood and urine tests, kidney ultrasound scanning, x-ray tests were.

The course of treatment of both groups lasted 3 months.

Research results

During the period before and after administration of the medicine no statistically significant changes were noticed in the main indicators of the body status. During treatment process, good tolerance was noticed to the medicine, allergic reactions were not observed.

The major criteria of effectiveness of the treatment was the effect on the clinic symptoms(alleviated pains in the lumbar region, dysuric cases), reduction in sizes, process of evacuation of concrement).

By the end of the second week of administration of Renalof, the main group was observed to feel better in terms of alleviated (in 27 patients) and lack of pains(in 14 patients). Dysuric cases were jugulated as of day 9 of medicine administration.

In Group 1, reduction in size of concrement was observed in 22 or in 53.6% of the patients. Evacuation of calculi fragments was observed in 17 (41.4%) patients. In Group 2, reduction in calculi sizes was observed in 7 (18.4%) patients, evacuation in the form of sand by itself was observed was observed in 9 (23.6%) patients.

Improvement of laboratory test results as reduction in leukocyturia, erythrocyturia, bacteriuria, oxaluria was obviously observed in the main group.

Table 5. The major criteria of assessment of treatment effectiveness in researched patients

Signs	Group 1		Group 2	
	Before treatment	After treatment	Before treatment	After treatment
Concrement size reduction	0.8±0.2	0.5±0.4*	0.6±0.3	0.5±0.2
Urine pH	5.04±0.7	6.79±0.12*	5.2±0.21	5.03±0.25
Urine citrate wet	320±12	640±18*	280±24	310±27
Presence of salts in urine	++++	-	++++	+

* $p \leq 0,05$

The preliminary trial of Renalof thus gives evidence of quite high effectiveness of this medicine in treatment of urolithiasis patients.

Beside monotherapy, we administered Renalof for pre-operative preparation of patients for lithotripsy. Introduction of remote lithotripsy in the 1980s have altered the treatment of urolithiasis patients. However, recently the effectiveness of remote lithotripsy is becoming debatable considering the forecast factors of disintegration of concrement (calculi size, their spotting, time of presence in urinary tracts). Analysis and taking into account these parameters affect the choice of effective

and safe mode of remote lithotripsy and thus reduce the frequency of side effects of the method.

The research group patients were administered Renalof as per standard scheme. The indicators were checked after one month.

Table 6. Calculi density variation in researched patients

Groups	Before treatment	After one month of treatment
Renalof	787±16,8	511±14.6*
Control group	792±17.5	782±19.2

$p < 0,04$ when indicators are compared against indicators before treatment

Having analyzed the acquired data, we may conclude that when Renalof is administered before remote lithotripsy, the calculi structural density obviously drops as compared with the control group. More favorable conditions are thus created for remote lithotripsy.

We have analyzed the number of cases with remote lithotripsy in these patients.

Table 7. Quantitative characteristics of lithotripsy runs in researched patients

Remote lithotripsy runs	Researched group (n-14)		Control group (n-11)	
	Absolute	%	Absolute	%
1	27	79.4±18.3*	16	51.6±12.4
2	7	20.5±4.9	9	29.0±11.7
Over 2	0	0	6	19.3±8.2

$p < 0,05$ when compared with the control group

The acquired data give evidence that preparation of patients with Renalof before remote lithotripsy allows to obviously reduce the number of runs.

Pre-operative preparation of urolithiasis patients with remote lithotripsy ensures reduction of the number of lithotripsy runs which is cost-effective for urologic hospitals.

CONCLUSIONS:

1. We have found out that administration of Renalof effectively alleviates pains and dysuria in urolithiasis patients.
2. Administration of Renalof obviously reduces the calculi sizes in urolithiasis patients.
3. Administration of Renalof improves pH status and increases urine citrate evidencing of significant litholytic effect.
4. Improvement in urine citrate values speaks for improvement in metabolic indicators in urolithiasis patients.

RECOMMENDATIONS:

1. It is necessary to administer Renalof as a litholytic medicine to patients with small concrements (up to 1 cm).
2. Administration of Renalof to patients with inflammation of urinary tracts produces a significant clinic effect.
3. Renalof is recommended to administer for pre-operative preparation for lithotripsy of urolithiasis patients in order to get highly effective lithotripsy.

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