Phytotherapy of calcium urolithiasis with extracts of medicinal plants: Changes of diuresis, urine pH and crystalluria

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At present the phyto-preparations is still widely used in the clinical practice. The simple extracts (infusions) from medicinal plants which have diuretic effect seem to be the most available for preparation and usage. Unfortunately, both physicians and patients consider that the extracts may be prescribed for a long time without limitation. Most of them are used only with purpose to increase diuresis. Meanwhile they have ability to change other urine parameters. We performed study of effect of the extracts from medicinal plants of the region on the diuresis and urine pH. Degree of crystalluria was determined as the criteria for evaluation of the activity of the process of stone formation. The results of investigations showed that the extracts from medicinal plants besides diuretic effect can in some cases reliably change urine pH and crystalluria degree.

Keywords: Calcium urolithiasis, extract of medical plants, phytotherapy of urolithiasis, urinary risk factors, diuresis, crystalluria, urinary pH

Introduction

The parameter urine pH is the leading factor that predominantly identifies the type of urine calculus. Unfortunately, in practice general practitioners at the first visit take no notice of this parameter and specialists frequently ignore and do not interpreter it in the processes of the urinary lithogenesis. Additionally due to incorrect collection of the urine samples and methods of measurement, the false result is frequently obtained.

According to the literature data (Majdrakov, 1973; Arustamov and Tarasenko, 1992; Stoller and Boulton, 2000), information based on the indicator allows us to get preliminary understanding about the type of stone formation. In parameter of urine pH 5.0 and less the pure uric acid is precipitated, and in the pH range from 5.2 to 5.8 - the salts of uric acid, in the range from 5.0 to 6.0 - oxalates, and in pH 7 - hydroxyl apatite. The alkalinuria occurs in the presence of nonspecific bacterial infection (UTI), and under this situation the infectious stones appear. If infection adds to the stones previously formed, than due to inflammation the salts specific for infectious nephrolithiasis begin to increase (brushit, struvite, ammonia magnesium phosphate) and the stones are infected. In healthy subjects without urolithiasis the pH indicator fluctuates in limits from 6.2 to 6.8. In this diapason, especially, the majority of the stone-forming substances are in the dissolved state and the precipitation and nucleation are not found.

To correct the urine pH in urolithiasis different combined preparations are used, more frequently the citrate mixtures - Magurlit, Blemaren, Urolit, Lithurex, Urocyt-K and others. The difficulty of correction is caused by the necessity of
continuous control of urine pH and titration of preparation dose in relation to changes. In these cases the sharp changes from acidic into alkaline state are observed. During prescription of preparation Urocyt-K due to use of the modern technologies of tablet forms preparation the stage releasing of the active substance occurs that allows to prevent of the pH sharp fluctuations.

These agents also include citric acid that impact on its content in the urine. However, they have no diuretic ability, though to stimulate urine production the thiazide diuretic preparations should be included additionally. At the same time it is impossible to exclude the situation when the combination of two or more preparations may result in changing of their characteristics.

At present the phytopreparations still remain the remedy widely used in the clinical practice. The simple extracts (infusions) from medicinal plants which have diuretic effect seem to be the most available for preparation and usage. Unfortunately, both physicians and patients consider that the extracts may be prescribed for a long time without limitation. Most of all they are used only with purpose to increase diuresis. Meanwhile they have ability to change other urine parameters (Kariev, 1999; Kariev et al., 2004; Gaybullaev et al., 2007). If these extracts are used for a long time ignoring their property to change some risk factors of urolithiasis, then undesirable effect of the therapy performed may be observed that, on the contrary, may intensify some processes of stone formation in the urinary tract.

Material and methods

We have carried out investigations of various properties of the phytopreparations, i.e. their effect on the urinary risk factors in the patients with calcium type of urolithiasis in the Urological Clinic of Tashkent Medical Institute of Postgraduate Education since 1993. The pH of urine is considered to be one of the most important categories for identification of the type of lithogenesis. We performed study of effect of the extracts from medicinal plants of the region (Table 1) on the diuresis and urine pH. Criteria for evaluation of the activity of the process of stone formation were chosen the degree of crystalluria.

<table>
<thead>
<tr>
<th>No.</th>
<th>Preparation</th>
<th>Patients quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Extract of Zizyphus Jujuba mill</td>
<td>22</td>
</tr>
<tr>
<td>2</td>
<td>Extract of Glycyrrhisa Glabra L. (roots)</td>
<td>23</td>
</tr>
<tr>
<td>3</td>
<td>Extract of Mentha piperita L. (leaves)</td>
<td>24</td>
</tr>
<tr>
<td>4</td>
<td>Extract of Bidens tripartita L.</td>
<td>24</td>
</tr>
<tr>
<td>5</td>
<td>Extract of Achillea millefolium L.</td>
<td>25</td>
</tr>
<tr>
<td>6</td>
<td>Extract of Helichrysum archarium Samarkand L.</td>
<td>27</td>
</tr>
<tr>
<td>7</td>
<td>Extract of Origanum L.</td>
<td>24</td>
</tr>
<tr>
<td>8</td>
<td>Extract of Maydis stigmatum</td>
<td>26</td>
</tr>
<tr>
<td>9</td>
<td>Extract of Aerva lanata (Pol-Pala)</td>
<td>27</td>
</tr>
<tr>
<td>10</td>
<td>Extract of Alhagi pseudalhagi (MB) Desv. (Yantak)</td>
<td>28</td>
</tr>
<tr>
<td>11</td>
<td>Extract of Hypericum perforatum L.</td>
<td>25</td>
</tr>
<tr>
<td>12</td>
<td>Extract of Hernia Glabra L.</td>
<td>21</td>
</tr>
<tr>
<td>13</td>
<td>Distilled water (Control)</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Total number of patients</td>
<td>316</td>
</tr>
</tbody>
</table>
In long-time metaphylaxis of stone recurrent formation in 316 adult patients suffering from calcium urolithiasis was carried out. Cases of uncomplicated urolithiasis were included, with patients living at homogeneous conditions (urban population). In accordance with the course of disease, patients were classified into three types of calcium urolithiasis: So, (first-time stoner without residual stone or fragments), Sres (first-time stoner with residual stone or fragments), and Rmo (recurrent stone former with mild disease and without residual stone(s) or fragments (Tiselius et al., 2009).

Mean age was 43.3±3.2 years (18-71 years). Extracts was administered as only therapeutic device at a daily dose of 1 ml on each 1.0 kg of body weight over a period of 2 months. Owing to seasonal changes in diuresis rate data were collected only in colder periods of the year (autumn, winter, spring) to ensure a correct interpretation; during summer season the hot temperatures in Uzbekistan may lead to a drastic decrease in the amount of urine.

Each participant was given verbal and written instructions about the collection of urine samples. Control of diuresis dynamics was carried out by patients’ diaries of diuresis. Improper collection of urine was excluded. Subjects were also instructed to collect the sample while on their usual diet and to avoid any medical therapy that may alter the urinary data. The daily fluid intake of every patient (via diary) was also taken into consideration.

According to the classification proposed by Kholmatov (1979) in relation to intensification of the diuretic effect the studied extracts from the medicinal plants of our region were divided into 3 groups:

- **Group 1** - active diuretics, increase of diuresis by 50% and more - included extracts of Alhagi pseudalhagi, Aerva lanata, Herniaria glabra L.
- **Group 2** - diuretics of moderate effect increase of diuresis by 25-50% from initial volume - included extracts from Maydis stigmatum, Glycirrhiza glabra L., Hypericum perforatum L., Achillea millefolium L.
- **Group 3** - mild diuretics - increase diuresis by less than 25% from initial volume - included extracts from Helichrysum archarium Samarkand L., Origanum L., Zizyphus Jujuba mill, Mentha piperita L.

**Technique of urine pH registration.** The parameters of urine pH were measured during 15 minutes after sample collection. After the contact with the environment the chemical properties begin to change and, consequently, urine response converted from acidic state more frequently into neutral and even alkaline, particularly in the hot periods of year. The urine collection was performed into the dry, clean, made of intact material (glass, plastic) containers with tightly closed cover. Measurement was performed with use of ionometer EV-74 after regularly calibration with use of standard buffer titre-solutions

**Technique of crystalluria investigation.** Evaluation of crystalluria was performed by technique offered by Klepikov et al. (1992). The fresh urine 100 ml was collected into the conic glass cylinder. After exposition during 2 hours in 37º C there were taken 2 ml of urinary sediment from the bottom of the cylinder that was intensively shaken in the tube. During the shaking 3 µl of the precipitate with use of micropipette were taken from the bottom of the tube and were put into the counter chamber after that calculation and analysis of the crystals was performed. Calcium oxalate (CaOx) in the urine presents as octahedral crystals of weddellite (“post envelopes”) of sizes from 5 to 15µm achieving 50-100 µm in some cases. CaOx was found more seldom in the sediment looking as watch glass, dumb-bells or ovals (uvellit). Both types of crystals CaOx may be adhered into aggregates forming microuroliths.

According to offered classification there are 3 grades of crystalluria intensity:
In the diagrams of Figure 1, Figure 2, and Figure 3 mean parameters of the changes of diuresis, urine pH and crystalluria were presented in our patients during 2 months of phytotherapy with extracts of studied medicinal plants. While studying the average daily indicator of urine pH we found that it changed and was independent on the force of diuretic effect and was different not only in every extract but also during 2-month course of treatment.

It was found out that the use of extracts from medicinal plants, besides diuretic effect, showed their effect on the urine pH and crystalluria. Only two preparations had the capacity to increase urine pH, they are diuretic of moderate action Hypericum perforatum L. and mild diuretic Bidens tripartita L. Unreliable tendency of pH growing was observed in use of strong diuretics Aerva lanata (Pol-Pala) and Herniaria glabra L., moderate diuretics Glycyrrhiza Glabra L. and Achillea millefolium L., as well as mild diuretic Zizyphus Jujuba mill.

At the same time the active diuretic Alhagi pseudalhagi (Yantak) demonstrated capacity to reduce the urine pH reliably and for a long time. Almost similar situation was observed in patients receiving Helichrysum Archarium Samarkand L.
The rest of studied extracts of medicinal plants induced only insignificant and unreliable urine pH fluctuations: extracts of Maydis stigmatum and Origanum L.
towards the increase and Mentha piperita L. towards the reduction of the urine pH.

The most marked capacity to reduce crystalluria was found in Yantak, then in Herniaria glabra L., they are strong diuretics. Then moderate diuretic Maydis stigmatum followed and weak diuretic Zizyphus Jujuba mill. The moderate diuretics Achillea millefolium L. and Glycyrrhiza glabra L., as well as weak extract Helichrysum archarium Samarkand L. were the following in the List and only then the strong diuretic Pol-pala came. After that there were weak diuretics - Bidens tripaprite L. and Origanum L. whose efficacy was lower than in the control group where the patients received distillated water. And during receiving of the extracts of Hypericum perforatum L. and Mentha piperita L., on the contrary, increasing of crystalluria was observed. This was expressed very brightly in the group of patients receiving extract of Hypericum perforatum L. when crystalluria increase was accompanied by frequent attack of renal colic. It was interesting that urine pH after phytotherapy with extract of Hypericum perforatum L. was close to the level of healthy individuals. And in group receiving Mentha piperita L. tendency to urine pH lowering was noted, that is, aggravation of the factor contributing to stone formation. The noted urine pH increase in prescription of Bidens tripaprite L. did not change activity of stone formation process and the degree of crystalluria did not change. If the crystalluria changes would be compared under the effect of distillated water and Pól-Pala extracts it may be noted that the former had stronger capacity to reduce crystalluria intensity with less diuretic capacity.

Discussion

In geographical areas with dry and hot continental climate the problem of increase in diuresis in patients with urolithiasis is the most important one. Enhancement of diuresis contributes to a decrease in stone-forming urine factors. Under the above mentioned climatic conditions increase in fluid consumption alone (daily fluid amount: 2.5-3.0 L), as advised by the guidelines from EAU (Türk et al., 2011), is not satisfying. Thus there is need of an additional stimulation of diuresis. In many cases phytopreparations with diuretic properties are of choice. In our opinion, supersaturation of urine with stone-forming components contributes not only to their increased excretion via kidneys but to a significant decrease in urine volume during hot seasons. The investigated herbal extracts are obviously able to improve several factors of calcium stone-formation, e.g. increase in diuresis and urine pH. Changes urinary risk factors were manifest more markedly after a prolonged treatment over a period of 1 month. Additionally a decrease in the crystalluria degree can be observed during the 2-month-course. For this reason it must be taken into account that plant medicines do not only possess diuretic properties but also have the ability to influence saluresis (increase of ion excretion).

Therefore the long-term administration of the herbal preparations able markedly affects several factors promoting stone formation (see Figure 1 and Figure 3). The important fact is that changes of crystalluria had not direct dependency only on diuretic force of investigated extracts. Thus, besides diuretic effect the extracts from medicinal plants may influence on the other urinary factors of lithogenesis. Such a multifactorial influence is considered as suitable for the prophylaxis of recurrences. The efficacy of phytopreparations should be evaluated upon prolonged follow-up of the results of metaphylaxis.

The results of investigations showed that the extracts from medicinal plants besides diuretic effect can in some cases reliably (p<0.05) change urine pH (Yantak, Hypericum perforatum L, Helichrysum archarium Samarkand L., Bidens tripaprite L.). The power of diuretic effect is different and maybe dependent on the chemical composition of the plant, i.e. contents of biological active substances and
their combinations. The observed changes are, first of all, natural result of the complex chemical contents of the medicinal plants and the extracts obtained from them. These shows that individual selection of the extracts from the medicinal plants should be performed taking into account their capacity to change some urinary risk factors. Thus, besides the expected increase in diuresis the urine pH can be also changed.

Taking into consideration the results obtained in different situations there may be the following recommendations:

- In cases when it is necessary, besides the increase in diuresis, to reduce urine pH in association with UTI the extracts having property to reduce urine pH should be prescribed. They are Alhagi pseudalhagi, Helichrysum areharium Samarkand L. and Mentha piperita L.;
- in cases when it is necessary to increase diuresis without changing of urine pH it may be recommended as monophytopreparation extracts of Maydis stigmatum, Glycyrrhiza glabra L., Achillea millefolium L., Zizyphys Jujuba mill, and Origanum L.;

The property to increase urine pH was found among studied medicinal plants only in extracts of Hypericum perforatum L. and Bidens tripartite L. Unfortunately this extracts property in the patients was not long-term and did not result in achievement of parameters of healthy individuals. At the same time the prolonged phytotherapy with Hypericum perforatum L. in the patients of this group resulted in marked increase in crystalluria degree which was accompanied by increase in number of cases of renal colic. That is, with purpose to increase the pH level the prescription of the extract Hypericum perforatum L. as monotherapy in the patients with urolithiasis is not rational due to presence of clinical complications.

Of course, the data of our investigation would be interesting to develop in further long-term placebo control studies for to get more information about the onwards trend of decrease of lithogenesis due to the effects of extracts components. However, under the conditions of our experience in urological praxis we consider the study results as very promising.

**Conclusion**

Thus, besides diuretic effect the extracts from medicinal plants may influence on the other urinary risk factors of stone formation. Consequently, these properties of the extracts should be noted in cases of their inclusion into the complex of therapeutic measurements in urolithiasis. Especially, the indicator of urine pH should be taken into account which is one of the parameters characterizing pathogenesis of stone formation. Unfortunately, among the studied extracts from medicinal plants were not found the ones which would be able to increase urine pH reliably without complications.

The property to acidate urine on the basis of strong diuretic effect was found in Alhagi pseudalhagi, and on the basis of moderate diuretic effect – not, and on the basis of weak diuretic effect this property was found in Helichrysum archarium Samarkand L. and Mentha piperita L.

Maydis stigmatum, Herniaria glabra L., Glycyrrhiza glabra L., Achillea millefolium L., Zizyphus Jujuba mill - increase diuresis without change of urine pH.

In cases of requirement of strong diuretic preparation with marked ability to reduce crystalluria then Alhagi pseudalhagi, Herniaria glabra or Maydis stigmatum may be the preparations of choice. In case of recommendation of extract Alhagi pseudalhagi it should correct pH with preparations having property to alkality urine. Evidently it would be more rationally to prescribe this extract in marked
Phytotherapy of calcium urolithiasis with extracts of medicinal plants

crystalluria (more frequently in phosphate) and alkaline urine (in UTI as well as after ending or during of its basic treatment), when there is need to increase diuresis and to acidate urine.

For moderate stimulation of diuresis without acute necessity of urine alkaliifying the preparations of choice included extracts of Herniaria glabra L., Maydis stigmatum, Glycyrrhis glabra L., Achillea millefolium L. and Zizyphus Jujuba mill.

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