EFFECTIVENESS OF USING THE DRUG CANEFPON®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 urolitiazei
Urolitiaza este cea mai răspândită patologie urologică în lume. Aceasta patologie este descrisă ca formarea calculilor în sistemul urinar. În conformitate cu pronosticul, urolitiaza are o continuă tendință ascendentă datorită schimbărilor semnificative în natură și în calitatea alimentelor, acțiunea nefastă a mediului ambiant și factorilor sociali, metabolici și infecțioși. Necătând la aplicarea și implementarea pe scara largă a metodelor eficiente în diagnosticarea și tratamentul urolitiazei, incidența formării calculilor și recurența rămâne 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 supersupersaturation 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] spasmyloytic [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±12 years old (from 20 to 62). All patients have undergone outpatient supervision 2-5 years.

Table 1

Baseline patient demographic and anamnestic characteristics

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

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).

\* - p<0.05.

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

**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 atît în terapie şi endocrinologie, cît şi în urologie, se ştie că maladiile inflamatorii ale rinichiului şi ale căilor urinare la bolnavii cu DZ este mai frecventă, decît la persoanele fără diabet şi se caracterizează prin o evoluţie gravă, deseori complicată de insuficienţă renală şi urosepsis, complicată cu sfârşit lethal.

Dezvoltarea formelor grave ale PA este, condiţionată de internarea tardivă, tabloul clinic neclar, diagnosticării tardive şi tratării neadevrate a acestui contingent de bolnavi. Combinăţia acestor două maladii grave, crează un pericol potenţial pentru viaţa acestor bolnavi.