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TOPIC PAPER

Dietary management of hypocitraturia in children with urolithiasis: results from a systematic review

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Abstract

Purpose Hypocitraturia is a low urinary excretion of citrate and a well-known risk factor for kidney stone development in children. This systematic review aimed to evaluate the dietary management of hypocitraturia in children with urolithiasis.

Methods Literature search was performed on 30th September 2022 using Embase, PubMed, and Cochrane Central Controlled Register of Trials. Studies were included if children with stones and hypocitraturia were managed with diet supplements.

Results Six papers were included. Four studies evaluated the role of oral potassium citrate associated with high fluid intake on stone resolution and recurrence. Two studies assessed the impact of oral potassium citrate on long-term stone recurrence after percutaneous nephrolithotomy and shock wave lithotripsy. All studies demonstrated that the association of potassium citrate and high fluid intake was well tolerated with no side effects and restored normal urine citrate excretion, allowed a reduction in stone size, and, following definitive treatments, was associated with a lower rate of stone regrowth and recurrence compared with controls. These effects were demonstrated across all pediatric ages.

Conclusions Our review infers that oral potassium citrate and high fluid assumption are safe and effective in restoring urine citrate excretion, treating and preventing stone recurrence with no serious adverse events, and should probably be the first-line treatment of pediatric patients with asymptomatic stones and hypocitraturia.

Keywords Hypocitraturia · Potassium citrate · Urolithiasis · Infant · Child · Adolescent

Introduction

Hypocitraturia is a low urinary excretion of citrate and a well-known risk factor for kidney stone development both in adults and children [1]. The incidence of hypocitraturia in children ranged from 10 to 64% [2]. Urine citrate is an inhibitor of stone formation functioning mainly in the renal tubule where citrate complexes with calcium, increasing its solubility and reducing the concentration of free calcium in the urine [1]. The calcium-citrate complex can limit calcium supersaturation in urine and inhibits nucleation of both calcium phosphate and calcium oxalate, partially through interactions with the Tamm-Horsfall protein [3]. The second effect of citrate is preventing crystal agglomeration and growth through its ability to prevent the adhesion of calcium oxalate to renal epithelial cells, increasing its solubility and reducing the concentration of free calcium in the urine [4]. Citrate excretion is related to urinary pH and, consequently, can influence the generation of different types of stones.

Hypocitraturia in children has been defined as 24 h citrate to creatinine ratio of < 400 mg/g or < 180 mg/g regardless of gender [5]. Other definitions consider gender-dependent values with the lower limits to be daily urine citrate to creatinine ratio of 125 mg/g in boys and 300 mg/g in girls or 1.9 mmol (365 mg)/1.73 m^2 in males and 1.6 mmol (310 mg)/1.73 m^2 in females [6]. Some authors have stressed the need to establish daily total citrate excretion values in

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children akin to adult reference values, and but, unlike adults, the actual urinary citrate concentration might be more important than the total 24 h urinary citrate output [7]. Kovacevic et al. proposed that hypocitraturia appears to be dietary in origin, correlated with low consumption of potassium and magnesium, and the presence of hypocitraturia overtook hypercalciuria as the most important metabolic abnormality in pediatric urolithiasis [8], particularly in certain regions such as in Turkey [9]. However, hypocitraturia has also been detected in distal renal acidosis and from low intestinal alkaline absorption [7].

In this paper, we aimed to review the dietary management of hypocitraturia in children suffering from urolithiasis.

Evidence acquisition

Literature search

We performed a systematic review assessing the influence of dietary supplementation on children with urolithiasis and hypocitraturia. The literature search was performed on 30th September 2022 using PubMed, EMBASE, and Cochrane Central Controlled Register of Trials (CENTRAL). The following term and Boolean operators were used: (hypocitraturia OR low urine citrate) AND (potassium citrate OR supplement OR food OR dietary OR citrate OR alkali citrate) AND (urinary calculi OR urinary stone OR urolithiasis). Only English papers were accepted. Prospective randomized studies, retrospective, and prospective non-randomized studies were included. Animal studies, case reports, letters to the editor, and meeting abstracts were excluded.

Selection criteria

The following PICOS (Patient Intervention Comparison Outcome Study type) model was used to frame and answer the clinical questions. *Patients*: infants/children/adolescents suffering from urolithiasis and with concomitant hypocitraturia; *Intervention*: treatment with potassium citrate, alkali citrate, or food/beverage; *Comparison*: no comparison; *Outcome*: increase in urine citrate levels and/or reduction in stone episodes; *Study type*: prospective randomized studies, retrospective, or prospective non-randomized studies.

Study screening and selection

All retrieved papers were screened by two independent authors through Covidence Systematic Review Management® (Veritas Health Innovation, Melbourne, Australia) and a third author solved discrepancies. Study inclusion was performed accordingly to PICOS criteria of eligibility. The full text of the screened papers was selected if found relevant to the purpose of the present review. The screening process was then refined by manually researching the references of the included full-text papers.

Evidence synthesis

Literature screening

Literature search recovered 1917 studies. After deleting 534 duplicates, 1383 studies were left for screening against title and abstract. Among these, 1253 studies were excluded because were deemed irrelevant to this review. The remaining 130 full-text papers were further assessed for eligibility and 125 papers were further excluded. Five studies were considered eligible and included [10–14], and one study was manually retrieved from the reference of included studies [15]. Figure 1 summarizes the flow diagram of the literature search.

Study characteristics

There were two retrospective [10, 14] and four prospective studies [11–13, 15], and one among the latter was randomized [12]. Table 1 shows the study characteristics.

Discussion

Diet and hypocitraturia in children

Incidence of nephrolithiasis in children increased in the past few decades especially due to changes in nutrition habits such as major consumption of salty food, high protein diets, and a low intake of fruit and vegetable which are rich in citrate and malate [7]. Such a diet promotes a low urinary pH which results in a low concentration of urinary citrate and hypercalciuria predisposing to calcium nephrolithiasis [16]. Indeed, a correlation between lower intake of potassium and magnesium with hypocitraturia has been well established, highlighting the importance of eating habits leading to stone formation in children [8]. As a consequence, hypocitraturia has been found to be the most common metabolic alteration in children older than 12 months suffering from stones [10]. Citrate takes part in the tricarboxylic acid cycle in mitochondria, is synthesized from oxaloacetic acid and oxidative decarboxylation of pyruvic acid [1]. Citrate is freely filtered at the glomerulus complex with calcium and magnesium and is finally excreted in urine [1]. Almost all the filtered citrate is reabsorbed in the proximal tube with a sodium-dicarboxylate co-transporter, and this uptake into the membrane is pH-dependent and decreases with alkaline pH [17]. These

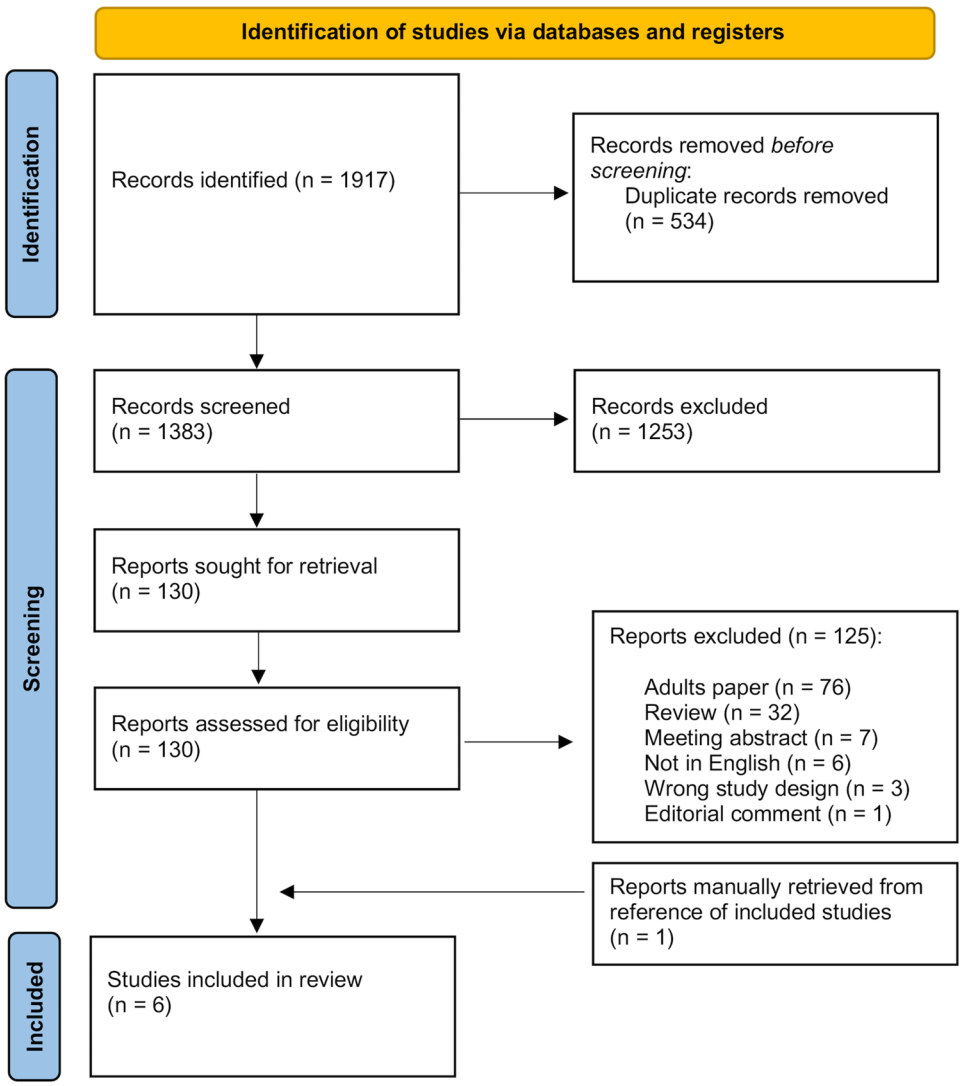

Fig. 1 Flow diagram of the literature search

properties reflect the important role of urinary pH in the regulation of the concentration of citrate in the urine. Several factors can contribute to reducing citrate levels on the nephron. Distal renal tubular acidosis is not only involved in decreasing urinary citrate excretion but systemic acidosis concurs in the partial reabsorption of the calcium and phosphate from the bone and its precipitation in the urine causing both calcium phosphate and calcium oxalate stones [18]. Net absorption of gastrointestinal alkalis is correlated with urinary citrate. A diet rich in animal protein tends to decrease the alkali absorbed determining a lower citrate excretion [19]. Gastrointestinal malabsorption causes hypocitraturia by losing gastrointestinal bicarbonate or potassium [20]. In addition, high sodium intake competes with calcium for passive reabsorption along the nephron resulting in hypercalciuria with mild acidosis, which ends in decreasing urinary citrate excretion [21].

Therapeutic options for hypocitraturia

In this review, we looked at the therapeutic outcomes of dietary management of hypocitraturia in children with urolithiasis. Six studies were included and among these, five used oral potassium citrate supplementation at 1 mEq/kg daily dose and one sodium citrate too. Dietary modifications such as increased fluid intake and sodium restriction were associated in most studies. Table 2 shows the main findings of the included studies.

Four studies showed the effect of conservative dietary therapy for hypocitraturia, evaluating its effectiveness on stone resolution and recurrence. The role of oral potassium citrate in children with calcium stones and idiopathic hypocitraturia was assessed in a prospective study of 64 children aged 1–15 years old by Tekin et al. [15]. Patients were treated with a daily dose of 1 mEq/kg of potassium

Table 1 Study characteristics

	Type of study	Population	Mean age (standard deviation)	Number of patients	Type of treatment	Study outcome	Length of follow-up
Baştuğ et al. [10]	Retrospective	Infants and children	39.5 (35) months	2513	Salt-restricted diet and hydration by increasing oral fluid intake; potassium citrate or Shohl's solution	Remission rate	1 year
Gürgöze and Sarı [11]	Prospective	Infants, children, adolescents	3.9 (range 0.1–18) years	112	Fluid intake (> 2.5 L/m^2 day); dietary sodium restriction; Potassium citrate solution contains approximately 2 mEq/ml potassium	Effect on stone size reduction	Mean 16.7 (range 1–36) months
Karsli et al. [14]	Retrospective	Infants, children, adolescents	Male: 9.7 (4.9) years Female: 6.7 (4.4) years	129	Potassium citrate (1 mEq/kg); restrict sodium intake	Recurrence rate	26.5 ± 9.4 months
Razavi et al. [12]	RCT	Children, adolescents	7.41 (2.71) versus 6.61 2.5(2.5) years	176	Polycitra-K versus Bicitra	Stone dissolution	6 months
Sarica et al. [13]	Prospective	Children	39.5 (35) months	96	Potassium citrate (1 mEq/kg daily)	Stone recurrence after extracorporeal shockwave lithotripsy	Mean 24.4 months
Tekin et al. [15]	Prospective	Infants, children, adolescents	Median 7.2 years	64	Potassium citrate (1 mEq/kg daily)	Restoring normal urinary citrate levels; prevention of stone recurrence	Mean 22 months

RCT randomized clinical trial

Table 2 Main findings of the included studies

	Localization of stones	Stone resolution with Potassium citrate	Stone resolution without Potassium citrate	Stone growth with Potassium citrate	Stone growth without Potassium citrate	Stone recurrence with potassium citrate	Stone recurrence without potassium citrate	Change in citraturia with Potassium citrate		Change in citraturia without Potassium citrate
Baştuğ et al. [10]	Pelvis-calix 1530 (63.2%) Parenchymal 688 (28.4%) Pelvis + parenchymal 88 (3.6%) Ureter 94 (3.9%) Bladder 19 (0.8%)	Most frequent in those with metabolic abnormalities (50.2 vs 33.6%)	Higher in patients with no metabolic abnormality (48.7 vs 29.1%)	NA	NA	NA	NA	NA		NA
Gürgöze and Sarı [11]	Kidney 105 (93.8%) Ureter 2 (1.8%) Both kidney and ureter 5 (4.4%)	52.7%	NA	8.9%	NA	NA	NA	NA		NA
Karsli et al. [14]	129 kidney stones after PCNL	NA	NA	NA	129	1 (1.4%)	11 (100%)	NA		NA
Razavi et al. [12]	Polycitra-K Kidney 40 Ureter 32 Bicitra Kidney 32 Ureter 28	Polycitra-K 3 months 36 (40.9%) 6 months 19 (21.6%) Bicitra 3 months 39 (44.3%) 6 months 20 (22.7%)	NA	NA	NA	NA	NA	NA		NA
Sarica et al. [13]	Renal pelvis stones treated with shock-wave lithotripsy 96	NA	NA	3/22 (13.6%)	9/22 (40.9%)	3/48 (6.2%)	16/48 (33.3)	Before treatment[a] 43.1%	2 years after treatment[a] 7%	None
Tekin et al. [9]	Renal 64	86%	NA	NA	NA	4.7%	NA	Before treatment 197 ± 72 mg/1.73 m^2	Last follow-up 632 ± 218 mg/1.73 m^2	NA

NA not available, *PCNL* percutaneous nephrolithotomy

[a]% of patients with Hypocitraturia (< 320 mg/1.73 m^2)

citrate divided into three administrations. In addition, an increase in daily fluid intake was also recommended with a restriction of dairy products and oxalate-rich foods. At a mean follow-up of 22 months, there were no serious adverse events, with patients' good compliance. Potassium citrate treatment restored normal citrate excretion with significant urinary pH elevation and a significant decrease in urinary calcium excretion in all children. From a clinical point, there were no stone recurrence episodes in initial stone formers and recurrence decreased from the preceding rate of 0.32–0.17 per patient-year during treatment in recurrent stone formers.

Gürgöze et al. evaluated 112 children with urolithiasis with a mean age at diagnosis of 3.9 years, and a follow-up duration of 16.7 months [11]. Ninety-two percent of patients had urine metabolic abnormalities and hypocitraturia was the most common finding (42%), followed by hyperoxaluria (32.1%), hypercalciuria (25%), hyperuricosuria (9.8%), and cystinuria (2.7%). Patients were treated according to their underlying metabolic abnormalities. Children with hypocitraturia were counseled to drink > 2.5 L/m^2 per day and potassium citrate was prescribed at the dosage of 4 mEq/Kg body weight divided into three doses a day. Overall, 52.7% of patients were stone-free or had their stone downsized at the last follow-up visit. Interestingly, 42.4% of those patients had hypocitraturia as the most frequent metabolic abnormality, confirming that correction of hypocitraturia plays a pivotal role in successful treatment and preventing recurrence.

Razavi et al. randomized 176 patients aged between 5 and 18 years old with kidney stones and hypocitraturia, and compared oral potassium citrate (1 mL/kg or 1–1.5 mg/kg, Polycitra-K) versus sodium citrate (Bicitra in the same dose) in terms of stone dissolution [12]. At 3 and 6 months follow-up, there was no significant difference between the two groups in terms of stone passage or dissolution but the incidence of hematuria and dysuria were significantly higher in patients taking Polycitra.

In a large multicenter study in Turkey, Bastug et al. retrospectively evaluated 2513 children with urolithiasis and a mean age of 39.5 ± 35 months, with half of them aged less than 12 months [10]. Metabolic abnormalities were identified in 61.5% of cases and hypercalciuria was the most prevalent one (26%) followed by hypocitraturia (24%) and hypomagnesuria (17.8%). However, hypocitraturia was the most frequent abnormality in children, whereas hypercalciuria was in infants. Patients were recommended to follow a salt-restricted diet, potassium citrate or Shohl's solution, and hydration by increasing oral fluid intake and frequent lactation for infants. At least one recommendation was followed by 55% of patients. Interestingly, a spontaneous stone resolution was higher in patients with no metabolic abnormality (48.7 vs 29.1%), whereas stone resolution with treatment was most frequent in those with metabolic abnormalities (50.2 vs 33.6%), confirming the important effect of dietary management in children.

The remaining two studies included in this review evaluated the role of potassium citrate supplementation after the active treatment of stones. Sarica et al. evaluated the preventive effects of potassium citrate therapy on stone recurrence and regrowth of residual fragments after shockwave lithotripsy for calcium stones in children with no renal malformation and urinary infections [13]. One month after shockwave lithotripsy, 96 children (52 stone free and 44 with < 5 mm fragments) aged 4–14 years (mean age of 6.6 years) were randomly assigned to receive potassium citrate (1 mEq/kg per day for 12 months) or no specific medication or preventive measure. Mean follow-up was 24.4 months. Patients with residual fragments and on potassium citrate treatment showed a lower rate of stone regrowth (18.1%) compared with controls (72.7%) and the latter demonstrated a more pronounced increase in mean stone size. Yet, stone-free patients on potassium citrate demonstrated a statistically significant low incidence of stone recurrence with only 7.6% suffering from a new stone episode compared with 34.6% of controls. Interestingly, hypocitraturia was the primary risk factor in most of the patients who had either stone recurrence or regrowth.

In a similar study, Karsli et al. evaluated the effect of potassium citrate supplementation on the long-term recurrence of urolithiasis in pediatric patients with hypocitraturia following percutaneous nephrolithotomy [14]. Eight two patients were included and all were advised to assume potassium citrate (dose of 1 mEq/kg) and to restrict sodium intake. Among them, 11 patients refused treatment and served as controls. After two years of follow-up, all patients who did not receive treatments experienced recurrence that occurred in only 1.4% of the patients who took potassium citrate. In patients who recurred, the most common metabolic abnormality was hypocitraturia-hypomagnesuria (45%), with calcium oxalate stones as the prevalent analysis (95.2%).

The analysis of these two studies confirms the important role of dietary management of children with hypocitraturia after definitive treatments to avoid recurrence, particularly in those who had residual fragments [13], although long-term compliance with potassium citrate therapy has not been assessed yet in children.

Our review infers that oral potassium citrate represents the cornerstone of the medical management of stones in children with hypocitraturia. However, the increase in urine volume due to the rise in fluid intake appears to facilitate the medical management of hypocitraturia and urolithiasis by reducing the concentration of potential stone-promoting factors. Akin to adults, the fluid consumption of at least 2500 mL/day or targeting a urine production of at least 2000 mL/day is the primary recommendation [22], as it

has been demonstrated that merely a high fluid intake alone (> 2500 mL/day) without other treatments was associated with a lower stone recurrence rate after a 5 years follow-up [23]. Most of the studies included in our review also suggested that their patients should increase fluid intake. This increases urine volume output in children with urolithiasis vis a vis a trend to a lower 24 h urine volume noted in controls [24]. Water is the ideal fluid in children because consumption of fructose-containing drinks and grapefruit juices increases urinary excretion of calcium and oxalate with an increased risk of stone formation [25, 26], even though fluids that increase urinary pH and citrate excretion such as orange juice, can reduce the risk of calcium stone formation [26]. Lemon juice or lemonade are high in citric acid or citrate and are often suggested for the treatment of hypocitraturia. However, there is little evidence that suggests these juices provide enough urinary citrate delivery to restore urine concentration of citrate [27]. The current recommendations for fluid intake in pediatric populations are the following: (i) 750 ml/day in infants; (ii) 1.000 ml/day in children < 5 years of age; (iii) 1.500 ml/day in children aged 5–10 years; (iv) 2.000 ml/day in adolescents and older (> 10 years of age) [7].

Last but not least, dietary sodium restriction is another important point in the management of urolithiasis. Indeed, sodium restriction was applied in some studies in our analysis, despite being solely a recommendation. Sodium restriction is of utmost importance particularly in children with calcium-based stones with hypocitraturia and hypercalciuria because several studies found an association between urinary sodium and calcium excretion and, as a consequence, between high dietary sodium intake and hypercalciuria [28], with the former also decreasing urinary citrate [25]. The optimal daily intake of sodium should not exceed 1.2 g in children aged 4–8 years and 1.5 g in adolescents, with upper limits of 1.9 g and 2.3 g, respectively [28]. However, the current average daily intake of sodium is 2–3 times higher in most Countries, confirming the role of diet in pediatric urolithiasis [28]. Therefore, an intake of less than 2–3 mEq/kg/day of sodium in children or less than 2.4 g/day in adolescents is advocated for patients with concomitant hypercalciuria or calcium-containing stones [26].

Key inferences from our review

1) All infants and children diagnosed with urolithiasis should undergo a full metabolic evaluation since urine abnormalities are commonly discovered in most of them.
2) Hypocitraturia is the most common metabolic abnormalities in infants, children, and adolescents with urolithiasis and is closely associated with hypercalciuria.
3) Dietary management of idiopathic hypocitraturia with oral potassium citrate is a safe approach for all age groups and is free of electrolyte anomalies and important side effects.
4) Oral potassium citrate is capable of restoring urine citrate levels and reducing calcium excretion. This action confirms its pivotal role in preventing the stone formation and could probably be considered the first-line treatment of asymptomatic stones.
5) Physicians must ensure proper compliance of children being treated whilst ensuring that they also hydrate adequately accordingly to their age.
6) Potassium citrate as a therapeutic supplement can be used for both treatment and prevention of recurrence.

Future directions

1) Role of dietary supplements that enrich urinary citrate levels needs validation.
2) Oral intake of formulations or drinks as therapeutic recommended helping increase urinary citrate in children needs further research.
3) Guidelines or consensus statements need to be researched on the role of potassium citrate as a recommended treatment for pediatric urolithiasis patients with associated hypocitraturia.
4) Oral potassium citrate is purportedly a safe option in treating both asymptomatic renal stones as well as preventing recurrence across different ages and this should be researched further to offer as primary therapy.

Study limitations

To the best of our knowledge, there are no randomized studies comparing oral potassium citrate with a placebo and this could be a study limitation. However, such a study in children is either difficult to be conducted or, probably, unethical since a large amount of data regarding potassium citrate safety and efficacy in both adults and children are available. In addition, we were able to find only one randomized trial that compared potassium citrate and sodium citrate and future studies should compare oral supplements of citrate with different medications.

Conclusion

Our review firmly reiterates that hypocitraturia is the most prevalent metabolic abnormality in pediatric urolithiasis and hence any child with stones needs an in-depth evaluation for the same. If established, oral potassium citrate in children is safe and efficacious in treating and preventing recurrence with no reported side effects or electrolyte anomalies. The therapeutic regime must ensure proper compliance and be supplemented by fluid intake to ensure proper hydration.

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Data availability Data is are available on request from the authors.

Declarations

Conflict of interest The authors have no competing interests to declare that are relevant to the content of this article.

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References

1. Zuckerman JM, Assimos DG (2009) Hypocitraturia: pathophysiology and medical management. Rev Urol 11:134–144
2. Bowen DK, Tasian GE (2018) Pediatric stone disease. Urol Clin North Am 45:539–550. https://doi.org/10.1016/j.ucl.2018.06.002
3. Hess B, Zipperle L, Jaeger P (1993) Citrate and calcium effects on Tamm-Horsfall glycoprotein as a modifier of calcium oxalate crystal aggregation. Am J Physiol 265:F784–F791. https://doi.org/10.1152/ajprenal.1993.265.6.F784
4. Ryall RL (1997) Urinary inhibitors of calcium oxalate crystallization and their potential role in stone formation. World J Urol 15:155–164. https://doi.org/10.1007/BF02201852
5. Srivastava T, Winston MJ, Auron A, Alon US (2009) Urine calcium/citrate ratio in children with hypercalciuric stones. Pediatr Res 66:85–90. https://doi.org/10.1203/PDR.0b013e3181a2939e
6. Kirejczyk JK, Porowski T, Konstantynowicz J et al (2014) Urinary citrate excretion in healthy children depends on age and gender. Pediatr Nephrol 29:1575–1582. https://doi.org/10.1007/s00467-014-2806-7
7. Baştuğ F, Düşünsel R (2012) Pediatric urolithiasis: causative factors, diagnosis and medical management. Nat Rev Urol 9:138–146. https://doi.org/10.1038/nrurol.2012.4
8. Kovacevic L, Wolfe-Christensen C, Edwards L et al (2012) From hypercalciuria to hypocitraturia—a shifting trend in pediatric urolithiasis? J Urol 188:1623–1627. https://doi.org/10.1016/j.juro.2012.02.2562
9. Tekin A, Tekgul S, Atsu N et al (2000) A study of the etiology of idiopathic calcium urolithiasis in children: hypocitruria is the most important risk factor. J Urol 164:162–165
10. Baştuğ F, Ağbaş A, Tülpar S et al (2022) Comparison of infants and children with urolithiasis: a large case series. Urolithiasis 50:411–421. https://doi.org/10.1007/s00240-022-01327-0
11. Gürgöze MK, Sarı MY (2011) Results of medical treatment and metabolic risk factors in children with urolithiasis. Pediatr Nephrol 26:933–937. https://doi.org/10.1007/s00467-011-1803-3
12. Razavi MR, Vahedian M, Motharinejad F et al (2022) Effect of polycitra-K and bicitra in the treatment of pediatric nephrolithiasis: a double-blind randomized trial. Med J Islam Repub Iran 36:70. https://doi.org/10.47176/mjiri.36.70
13. Sarica K, Erturhan S, Yurtseven C, Yagci F (2006) Effect of potassium citrate therapy on stone recurrence and regrowth after extracorporeal shockwave lithotripsy in children. J Endourol 20:875–879. https://doi.org/10.1089/end.2006.20.875
14. Karsli O, Izol V, Aridogan IA et al (2013) Metabolic risk factors and the effect of metaphylaxis in pediatric stone disease with hypocitraturia. Urolithiasis 41:9–13. https://doi.org/10.1007/s00240-012-0539-2
15. Tekin A, Tekgul S, Atsu N et al (2002) Oral potassium citrate treatment for idiopathic hypocitruria in children with calcium urolithiasis. J Urol 168:2572–2574. https://doi.org/10.1097/01.ju.0000037968.53708.1b
16. Adeva MM, Souto G (2011) Diet-induced metabolic acidosis. Clin Nutr 30:416–421. https://doi.org/10.1016/j.clnu.2011.03.008
17. Brennan TS, Klahr S, Hamm LL (1986) Citrate transport in rabbit nephron. Am J Physiol 251:F683–F689. https://doi.org/10.1152/ajprenal.1986.251.4.F683
18. Hamm LL, Hering-Smith KS (2002) Pathophysiology of hypocitraturic nephrolithiasis. Endocrinol Metab Clin North Am 31:885–93. https://doi.org/10.1016/s0889-8529(02)00031-2
19. Sakhaee K, Williams RH, Oh MS et al (1993) Alkali absorption and citrate excretion in calcium nephrolithiasis. J bone Miner Res Off J Am Soc Bone Miner Res 8:789–794. https://doi.org/10.1002/jbmr.5650080703
20. Rudman D, Dedonis JL, Fountain MT et al (1980) Hypocitraturia in patients with gastrointestinal malabsorption. N Engl J Med 303:657–661. https://doi.org/10.1056/NEJM198009183031201
21. Sakhaee K, Harvey JA, Padalino PK et al (1993) The potential role of salt abuse on the risk for kidney stone formation. J Urol 150:310–312. https://doi.org/10.1016/s0022-5347(17)35468-x
22. Jung H, Andonian S, Assimos D et al (2017) Urolithiasis: evaluation, dietary factors, and medical management: an update of the 2014 SIU-ICUD international consultation on stone disease. World J Urol 35:1331–1340. https://doi.org/10.1007/s00345-017-2000-1
23. Borghi L, Meschi T, Amato F et al (1996) Urinary volume, water and recurrences in idiopathic calcium nephrolithiasis: a 5-year randomized prospective study. J Urol 155:839–843
24. Miller LA, Stapleton FB (1989) Urinary volume in children with urolithiasis. J Urol 141:918–920. https://doi.org/10.1016/s0022-5347(17)41052-4
25. Tasian GE, Copelovitch L (2014) Evaluation and medical management of kidney stones in children. J Urol 192:1329–1336. https://doi.org/10.1016/j.juro.2014.04.108
26. Copelovitch L (2012) Urolithiasis in children. Medical Approach Pediatr Clin North Am 59:881–896. https://doi.org/10.1016/j.pcl.2012.05.009
27. Kurtz MP, Eisner BH (2011) Dietary therapy for patients with hypocitraturic nephrolithiasis. Nat Rev Urol 8:146–152. https://doi.org/10.1038/nrurol.2011.9
28. Alon US (2009) Medical treatment of pediatric urolithiasis. Pediatr Nephrol 24:2129–2135. https://doi.org/10.1007/s00467-007-0740-7