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Effect of Vitamin E Therapy on Children With Renal Stones

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ABSTRACT

Background and Aim: Urinary system stones, including kidney stones, are common diseases of the kidney and urinary tract that have increased over time. The treatment of these patients, especially in children, is of great importance. This study evaluated the effect of vitamin E on the treatment of children with kidney stones.

Methods: This double-blind, randomized controlled trial (RCT) was conducted on children between the ages of 2 and 18 years with a diagnosis of kidney stones. The samples were randomly divided into two groups: The intervention group, which received vitamin E in addition to standard treatment, and the control group, which received standard treatment. This division was blinded to the evaluator and the patients. Information about the condition of the stones before and after treatment was obtained from two sources and compared using SPSS statistical software.

Results: The mean age (P=0.595) and frequency distribution of gender (P=0.685) showed no statistically significant difference between the two groups. The mean number of stones before treatment in the intervention group was 3.04±1.87, while in the control group, they were 3.22±2.01, indicating no significant difference according to the independent t-test. After treatment, values were 1.15±1.3 in the intervention group and 2.34±1.75 in the control group. The mean size of the largest stone in the intervention group before treatment was 0.09±0.34 cm, and after treatment, it was 0.18±0.07 cm (P=0.964). In the control group, the size of the largest stone before treatment was 0.10±0.32 cm, and after treatment, it increased to 0.25±0.1 cm, which was significantly smaller in the intervention group based on the independent t-test.

Conclusion: The use of vitamin E can reduce the size and number of kidney stones in children.

Keywords: Vitamin E, Kidney stones, Children, Treatment

J Ped Nephrol
Journal of Pediatric Nephrology

Introduction

The occurrence of kidney stones in children has significantly risen over the past 20 years, though the exact reasons remain unclear. When diagnosing pediatric kidney stones, it is important to include metabolic investigations to identify and manage any factors that may increase the risk of recurrent stones. Treatment should focus on removing stones effectively while minimizing complications, radiation exposure, anesthesia risks, and other hazards [1]. Kidney stones affect approximately 11% of the U.S. population, a figure that continues to grow and drives higher healthcare costs. In children, the prevalence is lower, at around 1%. In the U.S., studies estimate that the yearly incidence of pediatric kidney stones was about 65 cases per 100,000 people between 2005 and 2016, a notable increase from the 18 per 100,000 reported in 1999. Globally, the prevalence of kidney stones is also rising, possibly due to dietary changes, climate shifts, new health conditions, and evolving living environments [2]. This upward trend in pediatric kidney stones over recent decades is worrisome and has become a significant public health issue.

Although the disease has been documented for centuries, today's landscape shows shifts influenced by lifestyle, diet, and environmental factors, which may be contributing to the increasing number of cases [3]. One of the characteristic features of kidney stone disease in children is undiagnosed metabolic causes. It has been observed that 50% of children under the age of 10 with kidney stones have an underlying metabolic disorder. An appropriate approach to children with kidney stone disease should include an evaluation for metabolic factors that increase the risk of kidney stone formation in children. Among these metabolic disorders are hypercalciuria, hyperoxaluria, hyperuricosuria, and cystinuria [4, 5].

One of the most common types of kidney stones is those resulting from oxalate compounds. Oxalate is the ionic form of oxalic acid, which is derived from a variety of plants and animals. This compound is primarily excreted through the kidneys. Hyperoxaluria is a type of metabolic disorder involving oxalate and is defined as an increase in urinary oxalate excretion [6]. Hyperoxaluria inherently has the potential to cause significant complications and consequences. This disorder can occur during infancy or in the sixth decade of life, and if not properly addressed, can lead to substantial mortality and morbidity. One of the most important complications of this condition is the development of end-stage renal disease (ESRD) [7]. An elevated plasma oxalate level leads to the deposition of oxalate in various body organs. This condition, known as systemic oxalosis, should be prevented. However, a noteworthy point is that the diagnosis of this condition is delayed in more than 40% of patients. One study revealed that approximately 30% of affected patients only become aware of the condition once they have already developed ESRD [8]. In other patients, the diagnosis is only made when the disease recurs after a kidney transplant [9, 10]. Hyperoxaluria is one of the most significant risk factors for the formation of calcium oxalate kidney stones in humans. Studies have shown that 60 to 80% of kidney stones in humans are composed of calcium oxalate [11]. In recent years, there have been substantial advancements in the diagnosis and early treatment of kidney stones. Various treatment options have been evaluated, including alkaline citrate, thiazides, dietary modifications, and reduction of animal proteins and foods rich in glycolate and glyoxylate, which have all contributed to the prevention of recurrent stones [12]. Numerous studies have shown that increased oxidative stress in the human body can lead to the formation of calcium oxalate crystals, and subsequently, stone formation [13, 14]. Therefore, if oxidative stress can be mitigated, it may be possible to prevent the damage it causes, including the formation of multiple kidney stones and a decline in kidney function.

Vitamin E is a fat-soluble antioxidant that can protect polyunsaturated fatty acids in cell membranes from oxidation. It also regulates the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS), and modulates signal transduction. The immunomodulatory effects of vitamin E have been evaluated in both animals and humans under healthy and diseased conditions [15]. As a non-specific antioxidant, vitamin E protects host cells from oxidative damage and prevents the potential binding of calcium oxalate crystals and the formation of kidney stones [16]. In their 2023 study, Baltusnikiene et al. stated that vitamin E may play an effective role in preventing or improving kidney damage and ultimately enhancing kidney function [17].

Children of all ages may experience kidney stones. In addition to a family history, unhealthy lifestyle and dietary habits—such as inadequate water intake and consumption of carbonated or caffeinated beverages—put children at greater risk of developing kidney stones compared to adults [18]. Since the most common cause of kidney stones is metabolic disorders [19], and due to the increasing prevalence of kidney stones in children, focusing on the treatment and management of metabolic disorders can significantly reduce the incidence in this population. Furthermore, considering the effectiveness

of vitamin E in reducing oxidative stress and improving clinical outcomes in children with kidney stones, it seems reasonable to use vitamin E to enhance clinical status by reducing the number and size of kidney stones. However, most previous studies have been conducted on animal models, and limited research has focused on children. Therefore, the present study was conducted to determine the effect of vitamin E in the treatment of children with kidney stones.

Materials and Methods

This study was a randomized controlled trial (RCT) with a double-blind design. The samples were selected through convenience non-random sampling from children aged 2 to 18 years diagnosed with kidney stones, who were referred to Amirkabir Hospital in Arak in 2023. Children were included after obtaining ethical approval, provided that their kidney stones were diagnosed by a specialist using ultrasound and they met the inclusion criteria. Sampling continued until the required sample size was reached. Based on the study by Anbazhagan et al. [20], vitamin E supplementation reduced oxalate excretion by 34%, compared to 27% in the control group. Using the formula for comparing proportions in two independent groups, a sample size of 43 patients per group was calculated. Accounting for possible dropouts, 50 patients per group (a total of 100 participants) were included.

The samples were randomly divided into two groups: The intervention group, which received vitamin E in addition to standard treatment, and the control group, which received standard treatment. Both the evaluator and the patients were blinded to group assignments. Due to the use of an intervention (oral vitamin E drops), the presence of a control group, and random assignment, this constituted an RCT.

Block randomization was applied. Participants were enrolled in order of arrival and randomly assigned to the intervention or control groups based on a pre-generated sequence. The sequence was unpredictable and completely random, using blocks of 8 created [21]. The order of letters A and B within each block served as the randomization sequence, and the process was entirely automated, keeping researchers blind to allocation.

This was a double-blind study, meaning that neither the patients nor the data collectors were aware of the treatment allocation. Patients were informed that, upon providing consent, they would be randomly assigned to one of the treatment groups. Once eligibility and consent were confirmed, participants were randomly assigned. At the end of the study, the effect of vitamin E on kidney stones was evaluated. A placebo was prepared for vitamin E in coordination with the pharmaceutical company that manufactured it and was administered to the control group. The intervention group received vitamin E in addition to standard treatment for one month, at the recommended dosage based on age and weight, as advised by the Behsā Pharmaceutical Company in Arak. The control group received a daily placebo along with standard treatment. Potential sensitivities and side effects of vitamin E were monitored weekly by phone.

To collect study data, participants were purposefully selected by the research assistant based on the study's inclusion criteria and randomly assigned to either the intervention or control group using simple randomization. At the beginning of the study, after explaining the study's objectives and obtaining written consent from the children's parents, a demographic checklist was completed for each participant. In cases where the parents were unable to complete the questionnaire, the research assistant filled it out for them. Additionally, based on the child's ultrasound results, a checklist of ultrasound findings was also completed by the assistant.

In the intervention group, starting from day one, an oral vitamin E drop (or vitamin E softgel for children over 12 years old) sufficient for one month's daily use was provided to the parents, along with instructions to administer it regularly each day. To ensure adherence throughout the month, a reminder text message was sent weekly to one of the parents' mobile phones (preferably the mother's, assuming a closer relationship with the child). If no response was received, follow-up phone calls were made.

After one month of vitamin E consumption in the intervention group, both groups were contacted, and the children were called in for a second ultrasound. The new ultrasound results were recorded to assess the number and size of kidney stones. In cases where more than one stone was present, the largest stone size was recorded both before and after the intervention for analysis. Since both the initial and follow-up ultrasounds (after one month) are part of routine clinical care and follow-up for pediatric kidney stone patients, no additional costs were incurred by the patients or their families.

In this study, kidney stone count and size were evaluated using renal and urinary tract ultrasound at the beginning of the study, and then reassessed after the 30-day treatment period to determine the impact of the intervention. Blinding was implemented, and no patient knew to which group they were assigned.

J Ped Nephrol
Journal of Pediatric Nephrology

Statistical analysis

Quantitative data were described using Mean±SD, while qualitative data were described using frequencies and percentages. The Kolmogorov–Smirnov test was used to assess the normality of quantitative variables. Independent t-tests or their non-parametric equivalents were used for comparing means between two groups. Pearson or Spearman correlation coefficients were used to evaluate the relationships between quantitative variables. The chi-square test was used to assess relationships between qualitative variables. All analyses were conducted with a 95% confidence level (CI) and a 5% alpha error using SPSS software, version 26.

Results

The effect of vitamin E on acute kidney stones was assessed in 100 patients across two groups.

As shown in Table 1, the mean children's age in the intervention group was 12.57±4.99 days, while in the control group, it was 12.42±4.79 days, with no significant difference observed between the two groups (P=0.595) (Figure 1).

On the other hand, regarding gender, the male-to-female ratio in the intervention and control groups was 30.20 and 28.22, respectively. Statistical evaluations also indicated no significant difference between the two groups in terms of gender distribution (P=0.685) (Figure 2).

The aim was to determine and compare the size and number of kidney stones in the intervention and control groups before and after treatment.

As shown in Table 2, the mean number of stones before treatment was 3.04±1.87 in the intervention group and 3.22±2.01 in the control group. According to the independent t-test, there was no statistically significant

Table 1. Mean age and gender distribution among patients

Variables		Mean±SD/No. (%)		P
		Group		
		Intervention	Control	
Age (y)		12.57±4.99	12.42±4.79	0.595*
Gender	Male	30(60)	28(56)	0.371**
	Female	20(40)	22(44)	

*Indpendent sample t-test, **Chi-square test.

Table 2. Comparison of the mean number of kidney stones before and after treatment in the two groups

Section	Mean±SD		t-test	
	Group			
	Intervention	Control	Independent	Paired
Before treatment	1.87±3.04	2.01±3.22	0.74	0.001
After treatment	1.30±1.15	1.75±2.34	0.001	

Table 3. Comparison of the mean largest size of kidney stones before and after treatment in the two groups

Section	Group		Independent t-test	P
	Intervention	Control		
Before treatment	0.34±0.09	0.32±0.1	0.964	0.001
After treatment	0.18±0.07	0.25±0.1	0.01	

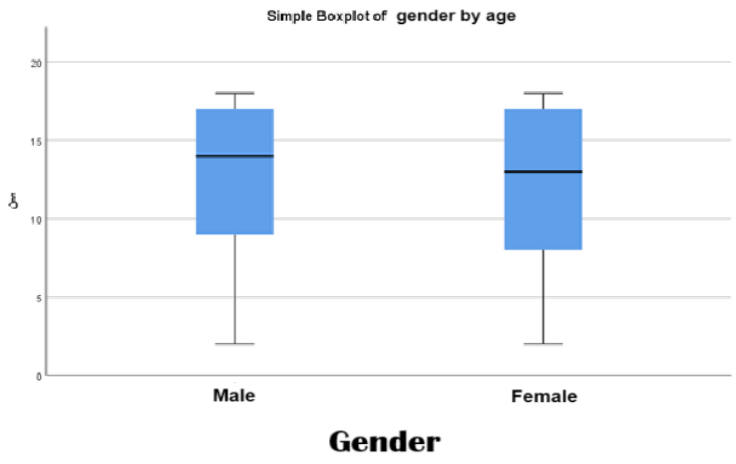

Figure 1. Mean patients' age in the two groups

difference between the two groups in this regard. After treatment, the values were 1.15±1.3 in the intervention group and 2.34±1.75 in the control group, and the independent t-test indicated that the number was significantly lower in the intervention group. Additionally, the comparison of the mean number of stones before and after treatment in both groups showed a statistically significant difference (P=0.001) (Figure 3).

As shown in Table 3, the mean size of the largest stone in the intervention group before treatment was 0.34±0.09 cm, and after treatment, it was 0.07±0.18 cm. According to the independent t-test, there was no statistically significant difference between the two groups in this regard (P=0.964). In the control group, the size of the largest stone before treatment was 0.32±0.1 cm, and after treatment, it was 0.1±0.25 cm, which was significantly lower in the intervention group based on the independent t-test (Figure 4).

Discussion

This RTC investigated the impact of vitamin E on kidney stones in children aged 2 to 18 years diagnosed with kidney stones, examining various clinical parameters,

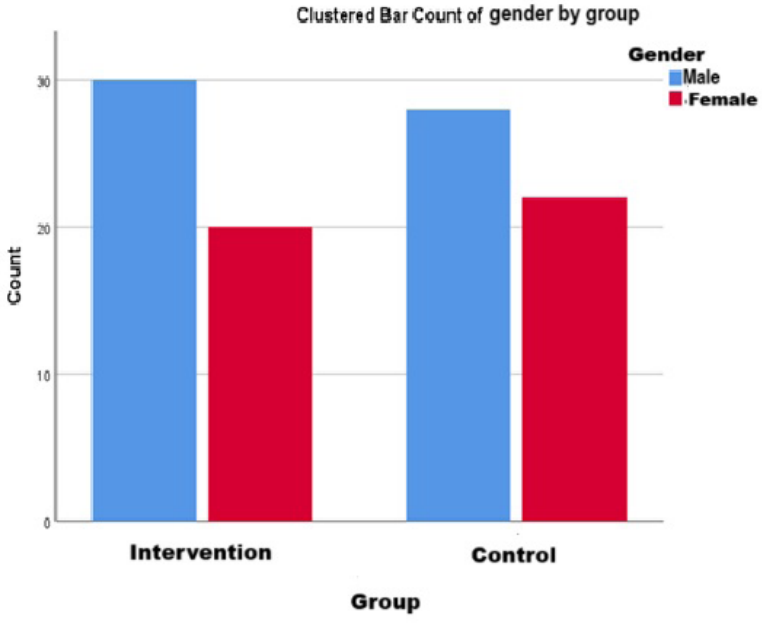

Figure 2. Gender distribution of patients in the two groups

J Ped Nephrol
Journal of Pediatric Nephrology

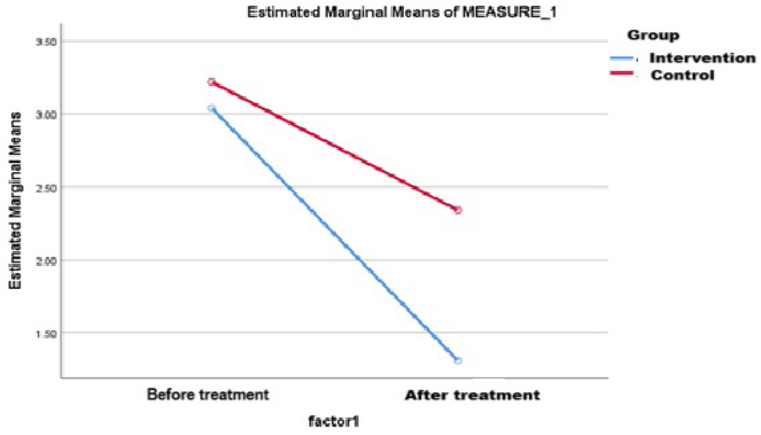

Figure 3. Comparison of the number of kidney stones before and after treatment in the two groups

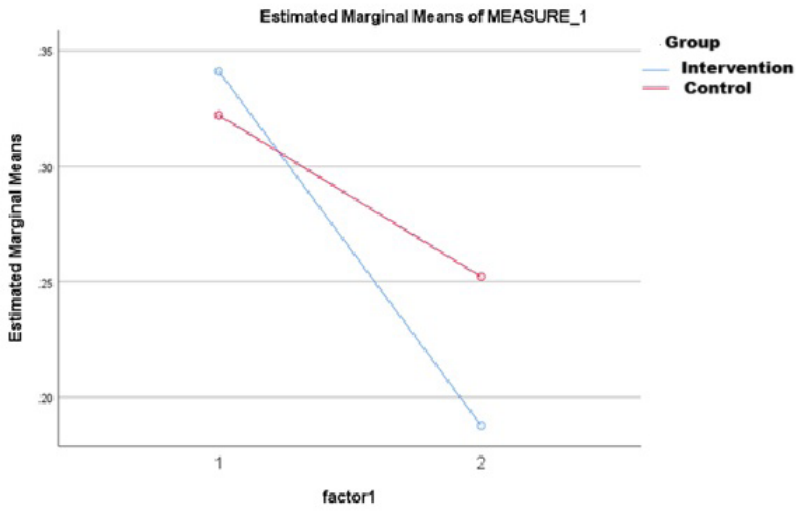

Figure 4. Comparison of the largest size of kidney stones before and after treatment in the two groups

including stone burden and demographic factors. The study found no significant differences in baseline age or gender distribution between the intervention and control groups, indicating that the groups were well-matched, thereby strengthening the validity of the outcome assessments.

Regarding the stone count, both groups demonstrated similar baseline numbers before treatment, with means of 3.04±1.87 and 3.22±2.01 for the intervention and control groups, respectively. Post-treatment, the intervention group showed a significant reduction in stone number (1.30±1.15) compared to the control group (2.34±1.75), confirming the effectiveness of the intervention in reducing stone burden (P=0.001). Additionally, the significant decrease in the size of the largest stone—from 0.34±0.09 cm to 0.07±0.18 cm in the intervention group—indicates that vitamin E may contribute to stone dissolution or prevent stone growth post-treatment. Although the increase in the largest stone size was not statistically significant between groups before treatment (P=0.964), the reduction within the intervention group suggests a potential therapeutic benefit. Bevill et al. emphasized the importance of evaluating metabolic risk factors in pediatric nephrolithiasis, noting that stones are often linked to underlying metabolic disturbances, such as hypercalciuria, cystinuria, or oxalate disorders. Their review underscores that management strategies focusing on metabolic correction can significantly influence stone recurrence and growth. Our study aligns with this perspective by demonstrating

that interventions—possibly including antioxidants, like vitamin E—might modulate stone progression, though further studies are necessary to elucidate the underlying mechanisms fully. This study showed the significance of comprehensive metabolic evaluation and targeted therapy, suggesting that antioxidant supplementation could be part of a broader metabolic management plan [3]. Moreover, current guidelines advocate minimizing radiation exposure and invasive procedures, highlighting the importance of non-invasive therapies that can effectively manage and prevent recurrent stones.

Bahadoran et al. observed that calcium oxalate deposition in mice receiving vitamin E, either alone or in combination, reduced oxidative stress and protected the kidneys from the formation of urinary stones [22], which aligns with the findings of the present study. Another study also demonstrated that hyperoxaluria causes peroxidative damage and the aggregation of calcium oxalate crystals in kidney tubules. Moreover, it was found that supplemental vitamin E completely prevented calcium oxalate deposition by preventing peroxidative damage and restoring antioxidants. Therefore, treatment with vitamin E may also prevent calcium oxalate stone formation in humans [11], which supports the effectiveness of vitamin E on kidney stones as shown in the present study. In another study by Thamilselvan et al., it was observed that treatment with vitamin E and mannitol completely prevented calcium oxalate deposition in kidney tubules by normalizing tissue oxalate concentration, mitochondrial oxalate-binding activity, and increasing antioxidant levels [23], which also corresponds to the recent evaluation results.

Anbazhagan et al. by evaluating the role of vitamin E supplementation in reducing hyperoxaluria, observed that citrate excretion increased following vitamin E intake, suggesting a reduction in calcium oxalate crystal accumulation and a lower likelihood of kidney stone formation [20], which is consistent with the recent findings. Huang et al. also stated that at the onset of the urolithiasis cascade, hyperoxaluria leads to increased production of free radicals in the kidneys, which in turn damages the tubular cells. As a result, antioxidant supplements can protect these membranes from damage and prevent stone formation [24]. Accordingly, similar to the present evaluation, it has been observed that vitamin E can improve the condition of patients with kidney stones.

Huang et al. found that vitamin E supplementation in kidney tissue via ethylene glycol could prevent the destruction and loss of osteopontin and Tamm-Horsfall protein. The beneficial role of vitamin E in reducing calcium oxalate accumulation is attributed to a decrease in tubular cell death and an increase in the defensive function of osteopontin and Tamm-Horsfall protein [25], once again demonstrating the effectiveness of this vitamin on kidney stones, similar to their previous study. Other study also showed that low levels of vitamin E cause disturbances in cellular balance and promote cell death, thereby contributing to the formation of oxalate urinary crystals [26]. However, in the current evaluation, the effectiveness of vitamin E on kidney stones was examined through an interventional study.

Kumar et al. found that supplementation with vitamin E + selenium reduced lipid peroxidation levels and the activity of oxalate-synthesizing enzymes, such as glycolic acid oxidase (GAO), lactate dehydrogenase (LDH), and xanthine oxidase (XO), while simultaneously increasing the activity of antioxidant enzymes, like superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and glucose-6-phosphate dehydrogenase (G6PDH). Additionally, levels of non-enzymatic antioxidants such as ascorbic acid and α-tocopherol were raised, and oxalate and calcium urinary excretion returned to normal. Ultimately, they concluded that vitamin E + selenium antioxidants protect against hyperoxaluria in mice [27]. However, in the present evaluation, only the effectiveness of vitamin E was studied.

Baltusnikiene et al. reported that vitamin E can have both beneficial and adverse effects on the kidney. High doses of vitamin E may cause renal effects, prompting comparison with upper toxicity limits. However, dietary vitamin E intake has been linked to a negative association with the prevalence of chronic kidney disease (CKD), suggesting a protective effect in adults. Therefore, the impact of vitamin E on kidney health appears to be dose-dependent, with potential benefits at lower intake levels and adverse effects at higher levels [17].

Accordingly, in most studies reviewed here, and in line with the present evaluation, vitamin E can be used to increase urinary oxalate levels and reduce the likelihood of kidney stones in children. However, further research is needed to confirm these results.

Conclusion

The use of vitamin E may reduce the size and number of kidney stones in children. Nonetheless, further studies are necessary to compare the efficacy of vitamin E with other established and potentially effective methods.

Research limitations

One limitation of this study was the death of some patients, referrals to other hospitals, and the unavailability of certain patients. However, by extending the sampling period, this issue was largely resolved.

Recommendations

It is recommended that further studies be conducted to resolve the existing contradictions in this field. If the effect of vitamin E on kidney stones is confirmed, it may be used to improve the condition of children with this disease. Additionally, future studies should assess the effectiveness of other potential methods that could positively impact kidney stones in children.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Authors' contributions

All authors equally contributed to the preparation of this article.

Conflict of interest

The authors declared no conflict of interest.

References

[1] Pecoraro L, Zuccato A, Vitella R, Pietrobelli A, Piacentini G, Brugnara M. Pediatric nephrolithiasis: A changing landscape through time and space. Medicina. 2024; 0(12):1993. [DOI:10.3390/medicina60121993] [PMID]

[2] Cao B, Daniel R, McGregor R, Tasian GE. Pediatric Nephrolithiasis. Healthcare (Basel). 2023; 11(4):552. [DOI:10.3390/healthcare11040552] [PMID]

[3] Bevill M, Kattula A, Cooper CS, Storm DW. The Modern Metabolic Stone Evaluation in Children. Urology. 2017; 101:15-20. [DOI:10.1016/j.urology.2016.09.058] [PMID]

[4] Valentini RP, Lakshmanan Y. Nephrolithiasis in children. Adv Chronic Kidney Dis. 2011; 18(5):370-5. [DOI:10.1053/j.ackd.2011.07.002] [PMID]

[5] Pietrow PK, Pope JC 4th, Adams MC, Shyr Y, Brock JW 3rd. Clinical outcome of pediatric stone disease. J Urol. 2002; 167(2 Pt 1):670-3. [DOI:10.1016/S0022-5347(01)69121-3] [PMID]

[6] Robijn S, Hoppe B, Vervaet BA, D'Haese PC, Verhulst A. Hyperoxaluria: A gut-kidney axis? Kidney Int. 2011; 80(11):1146-58. [DOI:10.1038/ki.2011.287] [PMID]

[7] Arena R, Cahalin LP. Evaluation of cardiorespiratory fitness and respiratory muscle function in the obese population. Prog Cardiovasc Dis. 2014; 56(4):457-64. [DOI:10.1016/j.pcad.2013.08.001] [PMID]

[8] Hoppe B, Langman CB. A United States survey on diagnosis, treatment, and outcome of primary hyperoxaluria. Pediatr Nephrol. 2003; 18(10):986-91. [DOI:10.1007/s00467-003-1234-x] [PMID]

[9] Spasovski G, Beck BB, Blau N, Hoppe B, Tasic V. Late diagnosis of primary hyperoxaluria after failed kidney transplantation. Int Urol Nephrol. 2010; 42(3):825-9. [DOI:10.1007/s11255-009-9690-2] [PMID]

[10] Bhasin B, Ürekli HM, Atta MG. Primary and secondary hyperoxaluria: Understanding the enigma. World J Nephrol. 2015; 4(2):235-44. [DOI:10.5527/wjn.v4.i2.235] [PMID]

[11] Thamilselvan S, Menon M. Vitamin E therapy prevents hyperoxaluria-induced calcium oxalate crystal deposition in the kidney by improving renal tissue antioxidant status. BJU Int. 2005; 96(1):117-26. [DOI:10.1111/j.1464-410X.2005.05579.x] [PMID]

[12] Tiselius HG; Advisory Board of European Urolithiasis Research and EAU Health Care Office Working Party for Lithiasis. Possibilities for preventing recurrent calcium stone formation: principles for the metabolic evaluation of patients with calcium stone disease. BJU Int. 2001; 88(2):158-68. [DOI:10.1046/j.1464-410x.2001.02308.x] [PMID]

[13] Habibzadegah-Tari P, Byer KG, Khan SR. Reactive oxygen species mediated calcium oxalate crystal-induced expression of MCP-1 in HK-2 cells. Urol Res. 2006; 34(1):26-36. [DOI:10.1007/s00240-005-0007-3] [PMID]

[14] Tungsanga K, Sriboonlue P, Futrakul P, Yachantha C, Tosukhowong P. Renal tubular cell damage and oxidative stress in renal stone patients and the effect of potassium citrate treatment. Urol Res. 2005; 33(1):65-9. [DOI:10.1007/s00240-004-0444-4] [PMID]

[15] Lee GY, Han SN. The role of vitamin E in immunity. Nutrients. 2018; 10(11):1614. [DOI:10.3390/nu10111614] [PMID]

[16] Chmiel JA, Stuivenberg GA, Al KF, Akouris PP, Razvi H, Burton JP, et al. Vitamins as regulators of calcium-containing kidney stones-new perspectives on the role of the gut microbiome. Nat Rev Urol. 2023; 20(10):615-37. [DOI:10.1038/s41585-023-00768-5] [PMID]

[17] Baltusnikiene A, Staneviciene I, Jansen E. Beneficial and adverse effects of vitamin E on the kidney. Front Physiol. 2023; 14:1145216. [DOI:10.3389/fphys.2023.1145216] [PMID]

[18] Panzarino V. Urolithiasis in children. Adv Pediatr. 2020; 67:105-12. [DOI:10.1016/j.yapd.2020.03.004] [PMID]

[19] Ahmad I, Pansota MS, Tariq M, Tabassum SA. Frequency of metabolic abnormalities in urinary stones patients. Pak J Med Sci. 2013; 29(6):1363-6. [DOI:10.12669/pjms.296.4007] [PMID]

[20] Anbazhagan M, Hariprasad C, Samudram P, Latha E, Latha M, Selvam R. Effect of oral supplementation of vitamin E on urinary risk factors in patients with hyperoxaluria. J Clin Biochem Nutr. 1999; 27(1):37-47. [DOI:10.3164/jcbn.27.37]

[21] Bahadoran H, Naghii M, Mofid M, Asadi M, Ahmadi K, Sarveazad A. Protective effects of boron and vitamin E on ethylene glycol-induced renal crystal calcium deposition in rat. Endocr Regul. 2016; 50(4):194-206. [DOI:10.1515/enr-2016-0021] [PMID]

[22] Sealedenvelope. Randomisation and online databases for clinical trials [Internet]. 2025 [Updated 2025 December 13]. Available from: [Link]

[23] Thamilselvan S, Selvam R. Effect of vitamin E and mannitol on renal calcium oxalate retention in experimental nephrolithiasis. Indian J Biochem Biophys. 1997; 34(3):319-23. [PMID]

[24] Huang HS, Chen CF, Chien CT, Chen J. Possible biphasic changes of free radicals in ethylene glycol-induced nephrolithiasis in rats. BJU Int. 2000; 85(9):1143-9. [DOI:10.1046/j.1464-410x.2000.00674.x] [PMID]

[25] Huang HS, Chen J, Chen CF, Ma MC. Vitamin E attenuates crystal formation in rat kidneys: roles of renal tubular cell death and crystallization inhibitors. Kidney Int. 2006; 70(4):699-710. [DOI:10.1038/sj.ki.5001651] [PMID]

[26] Huang HS, Ma MC, Chen J. Low-vitamin E diet exacerbates calcium oxalate crystal formation via enhanced oxidative stress in rat hyperoxaluric kidney. Am J Physiol Renal Physiol. 2009; 296(1):F34-45. [DOI:10.1152/ajprenal.90309.2008] [PMID]

[27] Kumar MS, Selvam R. Supplementation of vitamin E and selenium prevents hyperoxaluria in experimental urolithic rats. J Nutr Biochem. 2003; 14(6):306-13. [DOI:10.1016/S0955-2863(03)00033-0] [PMID]