

## EFFECTIVENESS OF USING THE DRUG CANEPHRON®N IN THE METAPHYLAXIS OF UROLITHIASIS

**Emil Ceban**

Department of Urology and Surgical Nephrology,  
State University of Medicine and Pharmacy “Nicolae Testemitanu”

### **Summary**

Urolithiasis is one of the most common urologic diseases in the world. It describes the formation of urinary calculi in the urinary system. According to forecasts, urolithiasis has a continuing upward trend due to a significant change in the nature and quality of nutrition, increase of negative environmental and social factors. Despite the large-scale implementation and application of highly effective methods for urolithiasis diagnosis and treatment, the incidence of stone formation and recurrence remains high (30-50%). In study was determine the effectiveness of usage Canephron®N (dragees) in the complex prophylaxis of recurrent stone formation in patients with urolithiasis.

### **Rezumat**

#### *Eficacitatea preparatului Canefron®N în metafilaxia urolitiaziei*

Urolitiază este cea mai răspândită patologie urologică în lume. Aceasta patologie este descrisă ca formarea calculilor în sistemul urinar. În conformitate cu pronosticul, urolitiază are o continuă tendința ascendentă datorită schimbărilor semnificative în natura și în calitatea alimentelor, acțiunea nefastă a mediului ambiant și factorilor sociali, metabolici și infecțioși. Necătfînd la aplicarea și implementarea pe scara largă a metodelor eficiente în diagnosticarea și tratamentul urolitiază, incidența formării calculilor și recurența rămîne înaltă (30 – 50 %). În studiu este determinată eficacitatea utilizării preparatului Canefron®N în metafilaxia complexă la pacienții cu urolitiază recidivantă.

### **Introduction**

Urolithiasis is one of the most common urologic diseases in the world. It describes the formation of urinary calculi in the urinary system. Currently, urolithiasis ranks first in the structure of diseases in the Urology Departments of the Republic of Moldova.

According to forecasts, urolithiasis has a continuing upward trend due to a significant change in the nature and quality of nutrition, increase of negative environmental and social factors. The topicality of the urolithiasis problem is conditioned by its frequent diagnosis in individuals of more able-bodied period of life (aged 20-60).

The pathophysiology of urolithiasis is still under debate and seems to be multifactorial such as physicochemical and metabolic trigger mechanisms. A main physicochemical trigger is supersaturation, e.g. as expressed as the ratio of urinary calcium oxalate or calcium phosphate concentration to the solubility, which is the driving force for stone formation. About 80% of stones are composed of calcium oxalate with variable amounts of calcium phosphate. Calcium oxalate supersaturation is independent of urine pH, but calcium phosphate supersaturation increases rapidly as urine pH rises from 6 to 7. Other triggers are of metabolic nature, such as imbalances between excretions of calcium, oxalate, and water which create supersaturation.

Despite the large-scale implementation and application of highly effective methods for urolithiasis diagnosis and treatment, the incidence of stone formation and recurrence remains high (30-50%).

A comprehensive, personalized metaphylaxis, with a change in lifestyle, diets, increased water consumption, use of phytomedicines increases the effectiveness of the treatment.

Herbal drugs play a specific role in the conservative treatment of urologic complaints, especially for secondary prevention of urinary tract infections and renal inflammation as well as for the prevention of renal gravel. In cases of urolithiasis herbal drugs as e.g. Equiseti herba, Levistici radix, Urticae herba/folium and Solidaginis herba are used since many centuries. The main therapeutic strategy is the increase of urinary flow and the dilution of the urine, resulting in a reduction of stone formation. The clinical efficacy is mainly due to several additive or synergistic pharmacodynamic effects. Herbal drugs for therapy of urolithiasis were shown to be safe during long-term therapy [1, 2]. Scientific monographs of the herbal urologicals are available from the ESCOP (European Scientific Cooperative on Phytotherapy; monographs from 2003 and 2009). For some drugs and preparations the traditional use in urology has been acknowledged by the European Committee on Herbal Medicinal Products (hitherto in monographs on Equiseti herba, Urticae herba and folium, and Solidaginis herba).

Canephron® N is a fixed combination of centaury herb (*Centaurium spec.*), lovage root (*Levisticum officinale* Koch) and rosemary leaves (*Rosmarinus officinalis* L.). Overall, the drugs exert diuretic [3, 4] spasmolytic [6, 7], anti-inflammatory [7, 8, 9], antimicrobial [10, 11, 12, 13], and nephroprotective effects [14].

In Moldova the combination is registered as diuretic for single or additive treatment of chronic infections of urinary tract, for non-infectious chronic inflammations of the kidneys and for urolithiasis. The combination had been introduced to the market in several countries more than 40 years ago. Some trials had shown its efficacy in the treatment of urinary tract diseases alongside with an excellent safety profile [1, 15, 16].

### **The aim of the study**

To determine the effectiveness of usage Canephron®N (dragees) in the complex prophylaxis of recurrent stone formation in patients with urolithiasis.

### **Materials and methods**

An open, single-center prospective randomized controlled study was conducted on the Clinic of Urology and Operational Nephrology of the State University of Medicine and Pharmacy, Chisinau, the Republic of Moldova.

A thorough clinical examination, including anamnestic data, previous treatment, identification of metabolic disorders, etc. were performed for all patients before inclusion in the study.

The inclusion criteria were:

- Men and women aged 18-70 years
- Presence of stones in kidney and ureters, which were treated by open surgery, ureteroscopy, ESWL or medical expulsion therapy.

The exclusion criteria were:

- Idiosyncrasy to drug components
- A pronounced accompanying pathology (Diabetes mellitus, coronary heart disease etc.)

All patients, included in the study, underwent a standard metaphylaxis of UL, which included the treatment, aimed at:

- liquidation of infectious-inflammatory process
- improvement of microcirculation in the kidney tissue
- fluid intake of no less than 2 liters per day in the absence of contraindications related with cardiovascular system
- prescription, depend on the chemical composition of stone and discovered metabolic disorders, of:

- diet therapy limiting the intake of stone forming elements or its precursors in the body
- medicamentous correction of hyperuricemia, hyperuricuria, hypercalciuria, hyperoxaluria, acid-base balance of urine

In addition to the standard metaphylaxis (Control group), patients in Study group were given **Canephron®N** – 2 dragées three times a day, during 3-month course, each 6 months.

Every 6 months, biochemical, microbiological, ultrasound and, if necessary, X-ray examinations were performed for patients, included in the study.

The main criterion of therapy effectiveness was occurrence of recurrent stone formation in the both groups.

Student's t test and Fisher's exact test were used to process the data. Statistical significance was considered achieved when  $p < 0,05$ .

## Results

A total of 86 patients with urolithiasis have been included in study (table 1). Patients distribution according to sex was 32 (37%) women and 54 (62%) men, average age  $42 \pm 12$  years old (from 20 to 62). All patients have undergone outpatient supervision 2-5 years.

Table 1

Baseline patient demographic and anamnestic characteristics

	<b>Group of study (n=50)</b>	<b>Control group (n=36)</b>
Age, years old	45±11,2 (22 – 61)	42±9,2 (20 – 62)
Gender, male/female (%)	31(62%)/19(38%)	23(64%)/13(36%)
Duration of the supervision, years	3,4±1,0 (2 – 5)	3,5±1,1 (2 – 5)
Duration of the disease, years	8,6±4,1 (2 – 15)	8,1±4,0 (2 – 14)
Recurrent stone formation in anamnesis	48 (96%)	32 (89%)
Urinary Tract Infection	31 (62%)	21 (58%)
Composition of concrements:		
Urates	11 (22%)	9 (25%)
Phosphates	12 (24%)	10 (28%)
Oxalates	27 (54%)	17 (47%)

*Note:* Data are expressed as absolute number (%) or Mean ± Standard Error (range);

Stone composition in anamnesis:

- in 44 (51%) patients - calcium oxalate,
- in 22 (25,5%) – phosphate,
- in 20 (23%) – uric acid.

By the beginning of prophylactic treatment, after operative removal of concrements, the disease lasted for 2 – 15 years, 80 (93%) patients had recurrent stone formation, 58 (67%) patients were underwent open surgery or ureteroscopy, 20 (23%) - ESWL, in 8 (10%) patients the stones eliminated spontaneous. Infectious-inflammatory process in the urinary system was diagnosed in 52 (60%) patients.

As it shown in Table 1, at the study beginning, statistically significant differences between treatment groups were not revealed.

In the group **Canephron®N** recurrent concrements have been revealed in 8 (16%) patients, while in the control group in 13 (36%) patients (figure 1). Use of **Canephron®N** allowed twice decrease frequency of recurrent stone formation in the investigated group (  $\chi^2=4,6$ ;  $p=0,03$ ).

Statistical data show a significant decrease in frequency of recurrence in case of phosphate urolithiasis (figure 2).

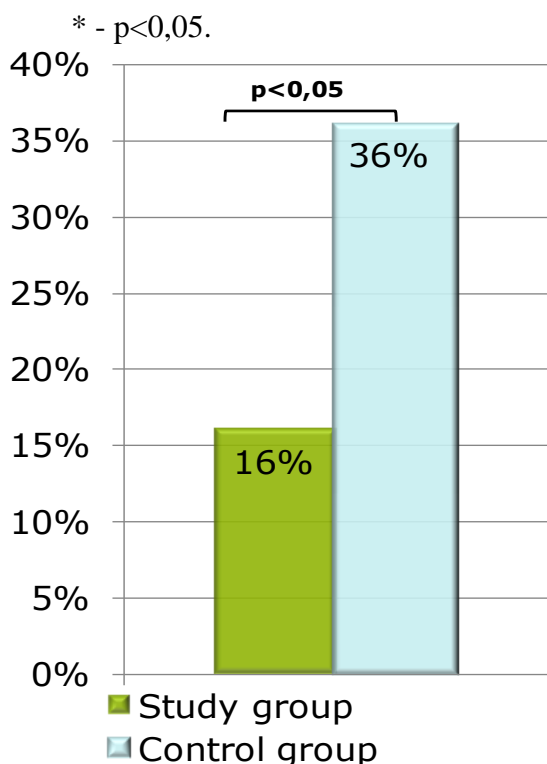


Fig. 1. Rate of recurrent concretions in studied groups.

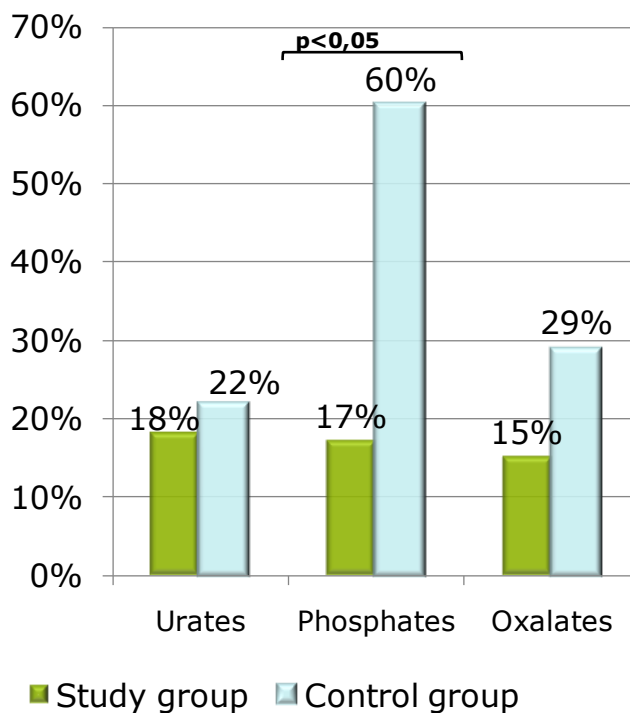


Fig. 2. Rate of stone recurrence according of chemical structure of the stones.

### Conclusions

Use of metaphylactic treatment of urolithiasis with **Canephron®N** allows reliably decrease the possibility of development of recurrent stone formation.

The complex of pharmacological effects of phyto-medicine **Canephron®N** (anti-inflammatory, antibacterial, antispasmodic, diuretic action) allows us characterizing it as a drug of choice for an effective, complex metaphylaxis of urolithiasis.

### References

1. Amosov AV. Herbal Canephron in urological practice. *Doctors* 2000; 6: 36
2. Piteli IUA, Amosov AV. Herbal Canephron in urological practice. *Attending Doctor* 1999; 6: 38–39
3. Haloui M, Louedec L, Michel JB, Lyoussi B. Experimental diuretic effects of *Rosmarinus officinalis* and *Centaureum erythraea*. *J Ethnopharmacol* 2000; 71: 465–472
4. Yarnell E. Botanical medicines for the urinary tract. *World J Urol* 2002; 20: 285–293
5. Ceban Emil. Efficacy of a fixed combination of *Centaurei herba*, *Levistici radix* and *Rosmarini folium* in urinary lithiasis. *Zeitschrift fur Phytotherapie* 2012; 33: 19–23
6. Yamahara J, Konoshima T, Sawada T, Fujimura H. Biologically active principles of crude drugs: pharmacological actions of *Swertia japonica* extracts, swertiamarine and gentianine. *Yakugaku Zasshi* 1978; 98: 1446–1451
7. Gracza L, Koch H, Luffler E. Isolierung von Rosmarinsäure aus *Symphytum officinale* und ihre antiinflammatorische Wirksamkeit in einem In-vitro-Modell. *Arch Pharm* 1985; 318: 1090–1095
8. Rampart M, Beetens JR, Bult H et al. Complement-dependent stimulation of prostacyclin biosynthesis; inhibition by rosmarinic acid. *Biochem Pharmacol* 1986; 35: 1397–1400

9. Valentao P, Fernandes E, Carvalho F et al. Hydroxyl radical and hypochlorous acid scavenging activity of small centaury (*Centaureum erythraea*) infusion. A comparative study with green tea (*Camellia sinensis*). *Phytomedicine* 2003; 10: 517–522
10. European Scientific Cooperative on Phytotherapy (ESCOP). *Centaurii herba* (Centaur herb). In: ESCOP Monographs. 2nd ed. Stuttgart, New York: Thieme; 2003: 70–73
11. European Scientific Cooperative on Phytotherapy (ESCOP). *Rosmarini folium* (Rosemary leaf). In: ESCOP Monographs. 2nd ed. Stuttgart, New York: Thieme; 2003: 429–436
12. Kumarasamy Y, Nahar L, Cox PJ et al. Bioactivity of secoiridoid glycosides from *Centaureum erythraea*. *Phytomedicine* 2003; 10: 344–347
13. Kumarasamy Y, Nahar L, Sarker SD. Bioactivity of gentiopicoside from the aerial parts of *Centaureum erythraea*. *Fitoterapia* 2003; 74: 151–154
14. Sterner W, Heisler E, Popp HO, Fischer H. Studien ber die Canephron-Wirkung bei chronischen Nierenerkrankungen. *Physikalische Medizin und Rehabilitation* 1973; 14:239–258
15. Kovalenko VN. *Compedium 2001/2002 –Medications*. Kiev: Morion; 2001: 1536
16. Lopatkin NA. *Manual of Urology*. Vol. 2, ch. 29: Urolithiasis. Moscow; 1998: 693–761

## **IMPORTANȚA TOMOGRAFIEI COMPUTERIZATE ȘI A ULTRASONOGRAFIEI ÎN DIAGNOSTICUL PIELONEFRITEI ACUTE LA BOLNAVII CU DIABET ZAHARAT**

**Eduard Pleșca, Adrian Tănase, Constantin Guțu**

Catedra Urologie și Nefrologie Chirurgicală USMF „Nicolae Testemițanu”

### **Summary**

#### *The Importance of the Computed Tomography and Ultrasonography in Diagnosing Acute Pyelonephritis in Patients with Diabetes Mellitus*

The impairment of the renal function in diabetics represents a serious problem in therapy, endocrinology as well in urology. The inflammatory renal and urinary pathways diseases are known to be more frequent in diabetics than in non-diabetics, and they have a severe development, complicated by the renal failure and urosepsis, with a lethal ending.

The development of severe forms of AP is determined by such factors as: the late hospitalization, the unclear clinical picture, the late diagnosis and the inadequate treatment of this category of patients. The association of these two severe diseases endangers the life of these patients.

This survey has determined us to realize the retrospective evaluation of the obtained clinical data and to advance some practical recommendations.

The algorithm of the emergency investigations includes the ultrasound scanning, radiologic and radionuclear procedures, but the top place is occupied by ultrasound scanning using the Doppler imaging and the computed tomography.

At present among the most used and effective methods of diagnosing acute pyelonephritis in diabetics is computed tomography.

### **Rezumat**

Afectarea rinichiului în cazul DZ constituie o problemă serioasă atât în terapie și endocrinologie, cât și în urologie, se știe că maladiile inflamatorii ale rinichiului și ale căilor urinare la bolnavii cu DZ este mai frecventă, decât la persoanele fără diabet și se caracterizează prin o evoluție gravă, deseori complicată de insuficiență renală și urosepsis, complicată cu sfârșit letal.

Dezvoltarea formelor grave ale PA este, condiționată de internarea tardivă, tabloul clinic neclar, diagnosticării tardive și tratării neadecvate a acestui contingent de bolnavi. Combinația acestor două maladii grave, crează un pericol potențial pentru viața acestor bolnavi.