

Alkalinization of the Urine and Lowering of Urine Uric Acid Content in Diabetic Patients with a Low Urine PH Results in Prevention and Dissolution of Uric Acid Stones - A Case Report and A Retrospective Outcome Study

David S. H. Bell^{1*} | Edison Goncalves²

*Correspondence: David S. H. Bell

Address: ¹Southside Endocrinology, Birmingham, AL; ²Grandview Medical Group, Birmingham, AL

e-mail ✉: dshbell@yahoo.com

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ABSTRACT

With insulin resistance there is a decreased production of ammonia in the proximal tubule of the kidney leading to a low urinary PH which results in precipitation of uric acid crystals which form the nidus for the formation of a uric acid kidney stone. Alkalinization of the urine and lowering of the urine uric acid levels can prevent formation of these stones as well as causing dissolution of existing stones. In this report we describe a patient who prior to this intervention had at least 130 events related to kidney stones and who following intervention had no further events. In addition, we describe a retrospective survey of outcomes of this intervention in twelve subjects with multiple kidney stone related events. There was no recurrence of events related to kidney stones in this group. Therefore, alkalinization of the urine and lowering of uric acid content in diabetic patients with a low urine PH is extremely effective in avoiding further kidney stone related events.

Keywords: Low Urine PH, Kidney Stone, Diabetes, Urine Alkalinization, Allopurinol Potassium Citrate, Obesity, Insulin Resistance

Introduction

While the majority of kidney stones (59%) are composed of calcium oxalate, in the type 2 diabetic patient, the incidence of uric acid stones (38%) is higher which is also true in the insulin resistant and obese non-diabetic subjects (Daudon *et al.*, 2006; Lieske *et al.*, 2006; Ferrannini *et al.*, 1999). High insulin levels decrease the production of uric acid in the proximal renal tubule leading to a low urine PH (Bell, 2012). Irrespective of the uric acid content of the urine a low PH causes uric acid crystals to come out of solution where they aggregate, expand and form the nidus for the formation of uric acid stones (Sakhaee *et al.*, 2002). Normally excretion of uric acid is less than 800 mg/day but at levels as low as 200 mg/day with a low urine PH precipitation of uric acid crystals occurs (Ngo and Assimos, 2007). By alkalinizing the urine and decreasing the urine uric acid content stone formation can be avoided and already formed uric acid stones may also be dissolved (Bell, 2012; Trinchieri *et al.*, 2009).

Based on this research over the past decade, we have assumed that in any diabetic patient with a history of nephrolithiasis accompanied by a low urine PH, that the etiology of their stone formation is precipitation of uric acid crystals and have initiated alkalinization of the urine with potassium citrate 30 mEq three times a day in addition to therapy with 100 mg of allopurinol daily (AK therapy) to prevent stone formation and potentially dissolve existing stones (Bell, 2012; Bell, 2015). To illustrate the success of this therapy, we describe a case where severe, frequent and chronic nephrolithiasis was resolved with this therapy in addition to a retrospective review of the outcomes of this therapy in our practice.

Case Report

A 67-year-old white male was admitted to hospital for coronary angioplasty and stent placement and was found to have a plasma glucose of 636 mg/dl. On being assessed as an outpatient for diabetes therapy he gave a history of multiple bouts of renal colic. Since age 26 he had at least three attacks per year so that over 41 years he estimated at least 130 nephrolithiasis related episodes. He had had open surgery on one occasion, non-invasive surgeries (basket procedure) on three occasions and lithotripsies on seven occasions. His urinalysis showed a PH of 5.0 and he was started on AK therapy. Following initiation of AK therapy he has not had renal colic or other evidence of a kidney stone for over seven years.

Based on the spectacular results of AK therapy in the patient described above we conducted a retrospective review of AK therapy in diabetic patients in our practice.

We identified 64 subjects with a history of diabetes and nephrolithiasis of whom 19 had been treated with AK. None of these 19 subjects had had a recurrence of symptoms of nephrolithiasis following initiation of AK. However, since only 31% of subjects presenting with symptoms of nephrolithiasis ever have a second event we eliminated from the analysis those who had only had a single event prior to AK therapy so that the remaining twelve subjects had had at least two events prior to starting AK.

In this group the average age of their first event was 37.7 ± 11.8 years and prior to AK therapy the number of events was 10.3 ± 15.8 . However, after the subject described above was removed from the analysis the number of events was 5.7 ± 2.6 . The phenotype features of this group were not surprisingly age 57.2 ± 11 years, BMI 32.5 ± 6.2 Kg/m² and a duration of diabetes of 15.2 ± 8 years.

Discussion

Based on the spectacular resolution of severe, frequent and chronic symptoms of nephrolithiasis in a single patient, and a retrospective analysis of diabetic patients with a low urine PH and nephrolithiasis

the use of urine alkalinization and lowering of urine uric acid content is efficacious in avoiding uric acid stone formation and further nephrolithiasis related events.

Since 2002 it has been known that a low urine PH was a major factor in the formation of uric acid stones (Moran *et al.*, 2002). Later it was proven that with either allopurinol or urine alkalinization there was both a decrease in stone formation and stone dissolution (Ettinger *et al.*, 1996). However, the combination of alkalinization of the urine and allopurinol (AK therapy) has been found to be additive and efficacious in lowering the stone burden (Sinha *et al.*, 2013).

To date a randomized, placebo-controlled, prospective study of AK therapy has not been performed in patients with a low urine PH and a history of symptomatic nephrolithiasis. Subjects with type 2 diabetes, based on our data, would be the ideal subjects for such a study which for several years we have been advocating. To date we have not been successful (Bell, 2012; Bell, 2015)

Conclusion

In diabetic subjects with a history of nephrolithiasis and a low urine PH, alkalinization of the urine accompanied by a reduction in urine uric acid content spectacularly reduces further events related to nephrolithiasis.

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