

The clinical course of urolithiasis in children under 3 years of age

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ABSTRACT

Purpose: Certain risk factors of urolithiasis may be diagnosed in 75% of children with stones. They include genetic, anatomic, metabolic and nutrition causes. The diagnostics' evaluation should determine and rule out anatomic factors and establish metabolic disorders. The treatment is based on an increased fluid intake, and alterations in the nutrition pattern. The aim was to analyze the clinical course of urolithiasis in children below 3, and detect the possible factors affecting the success of therapy.

Materials and methods: Between 2009 and 2013, we retrospectively investigated the cases of 68 children (34 boys and 34 girls) under 3 years who were treated in the clinic. Urolithiasis was diagnosed at the mean age of 10 months; the average follow-up lasted 26 months until reaching 3 years. The retrospective analysis was based on medical documentation and direct contact with parents.

Results: Among the risk factors, the most common was hyperciuria. The treatment of children was based on an increased daily fluid intake and dietary recommendations. Among the specific treatments, the most common were citrates (51%). In the majority of cases, the therapy lasted over a year after the clinical absence of stones. This therapy was successful in 62% of children. The factors contributing to the success of the treatment were: a negative family history of urolithiasis, unilateral stones, normal urinalysis, decrease of the Ca/Cr index, and compliance of dietary and medical recommendations.

Conclusions: The treatment is based on the elimination of risk factors, and alterations in the dietary pattern. High percentage of parents did not respect the medical recommendations.

Key words: Urolithiasis, pediatrics, treatment, risk factors.

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INTRODUCTION

In the process leading to urolithiasis, one of the most important roles is played by the risk factors leading to excessive urine crystal formation; in that genetic, environmental, and dietary disorders [1-3].

In recent publications concerning the European children, the presence of the risk factors reach up to 75% of children under 15 years [4-7]. As the most important we can outline as follows: metabolic disorders (up to 80%), infections of the urinary tract (46%), urinary system malformations (10-20%). Among the metabolic disorders, the most common are hipercalciuria (34%), hiperuricosuria (8%), cystinuria (7%) [4-7].

When considering the youngest children under 3 years of age, the diagnostic tract should be based on an accurate medical history, with regard to the urolithiasis risk factors, then on the exclusion of urinary tract malformations, and finally on the biochemical urine and serum analysis [8-10]. The therapy should be based on an extensive daily fluid intake (in all groups of urolithiasis), and on the specific treatment applied after determining the metabolic disorders [1]. The surgical treatment is reserved for the most severe cases of urolithiasis (even up to 20-30%) accompanied by urine tract malformations [11].

The aim of this paper is to analyze the clinical course of urolithiasis in children under 3 years, and detect the possible factors affecting the success of therapy.

MATERIALS AND METHODS

Between 2009 and 2013, we retrospectively investigated 68 children (34 boys and 34 girls) under the age of three, treated in the tertiary reference nephrological centre.

The selection criteria for the analysis were: diagnosis of urolithiasis before the age of 3 years based on USG or clinical criteria (the presence of the stone). Urolithiasis was diagnosed at the mean age of 10 months; the average follow-up lasted 26 months, until reaching 3 years (mean number of consultations – 5). The retrospective analysis was based on available medical documentation, and direct contact with parents.

We collected data, including the symptomatology, perinatal history, family history, results of imaging and biochemical tests, including parameters such as the concentration of serum creatinine, uric acid, calcium, phosphorus, magnesium, alkaline phosphatase, and the crystallization indexes in urine. We estimated the prevalence of urinary tract infection; we analyzed the medical recommendations – daily fluid intake, dietary orders, vitamins intake and pharmacological treatment.

We established hipercalciuria, when the Ca/Cr index reached above 0.81 mg/mg for children under 1 year, and above 0.53 mg/mg for children under 3 years, hiperuricosuria with UA/Cr above 1.9 mg/mg, and hipomagnesuria when Mg/Cr index decreased under 0.13 mg/mg [12]. Because of the retrospective nature of the investigation, we could not determine the Ox/Cr and citrate indexes.

In our research, we divided children into two groups with respect to the effectiveness of the treatment. To the first group, we qualified children with observed absence of calculi in subsequent imaging tests by the end of the follow-up 42 (62%) (Group 1). To the second group (Group 2), we qualified children with remaining calculi despite the appropriate therapy 26 (38%).

For the imaging of calculi, we used the ultrasound Aloca prosound Alfa 7.

Statistical analyses were performed with SigmaPlot for Windows version 11.0. Data were expressed as mean, absolute values and percentages. Chi-square test was used to investigate the relationship between nominal variables. The paired t-test was used to compare the outcome of the treatment (the normality of distribution of differences). A $p < 0.05$ was considered to be statistically significant.

This study was approved by the Ethics Committee of Polish Mothers Memorial Hospital Research Institute.

RESULTS

All children had normal kidney function. Among our children, urolithiasis was observed at the mean age of 10 months (ranging from 2 days to 35 months of age). The stones were most commonly small, under 2 mm with unilateral and bilateral localization in equal proportions (46% vs 54%). The stones bigger than 2 mm, were localized more often unilateral with a prevalence of left kidney (left-side side – 31%, right side – 69% $p=0.017$). Unilateral urolithiasis was diagnosed in 45 (66%) children, bilateral in 23 (34%). Family history was positive in 35 (52%) children.

During the first hospitalization 66 (97%), children received the dietary recommendations (fruits and vegetables, sodium-low diet, purine-low diet, or magnesium-high diet), 64 (94%) daily fluid intake recommendations (in that water intake above 700ml in children under 1 year of life, and water, tea, juices intake above 1000ml in children over 1 year) (Table 1), 32 (47%) vitamins intake restrictions (including total limitation of vitamin D3 and multivitamins), specific pharmacological treatment was necessary for 30 (44%) children.

Table 1. Dietary initial recommendations.

| Dietary recommendations | Patients |
|-------------------------|----------|
| Fruits and vegetables | 26 |
| Low-sodium diet | 15 |
| Low-purine diet | 5 |
| High magnesium diet | 2 |
| Non specified diet | 18 |

Among the specific treatments, the most common were citrates 18 (60%) at a dose corresponding to the body weight (combined formulation of sodium citrate and potassium citrate at a dose of 0.3g/kg/day), as well as the supplementation of magnesium 6 (21%) (at a dose of 5–10 mg/kg/day of magnesium citrate). Initially, psychomotor retardation was diagnosed in 13 (19%) children. The height and weight of children are shown on Fig. 1, Fig. 2. The alterations of biochemical indexes were present in 55 (81%) children, in that hypercalciuria – 8 (15%), hiperuricosuria – 2 (4%), hipomagnesuria – 23 (42%), abnormal Mg/Ca index 22 (39%). Abnormalities in urinalysis occurred in 56 (83%) cases, whereas 38 (56%) children showed symptoms connected to urolithiasis (mainly restlessness, nausea, vomiting, dysuric symptoms).

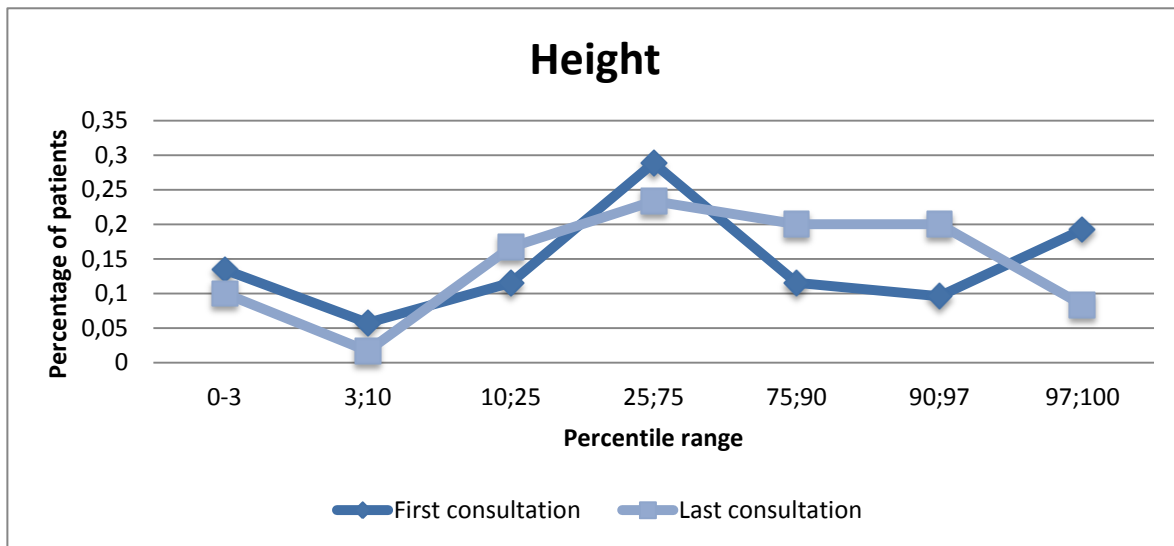


Figure 1. The height of children with urolithiasis.

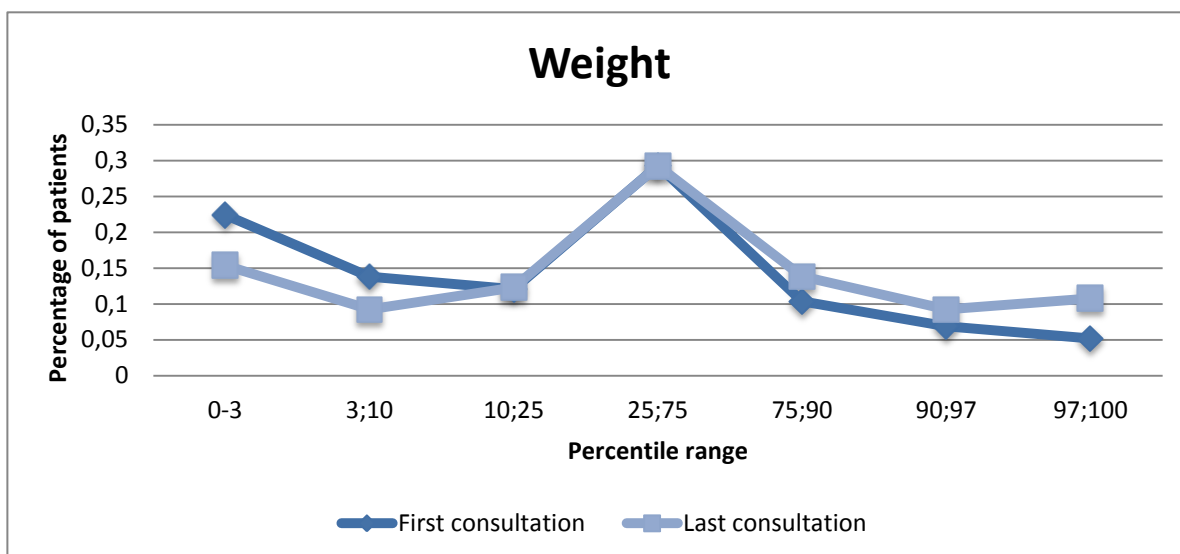


Figure 2. The weight of all children with urolithiasis.

At the end of the follow – up period the dietary recommendations were maintained in 62 (91%) children, daily fluid intake recommendations in 63 (93%), vitamin restrictions in 12 (18%), and pharmacological treatment in 24 (35%). The psychomotor retardation was present in 6 (9%) cases. The alterations of biochemical indexes were present in 21 (31%) children in that: hipercalciuria – 2 (9%), hiperuricosuria – 0 (0%), hipomagnesuria – 11 (52%) abnormal Mg/Ca in 8 (39%). Abnormalities in urinalysis occurred in 44 (65%) cases, whereas 11 (16%) children showed symptoms connected to urolithiasis.

We can see that during the treatment there was no necessary to keep the dietary recommendations (according to medical documentation) in 4 (6%) cases, the daily fluid intake recommendations in 1 (2%), the vitamin restrictions in 20 (30%), whereas the pharmacological treatment in 6 (10%) children. 34 (50%) less children revealed the biochemical alterations (the absolute value of hipercalciuria was lower by 6, hiperuricosuria by 2, the abnormalities In Mg/Cr index by 12, and Mg/Ca by 13). The alterations in urinalysis were present in 12 (18%) less children, in addition 27 (40%) less patients showed any symptoms connected to urolithiasis. (Table 2).

Table 2. Percentage before and after the therapy.

| Characteristics | Initial | Final |
|------------------------------|---------|-------|
| Dietary recommendations | 97% | 91% |
| Fluid intake recommendations | 96% | 93% |
| Pharmacotherapy | 45% | 35% |
| Vitamin restrictions | 47% | 18% |
| Biochemical abnormalities | 81% | 31% |
| Abnormal urinalysis | 83% | 65% |
| Symptoms | 56% | 16% |

At the age of three, 42 (62%) had no clinical and radiological manifestations of stones in subsequent tests. The mean time from the start of the treatment, to the absence of radiological manifestations of stones is half a year, however considering the specific treatment – the vitamin restrictions lasted usually 6 months after the absence of stones, the pharmacotherapy – a year, the dietary and fluid intake recommendations – to the end of the follow – up period (3 y of age).

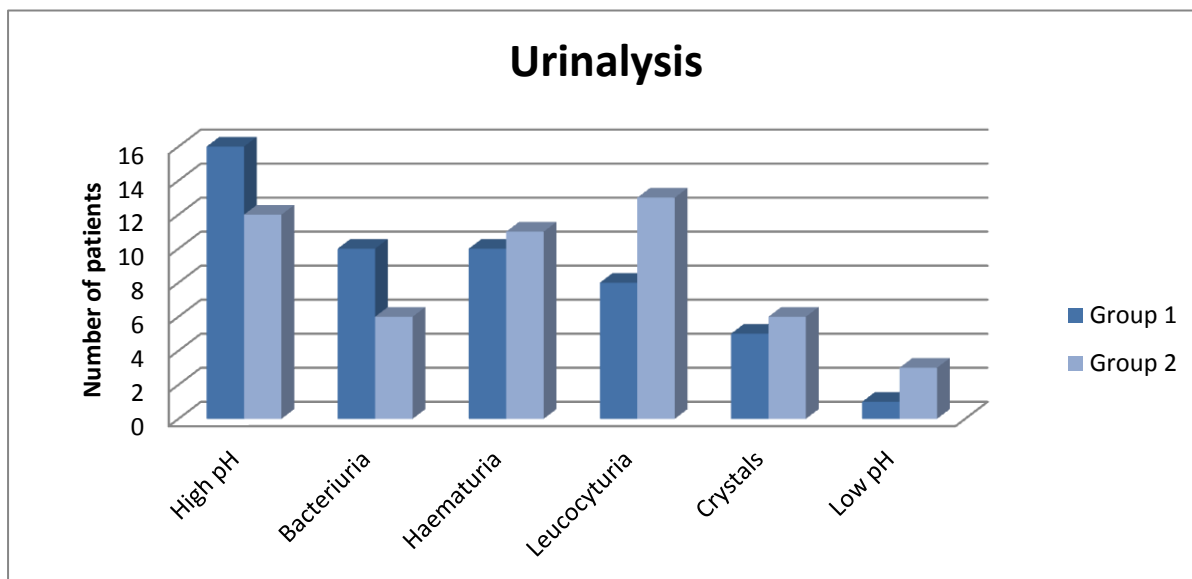


Figure 3. Differences between groups – urinalysis.

When considering the two researched groups (Group 1 and Group 2) – Group 1 (successful treatment) and Group 2 (persisting stones). Group 1 had statistically lower Ca/Cr index after the treatment (p=0.03). In Group 2, there was no such difference. In Group 1 the stones were more frequently unilateral (78% vs 52%) (P<0.05), there were less abnormalities in the results of urinalysis (65% vs 80%), in that bacteriuria (38%

vs 48%), hematuria (23% vs 44%), leucocyturia (19% vs 52%) low urine pH (pH<5) 3% vs 12% (all of the above statistically significant, p<0.05) (Figure 3).

The children from Group 1 received the treatment based on citrates and thiazide diuretics less often 36% vs 58% and 2% vs 8% (p<0.05). However, the restrictions concerning vitamins (in that vitamin D and multivitamins), were more often: 52% vs 23% (p<0.05). We can conclude that

the treatment was less specific, however more restricted.

Considering the family history, the overall adherence to the therapy, and compliance with the restrictions, we observe, that the positive family history was present in fewer children of Group 1 (43% vs 68%) ($p < 0.05$).

What is more, the compliance and adherence to the therapy were better in Group 1, the parents more frequently admitted, that they obeyed the restrictions 75% vs 57% ($p < 0.05$). All of the differences above were statistically significant (Figure 4).

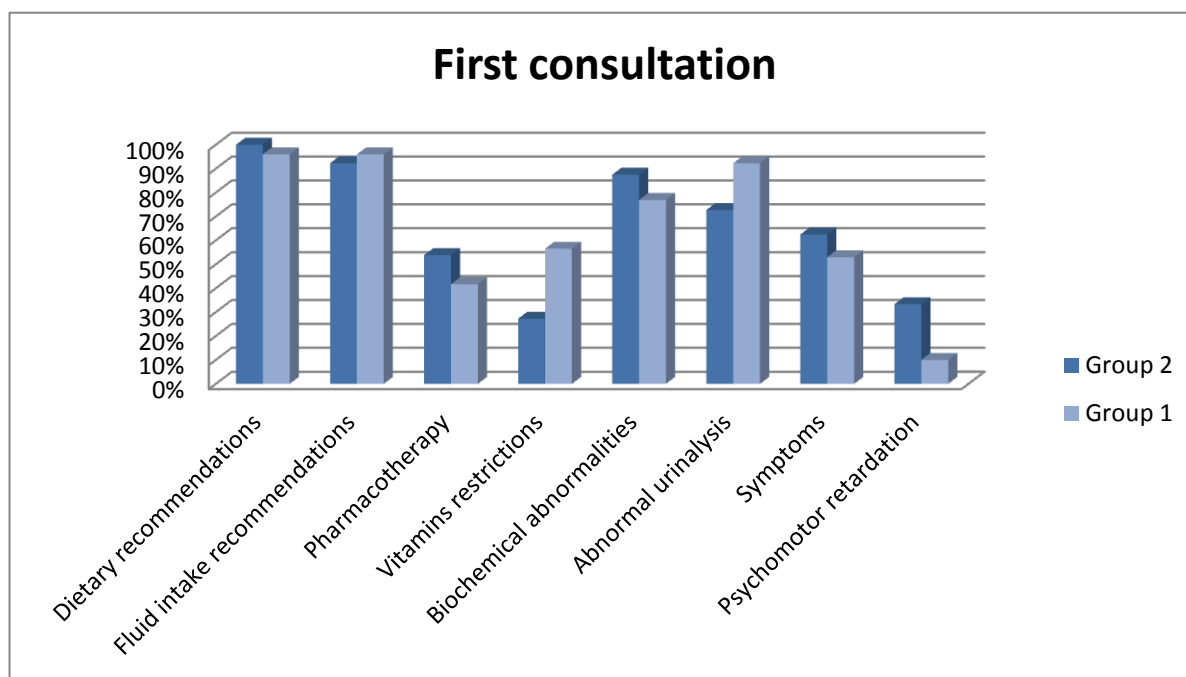


Figure 4. Differences between groups – first consultation.

We investigated also the correlations between other therapeutical recommendations (dietary alterations, daily fluid intake, supplementation of magnesium), initial indexes of crystallization in urine, comparison of initial to final indexes of crystallization, the size of calculi, the initial age, and the height and weight of children; however, we discovered no statistically significant correlations.

DISCUSSION

In our paper, we focused on the analysis of the factors affecting the efficacy of the therapy, and the effectiveness of various therapies recommended in treating urolithiasis. The treatment applied to 97% of children was focused on an increased daily fluid intake. The study by Bastug et al. recommended 750ml fluid intake for children under 12 months, and above 1000ml for children under 5 years of age [1]. This intake of drinks per day reduces the risk of precipitation of crystals in the urine. However, not only the amount and nature of the fluid intake affect the efficacy of treatment. It has been found that specific drinks prevent the precipitation of crystals in the urine better than others: coffee with or without caffeine, tea, water

and wine. However, there are also drinks causing the precipitation of urine crystals, in that: apple and grapefruit juice. Among the children in our study, the most commonly recommended for infants fluid was boiled water; in the case of children, over 1 year of age there was not only water, but also tea and juices. So far, the data on dietary recommendations applied to the youngest children were very scarce, hence it is difficult to conclude whether in this age, there are also such differences in the impact of various liquids on the crystallization of stones [13-17].

The second most important components of the therapy were dietary alterations - a low-sodium and low peptide diet. In other papers, both diets have their reasons. It has been demonstrated that there is a positive correlation between the ratio Na/Cr and Ca/Cr in children under 5 years of age [18]. What is more, there is an inverse correlation between K /Cr and Ca /Cr in random urine samples. Therefore, children with higher Ca/Cr index should obtain a low-sodium diet, even if we could not measure the Na/Cr ratio [18].

On the other hand, the low peptide diet is proven to reduce the risk of the recurrence of kidney stones. In a study where adults were investigated; the daily calcium excretion has not

diminished after reducing the purines' intake, but oxalate excretion was reduced by about 80 micromoles per day. That proved the inverse correlation between the intake of purines and the excretion of oxalates Borghi et al. [19]. The diet should be applied in the case of oxalate stones; however, in other papers it is widely recommended also for other types of urolithiasis [18].

In recent publications, it is recommended to begin the treatment with the high daily fluid intake and dietary alterations consistent with the metabolic disorders, a low-sodium diet for hypercalciuria, oligopurine diet for hyperoxaluria Bastug et al. [1]. Only in the case of ineffectiveness of such therapy (bigger stones, recurrence of urolithiasis) specific pharmacological treatment should be given - about 30-40% of cases [1]. This is consistent with our results, in which 45% of children required the pharmacological therapy; the others were treated alone with the diet and water saturation. In the case of children treated pharmacologically, the dietary treatment was continued [16].

According to Bastug et al. [1] the pharmacological treatment should be based on oral administration of potassium citrate at a dose 0.2-0.3 g per kg per day to alkalize the urine of patients with calcium, oxalate, cystine, urine stones and to reduce their urine crystallization. It is also recommended to prevent excessive acidification of the urine below pH 5 which is an important risk factor for urolithiasis. Our patients were treated mostly with citrates at a dose appropriate to the body-mass.

In a study concerning the compliance with medical orders in patients with urolithiasis, it was observed that the 100% compliance was responsible for 55% of the success (reduction in the risk of recurrence). In contrast, the compliance level of 25% reduces the chance of success by 80%. In our study, the group in which there were no present calculi in the stone tract by the end of the follow-up reached the compliance with therapy of 75%, while in the other group, it was only 57% of parents. This is an important difference [20].

There also are publications showing that the long-term adherence (five years) to diets that feature normal levels of calcium intake, low protein and low salt, may reduce numbers of stone recurrences [21]. Adherence to a low salt, normal calcium level diet for some months can reduce calciuria and oxaluria. However, the other dietary interventions examined did not demonstrate evidence of significant beneficial effects. We can conclude, that the most important issue in compliance and adherence to the therapy not the pharmacological issue, but the dietary one, which is also the more difficult part of the treatment to maintain [21].

In the paper of Parks et al. [22] it has been proven, that at best and despite the therapy, only 70% of patients with urolithiasis retain the treatment in a 5 year follow-up. It is a little more than in our research, as we reached the adherence of around 65% in a mean follow-up time of around 2 years, we can forecast, that in 5 years follow-up this index would be even lower.

CONCLUSIONS

Urolithiasis in children under 3 years is oligosymptomatic, and the treatment is based on the elimination of risk factors, and alterations in the dietary pattern lasting until the age of three. Specific pharmacological treatment is indispensable to 45% of children and it last over a year after the clinical absence of stones. High percentage of parents did not respect the dietary and medical recommendations (34%). The factors predisposing to the success of the treatment were: a negative family history of urolithiasis, unilateral stones, normal urinalysis after treatment, decrease of the Ca/Cr index, and compliance of dietary and medical recommendations.

Conflicts of interests

The authors declare no conflicts of interest.

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