

General and dietary oxalate restriction advice reduces urinary oxalate in the stone clinic setting

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Background: Idiopathic hyperoxaluria is a risk factor for developing calcium oxalate nephrolithiasis. Dietary oxalate's effect on urinary oxalate is not well studied. The aim of this study is to assess the effect of advice focused on reducing dietary oxalate in a cohort of idiopathic hyperoxaluric patients.

Methods: Patients referred to the Groote Schuur Hospital Stone Clinic from 2015 to 2017 were considered eligible, if they were an idiopathic hyperoxaluric stone former, excreting > 40 mg/d of urinary oxalate on a pre-intervention 24-hour stone study urinalysis. Patients were asked to adhere to a diet sheet which included general stone prevention advice (low salt diet, increased fluid intake and moderate protein intake) and specific low oxalate diet advice. A post-intervention 24-hour urinalysis was performed at six weeks.

Results: Nineteen patients had hyperoxaluria (eight men and 11 women) with a mean age of 49 years (range 25–76 years). The mean BMI of the group was 28.4 kg/m² (17.4–50). All patients had mean number of 1.9 range prior stone episodes (range 1–6 stone episodes). Fourteen (14/19) patients completed the study. The mean pre-dietary advice urinary oxalate was 53.2 mg/24 hours ($n = 14$), SD while the post-intervention was 29.6 mg/24 hours SD ($p = 0.0002$). Only 3/14 patients who completed the assessment failed to normalise their urinary oxalate on the diet.

Conclusion: In the stone clinic setting, general advice of low salt diet, increased water intake, moderate protein intake and specific oxalate restriction can significantly reduce oxalate excretion in hyperoxaluric stone formers. Sustained reduction of oxalate excretion and longitudinal clinical benefit are worthy of study in larger cohorts.

Keywords: kidney stones, hyperoxaluria, nephrolithiasis

Introduction

The lifetime prevalence of nephrolithiasis in the United States is estimated to be 12% in men and 7% in women.¹ Calcium oxalate stones account for roughly 70% of kidney stones, with hyperoxaluria, among other factors, promoting calcium oxalate supersaturation and resultant calculi. The calcium salt of oxalate has a low solubility leading to crystal precipitation in urine. Hyperoxaluria is of more importance than urinary calcium in the supersaturation that leads to calcium oxalate stones. Thus, hyperoxaluria has in recent years gained more attention in attempts to understand its pathophysiology and to devise potential strategies to prevent kidney stone recurrence.²

Hyperoxaluria is defined as excretion of urinary oxalate above 40 mg/day.³ Hyperoxaluria can be classified as either *primary* due to a genetic metabolic disorder causing excess endogenous (liver) oxalate production, *enteric* (secondary) due to excessive absorption in the intestinal tract due to bowel disease, or *idiopathic* due to an exaggerated absorption of dietary oxalate.

The prevalence of hyperoxaluria is poorly studied. In the systematic review by Spradling et al. on the epidemiology and geographical variation of hyperoxaluria, it has been

noted that hyperoxaluria prevalence has increased from 24% (1983) to 45% (2013).⁴ There are no reports of the prevalence of hyperoxaluria among the South African population.

Oxalate is mainly produced endogenously as an end-product of metabolism in the liver. Dietary contribution is variable among individuals ranging as high as 50% of urinary oxalate.⁵ This contribution of dietary oxalate to urinary oxalate was in earlier decades thought to be low, and this resulted in it being largely ignored.⁶

Accepted risk factors for hyperoxaluria include: male gender, obesity, dietary oxalate intake (oxalate is rich in spinach and rhubarb, nuts, plums, chocolate, beetroot, and strawberries), lack of oxalate degrading bacteria in the gut, and supernormal vitamin C intake.⁶ A landmark article by Curhan et al. established that an inverse relationship exists between calcium intake and levels of oxalate of the urine in stone formers.⁷ This study underscored the importance of maintaining adequate calcium intake to reduce urinary oxalate in calcium oxalate stone formers.

Hyperoxaluria increases urine calcium oxalate supersaturation and, therefore, the risk of kidney stone formation. A relatively small increase in urinary oxalate levels has significant effects on urinary supersaturation.² The

importance of this was highlighted by Voss et al. who showed that recurrent calcium oxalate stone formers have higher absorptive ability of oxalate compared to non-stone formers after an oral oxalate load.⁸

Despite what is known about stone formation, it remains unclear whether extensive metabolic evaluation and tailored dietary advice reduces stone recurrences overall compared to a general diet of low salt, increased fluid intake and moderate protein intake.

At the Groote Schuur Hospital Stone Clinic, patients are given a general diet sheet of low salt intake, increased fluid intake and moderate protein intake to address dietary factors contributing to stone recurrence. However, little is known of its effect to urinary oxalate parameters. Measuring urinary oxalate pre-diet and post-diet could provide support for the effectiveness of diet in the management of idiopathic hyperoxaluria in stone formers.

The aim of this study is thus to assess the impact, in a “stone clinic setting”, of advice focused on reducing dietary oxalate in addition to general advice in a cohort of idiopathic hyperoxaluric patients.

Methods

All patients referred to the Groote Schuur Hospital Stone Clinic from 2015 to 2017 were considered potentially eligible for the present study.

Inclusion criteria

To be included in the study, the patients had to fulfill the following requirements: (a) hyperoxaluria (> 40 mg/d) on a 24-hour stone study urinalysis; (b) absence of any known secondary causes of stone disease, including primary hyperoxaluria; and (c) not be taking medications known to affect urinary indexes such as diuretics, vitamin D, vitamin C, vitamin B₆, calcium, or magnesium supplements, bisphosphonates, and oestrogens.

Laboratory procedures

In the 24-hour urine sample, the urinary stone risk profile was assessed by measuring the following parameters: daily volume, pH; creatinine; sodium, potassium, calcium, magnesium; uric acid phosphate, citrate and oxalate at the NHLs laboratory.

Dietary intervention

The patients were all given a standardised diet sheet which emphasises dietary sodium and protein restriction. They were also instructed to avoid oxalate-rich foods such as spinach, rhubarb, beets, chocolate, cereals, nuts, tea, wheat bran, and strawberries, and to drink water in amounts of roughly 2 L during cold weather and 3 L during warm/hot weather. No incentive was given to the participants to enroll in the present study or to comply with the dietary advice. Following the dietary advice, a repeat 24-hour urine analysis at six weeks from dietary intervention was requested. Demographic, weight and height data was also collected.

Statistical analysis

Data was collected on a spreadsheet and baseline differences in continuous variables were examined by the one tailed paired *t*-test (using Graphpad Prism, version 5.03). $p < 0.05$ was regarded as statistically significant.

Results

Nineteen (19) patients were identified as having hyperoxaluria and met the inclusion criteria. There were eight men and 11 women with a mean age of 49 years. The mean BMI of the group was 28.4 kg/m² putting them in the overweight group with 5/19 patients > 30 kg/m² being obese.

Fourteen of the nineteen (14/19) patients completed the study; 3/19 patients failed to provide a post diet 24-hour urinalysis and in 2/19 the 24-hour collections were of inadequate volume, implying poor compliance with collection. A positive family history was found in 7/19 and all patients had had prior stone episodes, with a mean number of 1.9 prior stone episodes.

The normal upper level of absolute urinary oxalate excretion is 40 mg (440 μmol) in 24 hours. The mean pre-diet urinary oxalate was 53.2 mg/24 hours ($n = 14$), while the post intervention was 29.6 mg/24 hours ($p = 0.0002$). Only 3/14 patients who completed the trial failed to normalise their urinary oxalate on the diet.

Discussion

Dietary oxalate contributes up to 50% of urinary oxalate excretion.⁵ The importance of dietary oxalate's contribution was previously underestimated.⁶ The main sources of dietary oxalate are plants, principally seeds/nuts and leafy plants related to spinach and rhubarb.

Our study has contributed to a growing body of literature which supports oxalate restriction in the diet as a potential preventive strategy to reduce the risk of recurrence in calcium oxalate stone formers. We demonstrated a statistically significant drop in urinary oxalate to within normal levels in a group of hyperoxaluric stone formers on general preventive advice and specific oxalate dietary restriction (53.2 mg to 29.6 mg/24 hour, $p = 0.0002$).

Besides dietary oxalate restriction, additional preventive measures should include encouraging adequate fluid intake, urinary alkalinisation, caution with excess sodium and protein intake, and a normal calcium intake.

It is debated in the literature whether extensive metabolic evaluation and tailored dietary advice reduces stone recurrences overall compared to a general diet. Our study would appear to support a more intensive approach, such as practised at the Groote Schuur Hospital Stone Clinic. This approach is supported by Kocvara et al. who in a randomised study found a lower recurrence rate in subjects who underwent an extensive metabolic evaluation and tailored diagnosis compared to general diet.⁹

Studies have supported our findings that dietary instructions can effectively reduce urinary oxalate levels in a stone clinic setting. However, controversy exists as to the optimal diet to advise. For example, Nouvenne et al. were able to demonstrate a significant reduction in urinary oxalate with merely a normal-calcium, low-animal protein, low-salt diet.¹⁰ This finding led Noori et al. to compare a dietary approach to stop hypertension (DASH – high vegetable/fruit, low animal protein diet) with an oxalate restricted diet and showed that the DASH diet might be as effective as the low-oxalate diet in reducing calcium oxalate supersaturation.¹¹ Our study attempted to use both strategies by combining standard advice (akin to a DASH diet) with an oxalate reduced diet. Taking another strategy to mild idiopathic hyperoxaluria, Nakada showed that taking calcium citrate with meals is an effective clinical strategy for hyperoxaluria reduction.¹²

Our study has important limitations. Our sample size was small with 5/19 patients failing to complete or provide an adequate second (post-diet) 24-hour urinalysis. Two of the patients had pre-diet 24-hour urinalysis > 6 months prior to being recruited into the trial. Besides dietary advice and providing a diet sheet, we did not objectively monitor the compliance to the diet. Lastly, we did not calculate calcium oxalate supersaturation, but merely pre- and post-diet oxalate.

Conclusion

In the stone clinic setting, specific oxalate restriction in addition to general dietary advice of low salt intake, increased fluid intake and moderate protein intake can significantly reduce oxalate excretion in hyperoxaluric stone formers. The finding encourages metabolic evaluation and tailored treatment advice. These findings need further evaluation to determine if such dietary restriction can impact a general population of oxalate stone formers.

Conflict of interest

The authors declare no conflict of interest.

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Ethical approval

The study was approved by the Human Research Ethics Committee of the University of Cape Town; HREC 798/2014.

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