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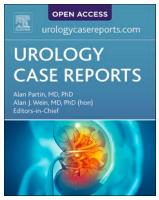

Endourology

# Refractory uric acid nephrolithiasis dissolution using phentermine/topiramate: A case report

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ABSTRACT

Uric acid is one of the few kidney stone minerals that can dissolve using oral alkalinization therapies such as potassium citrate. We report an obese female whose recalcitrant uric acid stones were eliminated using the weight loss medication phentermine/topiramate (Qsymia), a metabolic stimulant and carbonic anhydrase inhibitor. Pre- and post-dissolution 24-h urine studies and computed tomography images are included with a proposed mechanism of action of this medication. This is the first description of a non-alkaline oral therapy used alone for uric acid stone dissolution. Additional investigation of this medication in obese or diabetic uric acid stone formers is warranted.

## 1. Introduction

Uric acid nephrolithiasis (UAN) accounts for approximately 10 % of all kidney stone cases in the US with higher risk seen in patients with male sex, obesity (define as body mass index [BMI] > 30, and type 2 diabetes mellitus.[1,2] Excessive ingestion of dietary acids combined with a compromised urinary buffering system by impaired renal ammoniagenesis are risk factors that contribute to kidney stone formation in these populations.[3] These increases in urinary acid excretion and decreases in urine pH raise uric acid supersaturation and result in UAN.[4] For uric acid stone formers, guidelines of both the American Urological Association and the American Family Physician recommend oral alkalinizing agents such as potassium citrate or sodium bicarbonate to prevent or even dissolve uric acid stones by raising urine pH.[5] Additionally, lifestyle modifications, such as Dietary Approaches to Stop Hypertension (DASH) diet and/or increases in fluids, vegetables, and fruit, have been shown to improve the urinary factors that increase stone risk.[6] However, literature related to the impact of weight loss on stone formation is limited, and no standard of care or graded recommendation exists regarding the use of weight loss medication for the treatment of UAN. Thus, we report a novel approach toward the pharmacological treatment of refractory UAN using Qsymia, a weight-loss medication with the side effect of urinary alkalinization.

## 2. Case presentation

A 57-year-old morbidly obese (320 pounds, BMI = 53) female with type 2 diabetes mellitus presented to nephrology in 2012 for recurrent passage of uric acid stones. In light of normal serum uric acid level, her stone disease was managed using oral alkalinization medications. In 2013, she switched from potassium citrate (20 meq BID) to low dose sodium bicarbonate (1300 mg BID) due to diarrhea, nausea, and vomiting. The patient continued to pass stones and was unable to tolerate increases in sodium bicarbonate dosing. Two separate 24-h urine samples were collected during this time (Table 1 - May 2012, December 2016), both demonstrating low urine volume (1.4–1.5l), low urine pH (5.25–5.33), and elevated uric acid supersaturations (2.17–3.45). In 2017, she was referred to urology for surgical management of an obstructing 12 mm left ureteral stone. Over the subsequent four years, she had 16 different abdominal and pelvic computed tomography (CT) scans and five separate ureteroscopies.

On January 25, 2021, the patient had a CT scan performed (see Fig. 1 A/B insets) showing five new bilateral kidney stones roughly 4 months after bilateral ureteroscopic stone removal. We explored the option of weight loss and urinary alkalinization with pharmaceutical Qsymia®, a combination of phentermine, a sympathomimetic amine anorectic that increases metabolism, and topiramate, an anti-epileptic carbonic anhydrase inhibitor that reduces cravings. The patient collected a 24-h

*Abbreviations:* SS, supersaturation; CT, computed tomography; UAN, uric acid nephrolithiasis.

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**Table 1**
Recurrent uric acid stone former 24 hr urine values, variables labeled with normal range per day.

| Date | Volume (>2 L) | SS CaOx (<2) | Calcium (<200mg) | Oxalate (<40 mg) | Citrate (>550 mg) | SS CaP (<2) | pH (5.8–6.2) | SS UA (<2) | Uric Acid <0.75 gm) |
|---|---|---|---|---|---|---|---|---|---|
| 5/8/23 | 1.25 | 11.00 | 245 | 36 | 413 | 0.48 | 5.289 | 4.40 | 0.946 |
| 12/15/22[c] | 1.22 | 12.19 | 166 | 48 | 978 | 1.82 | 6.144 | 1.55 | 1.267 |
| 11/10/22[b] | 1.98 | 8.41 | 362 | 39 | 531 | 1.64 | 5.934 | 1.71 | 1.517 |
| 10/7/21[a] | 2.66 | 3.41 | 188 | 34 | 630 | 0.78 | 6.446 | 0.32 | 1.057 |
| 5/18/21 | 1.51 | 8.30 | 178 | 41 | 972 | 0.37 | 5.326 | 3.08 | 0.830 |
| 3/25/20 | 1.46 | 6.64 | 111 | 39 | 734 | 0.21 | 5.325 | 2.70 | 0.437 |
| 12/5/16 | 1.50 | 5.71 | 138 | 33 | 889 | 0.28 | 5.253 | 3.45 | 0.357 |
| 5/25/12 | 1.60 | 6.59 | 178 | 30 | 855 | 0.44 | 5.483 | 2.17 | 0.744 |

| Date | Sodium (<150 mmol) | Potassium (<100 mmol) | Magnesium (<120 mg) | Phosphorus (<1.2 mg) | Ammonium (<60 mmol) | Chloride (<250 mmol) | Sulfate (<80 meq) | Urea Nitrogen (6–14 gm) | Catabolic Rate (0.8–1.4 gm/kg) |
|---|---|---|---|---|---|---|---|---|---|
| 5/8/23 | 161 | 62 | 84 | 0.934 | 70 | 198 | 49 | 12.89 | 0.8 |
| 12/15/22[c] | 181 | 51 | 41 | 1.043 | 45 | 143 | 32 | 9.56 | 0.6 |
| 11/10/22[b] | 284 | 55 | 65 | 1.423 | 64 | 266 | 51 | 14.4 | 0.9 |
| 10/7/21[a] | 369 | 52 | 42 | 0.859 | 40 | 347 | 35 | 11.13 | 0.7 |
| 5/18/21 | 187 | 56 | 55 | 1.280 | 67 | 185 | 42 | 12.05 | 1.3 |
| 3/25/20 | 158 | 66 | 27 | 1.037 | 33 | 153 | 43 | 11.03 | 0.7 |
| 12/5/16 | 183 | 72 | 28 | 1.518 | 28 | 170 | 46 | 13.32 | 0.8 |
| 5/25/12 | 177 | 56 | 50 | 1.049 | 23 | 144 | 26 | 10.67 | 0.7 |

[a] 24 hour urine performed while patient on phentermine/topiramate 7.5 mg/46 mg.
[b] 24 hour urine performed while patient on topiramate 25 mg alone.
[c] 24 hour urine performed while patient on topiramate 50 mg alone.

urine specimen on 5/18/21 and began taking low dose Qsymia 3.75 mg/23 mg on 5/20/21. Fourteen days later, her dose escalated to 7.5 mg/46 mg. On July 12, 2021, seven weeks after beginning her medication, the patient had a follow-up CT scan, demonstrating complete dissolution of all five kidney stones (Fig. 1 insets C/D). A follow-up 24-h urine on 10/7/21 showed an increase in urine volume to 2.66 L and in urine pH to 6.45 with a drop in uric acid supersaturation to 0.32. Over the next six months, the patient lost 33 pounds (287 pounds) and had no ED visits or reports of stone passage. She remained on this medication until the fall of 2022. Due to financial reasons, she stopped Qsymia and was placed on generic topiramate 25 mg with repeat 24-h urine testing done on 11/10/22 showing a decrease in her urine pH to 5.934. As a result, her topiramate dose was escalated to 50 mg, and repeat testing on 12/15/22 showed a maintained urine pH of 6.144. Five months later, the patient self-discontinued the topiramate citing "brain fog," and a follow-up 24-h urine 5/8/23 showed urine volume, pH, and uric acid SS had all regressed back to pre-medication levels. At her most recent urology clinic visit in October 2023, she had weight regain to 310 pounds. Although she reported recurrence in monthly passage of small kidney stones, abdominal CT showed no stones or hydronephrosis in either kidney and, notably, she has not required surgical intervention for stone disease since 2020.

## 3. Discussion

The cornerstone of medical management for uric acid stones is urinary alkalinization to achieve a pH ranging 6.5–7, rendering uric acid stones completely soluble in the urine.[7] Unfortunately, patients are often non-compliant due to the high pill burden and gastrointestinal side effects, namely abdominal pain, nausea, or diarrhea.[8]

Given our patient's citrate intolerability and symptomatic recurrences requiring surgical intervention, we started Qsymia® (combination phentermine/topiramate), an FDA-approved medication for weight loss in patients with morbid obesity.[9] Topiramate inhibits carbonic anhydrase activity in the proximal convoluted tubule of the kidney, reducing bicarbonate reabsorption and raising urine pH to the point that calcium phosphate stone formation has been reported as a side effect of this medication when the urine is over alkalinized.[10–13] Based on our patient's lab values and imaging, Qysmia was effective for weight loss and urinary alkalinization. Not only did her existing uric acid stones completely dissolve within 4 months by moderate dose (7.5 mg/46 mg) therapy, but their formation was completely inhibited while the patient was compliant on medication. Coincidentally, her urine volume increased as the supersaturation of uric acid (SS UA) decreased while on Qsymia therapy. Although increase in urine volume may account for a small decrease in SS UA, the large drop in SS UA after initiation of treatment suggests a pharmacological rather than physiologic etiology. Interestingly, she continued topiramate alone after discontinuing Qsymia, and this by itself also seemed to effectively raise her urine pH. Her 24-hr SS UA was lowest while on topiramate therapy, highlighting the importance of a high urine pH to medically treat uric acid stones. Commonly seen with topiramate use, the patient reached her weight loss plateau roughly 6 months after initiation of Qysmia. The development of "brain fog" cognitive deficits that led to medication cessation is also a commonly reported side effect that has been shown to improve once the medication is stopped. Finally, the kidney responds to excessive urinary alkalinization and metabolic acidosis by reducing the excretion of urinary citrate. Our patient's decrease in urine citrate while on topiramate did not seem to adversely affect her clinical stone formation nor her uric acid supersaturation.

This is the first description of a non-alkaline-based, oral therapy used alone to dissolve uric acid stones. Based on our patient's improved

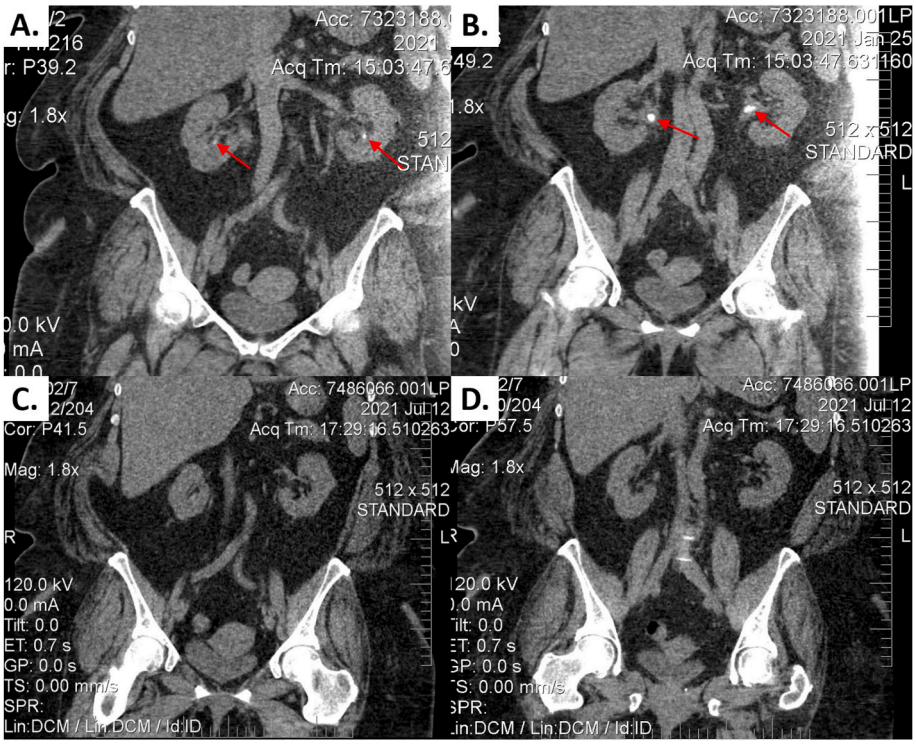


**Fig. 1.** Abdominal computed tomography (CT) of a patient with bilateral uric acid kidney stones before (A, B) and after (C,D) administration of Qsymia® 7.5 mg/46 mg. (A, B) Coronal CT sections demonstrating lower pole and renal pelvis calculi (red arrows). (C, D) Coronal CT demonstrating complete stone dissolution after 3 months on phentermine 7.5 mg/topiramate 46 mg (Qsymia®). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

clinical and urinary parameters, further investigation of this class of medications in the setting of refractory uric acid nephrolithiasis is warranted. Perhaps a multipronged treatment strategy that comprehensively targets weight loss, insulin resistance, and urine pH while providing more patient-friendly medications may be the key to more effective and personalized UAN therapies in the future.

## CRediT authorship contribution statement

**Logan Buchanan:** Writing – review & editing, Project administration, Formal analysis, Conceptualization. **Benjamin Canales:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Akira Yamamoto:** Writing – original draft, Conceptualization.

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