Published in final edited form as:

Int Urol Nephrol. 2011 September ; 43(3): 813–819. doi:10.1007/s11255-010-9824-6.

Thiazides diuretics in the treatment of nephrolithiasis: are we using them in an evidence-based fashion?

Rebecca Vigen,

Department of Medicine, VA North Texas Health Care System, The University of Texas Southwestern Medical Center at Dallas, Dallas, TX 75390-8856, USA

Rick A. Weideman, and

Pharmacy Service, VA North Texas Health Care System, Dallas, TX 75216, USA

Robert F. Reilly

VA North Texas Health Care System, The University of Texas Southwestern Medical Center at Dallas, Dallas, TX 75390-8856, USA. Section of Nephrology, VA North Texas Health Care System, Mail code-111, 4500 S. Lancaster Rd, Dallas, TX 75216, USA

Robert F. Reilly: Robert.Reilly2@VA.gov

Abstract

In the 1980s a change occurred in hydrochlorothiazide prescribing practices for hypertension from high-dose (50 mg/day) to low-dose (12.5–25 mg/day) therapy. However, randomized controlled trials (RCT) for prevention of calcium-containing kidney stones (CCKS) employed only high doses (≥ 50 mg/day). We hypothesized that these practices have resulted in underdosing of hydrochlorothiazide for prevention of CCKS. Patients with a filled prescription for thiazide diuretics that underwent a 24-h urine stone risk factor analysis were eligible. Those with evidence that thiazide was prescribed for CCKS were further analyzed. Of 107 patients, 102 were treated with hydrochlorothiazide, 4 with indapamide, and one with chlorthalidone. Only 35% of hydrochlorothiazide-treated patients received 50 mg/day; a dose previously shown to reduce stone recurrence. Fifty-two percent were prescribed 25 mg and 13% 12.5 mg daily, doses that were not studied in RCT. Evidence-based hydrochlorothiazide use was suboptimal regardless of where the patient received care (Nephrology or Endocrinology clinic). In a small subset of patients ($n = 6$) with 24-h urinary calcium excretion measured at baseline and after 2 hydrochlorothiazide doses (25 and ≥ 50 mg), there was a trend toward decreased urinary calcium excretion as the dose was increased from 25 to ≥ 50 mg/day ($p = 0.051$). Low-dose hydrochlorothiazide was often used for prevention of CCKS despite the fact that there is no evidence that it is effective in this setting. This may have resulted from a practice pattern of using lower doses for hypertension therapy or a lack of knowledge of RCT results in treatment of CCKS.

Keywords

Nephrolithiasis; Thiazide diuretics; Thiazide-like diuretics; Prescribing practices; Dose–response

Introduction

The modern era of diuretic therapy began in 1957 when Novello and Sprague synthesized the thiazide diuretic chlorothiazide [1]. In 1958 Beyer reported that the drug had natriuretic

properties [2]. Further modification of the benzothiadiazine core led to hydrochlorothiazide and the thiazide-like diuretics: chlorthalidone (phthalimidine); metolazone (quinazolinone); and indapamide (indoline). Thiazide-like diuretics bind and inhibit the Na–Cl cotransporter in distal convoluted tubule and connecting tubule but do not contain the benzothiadiazine core. The term thiazide diuretics will be used here subsequently to refer to both thiazide and thiazide-like diuretics. In 1959 Lamberg and Kuhlback found that chlorothiazide (1 gm BID) and hydrochlorothiazide (100 mg BID) reduced urinary calcium excretion [3]. Lichtwitz suggested this property might be exploited to prevent calcium-containing kidney stone recurrence [4], and in 1970 Yendt in uncontrolled studies reported reduced stone recurrence rates using hydrochlorothiazide in doses from 100 mg daily to 100 mg BID [5].

This was subsequently followed by at least 10 randomized prospective trials (RCT) using a variety of thiazide diuretics, eight of which showed reduced recurrence rates of calcium-containing kidney stones [6–15]. In these studies when hydrochlorothiazide was used, it was prescribed in high dose. The lowest dose employed was 50 mg daily. Seven of these studies were conducted in the 1980s, two in the early 1990s, and only one in the last 15 years [15].

In the 1980s a paradigm shift occurred in prescribing practices of hydrochlorothiazide for hypertension, and lower doses (12.5–25 mg daily) were increasingly employed [16]. In addition, clinical and biochemical side effects were noted to be dose dependent, especially hypokalemia [17]. This led to the current practice of using hydrochlorothiazide in lower doses for treatment of hypertension.

We hypothesized that in our institution thiazide and thiazide-like diuretics, especially hydrochlorothiazide were no longer being used in adequate, evidence-based doses to prevent calcium-containing kidney stone recurrence. This may be the result of a combination of factors including: a practice pattern of using lower doses of hydrochlorothiazide for the treatment of hypertension that has carried over to the treatment of stone disease and/or a lack of knowledge of RCT of thiazide diuretics in the treatment of calcium-containing kidney stone recurrence.

Materials and methods

Study design

Eligible patients were identified by querying the pharmacy database in the VA North Texas Health Care System for patients that filled a prescription for a thiazide diuretic in the past 10 years. Only those patients that also underwent a 24-h urine stone risk factor analysis were subsequently evaluated ($n = 223$) in order to better identify patients that were prescribed thiazides for nephrolithiasis and not hypertension. Since thiazide diuretics can be employed for both conditions, only those 115 patients with documented evidence in the medical record that the drug was prescribed for stone disease were included in the final analysis. Data were abstracted from VA's electronic medical record system—CPRS (Computerized Patient Record System). Eight patients were excluded because they either had side effects with up-titration of drug or were taking the diuretic for <6 months.

Urinary risk factor analysis was performed in the Mineral Metabolism Laboratory at the University of Texas Southwestern Medical Center at Dallas. Risk factors for calcium-containing kidney stone formation were defined as: low urine volume—<2 l/day; hypercalciuria (classic definition)— ≥ 300 mg/day in men and ≥ 250 mg/day in women; hypercalciuria (modified definition)— ≥ 250 mg/day regardless of gender; hypocitraturia—<320 mg/day in men and <500 mg/day in women; hyperoxaluria— ≥ 45 mg/day in men and ≥ 40 mg/day in women; hyperuricosuria— ≥ 800 mg/day in men and ≥ 750 mg/day in women. A risk factor was considered present if it was detected in one or more 24-h urine collections.

For 24-h urines to convert from mg/day to S.I. units: calcium—to convert to mmol/day multiply by 0.025; uric acid—to convert to mmol/day multiply by 0.0059; oxalate—to convert to $\mu\text{mol/day}$ multiply by 11.1; and citrate—to convert to mmol/day multiply by 0.0052.

Stone analysis was performed at the National VA Crystal Identification Center, Zablocki VA Medical Center, Milwaukee, WI using high-resolution X-ray powder diffraction and Fourier transform infrared spectroscopic techniques.

To determine if a dose–response effect of hydrochlorothiazide could be detected in the clinical setting, those patients with 24-h urinary risk factor analyses that were performed prior to onset of therapy and after 2 different doses of hydrochlorothiazide (25 and ≥ 50 mg) were identified. Pharmacy records were checked to verify that the patient had a filled prescription at the indicated dose in the month prior to the collection of the 24-h urine. If more than one 24-h urine was collected either at baseline or on a given dose of hydrochlorothiazide, the values were averaged.

Statistical analyses

The Chi-square test was used to compare the evidence-based use of hydrochlorothiazide in two of the three areas where patients received their care (Nephrology and Endocrinology clinic). Only 7 patients were cared for outside of Nephrology and Endocrinology clinics and due to the small numbers were not included in the analysis. To evaluate whether a dose–response effect was present with increasing dose of hydrochlorothiazide, a test of sphericity was first performed. The result was not significant and therefore, a repeated-measures ANOVA was employed to determine whether there was a significant difference between three doses of hydrochlorothiazide (control, 25 mg and ≥ 50 mg).

Results

Medical records of 107 patients prescribed a thiazide diuretic for ≥ 6 months for prevention of calcium-containing kidney stone recurrence were analyzed. Demographic characteristics of the patients are shown in Table 1. Most patients were male as expected given the preponderance of men in the VA system, as well as the increased prevalence of nephrolithiasis in men. Caucasians made up the majority of patients with the remainder largely African American. All patients had at least one 24-h urine stone risk factor analysis collected. The most common risk factor was low urinary volume (68.2%). The prevalence of other risk factors was: hypercalciuria (classic definition)—48.6%; hypercalciuria (modified definition)—59.8%; hypocitraturia—43%; hyperoxaluria—61.7%; and hyperuricosuria—37.4%. In sixty-three patients, at least one stone was chemically analyzed. As expected, the majority of stones submitted for analyses were pure calcium oxalate (54%) or a combination of calcium oxalate and calcium phosphate stones (30.1%). Fewer patients passed stones containing only calcium phosphate (7.9%). Stones composed of a combination of calcium oxalate and uric acid (3.2%), calcium oxalate and struvite (1.6%), or uric acid alone (3.2%) were much less common.

The highest dose of thiazide diuretic employed for prevention of stone recurrence was determined by chart audit. Of 107 patients, 102 were treated with hydrochlorothiazide, 4 with indapamide, and one with chlorthalidone (Table 2). Indapamide and chlorthalidone were prescribed at doses reported to reduce recurrence in randomized prospective trials, 2.5 mg indapamide and 25 mg chlorthalidone, respectively. However, of 102 patients treated with hydrochlorothiazide only 35% received ≥ 50 mg/day; doses previously shown in randomized prospective trials to reduce stone recurrence. All but two of these patients

received hydrochlorothiazide once daily. The remaining 65% were prescribed either 25 mg (52%) or 12.5 mg (13%) once daily; doses that were not studied in RCT.

We further examined the evidence-based use of thiazide diuretics based on where the patient received their care for stone disease. Patients were seen either in Nephrology clinic, Endocrinology clinic or other locations (Table 3). Regardless of where the patient was cared for evidence-based use of thiazide diuretics was suboptimal. In Endocrinology clinic, 57% of patients received evidence-based doses compared to 36% in Nephrology clinic and 29% in other locations. These differences were not statistically significant.

Little data is available regarding the dose–response curve of hydrochlorothiazide with respect to lowering urinary calcium excretion. Therefore, we examined patients prescribed hydrochlorothiazide with baseline 24-h urine stone risk factor analyses performed prior to therapy and at doses of 25 and ≥ 50 mg/day. Six patients were identified and their urinary calcium excretion is shown in Table 4. Pharmacy records were examined to verify that the patient had a filled prescription at the indicated dose for hydrochlorothiazide in the 30 days prior to the collection of the 24-h urine. In 5 of 6 patients, there was a further decline in urinary calcium as hydrochlorothiazide dose was increased from 25 to ≥ 50 mg/day. Baseline urine calcium excretion was 306.3 ± 70.9 mg/day; this decreased to 261.2 ± 106.1 mg/day at 25 mg, and to 183.3 ± 60.9 mg/day at doses ≥ 50 mg/day. Urinary calcium excretion was significantly lower comparing the 50-mg dose to control. There were no significant differences between control and the 25-mg dose. However, the decline in urinary calcium excretion when hydrochlorothiazide dose was increased from 25 to ≥ 50 mg/day was of borderline statistical significance ($p = 0.051$).

Discussion

Our patient population has many characteristics that are similar to that of calcium-containing stone formers previously reported. The majority are white Caucasian males. Prevalence of urinary stone risk factors is similar to that previously reported by Preminger except that hyperoxaluria was more frequent than expected [18]. In addition, chemical stone analyses were similar to that in the nonveteran population in Dallas reported by Pak [19].

RCT are critical in the evaluation of stone therapies [20, 21]. Referral of patients to a stone clinic is often followed by a reduction in stone-formation rate (stone clinic effect) independent of drug treatment [20]. This likely is the result of changes in fluid intake.

At least 10 randomized controlled trials examined the effect of thiazide diuretics on preventing CCKS recurrence. Seven of ten reported a reduction in recurrence rate in treated patients [8–15]. Two trials that showed no difference in outcome were limited by their short follow-up duration of less than 2 years [6, 7]. A consistent finding in these trials is that stone-formation rate between treated and control groups did not diverge until after at least one year of therapy. Stones too small to be detected by ultrasound or KUB may be passed in the first few months and obscure beneficial effects of treatment [12].

In the four trials that utilized hydrochlorothiazide, it was prescribed in doses of 50–100 mg daily [7–9, 15]. No randomized prospective trial that we are aware of has employed low-dose hydrochlorothiazide (12.5–25 mg daily) to examine reduction in calcium-containing-stone recurrence. Whether this dose would be effective is unknown. Of the three thiazide diuretics used in our study, evidence-based therapy would require the use of either: indapamide 2.5 mg/day; chlorthalidone ≥ 25 mg/day; or hydrochlorothiazide ≥ 50 mg/day. With regard to the use of antihypertensive drug therapy, Ernst has stated that “the practitioner who bases decisions on evidence from randomized trials expecting to see similar

benefits in practice should use the doses of antihypertensive drugs that were used in trials” [22]. The same can just as reasonably be stated for the treatment of stone disease.

Only 35% of patients prescribed hydrochlorothiazide were on relatively higher doses (≥ 50 mg/day) shown to be effective in RCT (Table 2). Reasons for this are unclear and may result from several factors including: lack of awareness of doses used in RCT and/or a practice pattern of using lower hydrochlorothiazide doses for hypertension treatment that has carried over to its use for treatment of stone disease.

In the 1980s a paradigm shift occurred toward the use of lower doses of hydrochlorothiazide in the treatment of hypertension. Hydrochlorothiazide at a dose of 12.5 mg/day has been compared to 25 mg/day in at least 6 studies involving 455 patients [23–28]. Doubling the dose of hydrochlorothiazide did not significantly improve blood pressure control. This has been used to make the argument that the dose–response curve of hydrochlorothiazide for the control of hypertension was relatively flat above doses of 25 mg/day [29].

The hypocalciuric action of thiazides is the most likely mechanism whereby this drug class reduces stone recurrence. Experimental studies in humans and laboratory animals suggest that there may be qualitatively different effects of high-dose and low-dose thiazide diuretic dose on renal calcium reabsorption. When thiazides are given in high dose, and there is a decline in extracellular fluid (ECF) volume, the resultant decline in ECF volume is thought to increase proximal tubular reabsorption of sodium and calcium [30–32]. The same is true in rats where molecular studies have shown that distal tubular transport proteins are not upregulated in response to high-dose thiazide diuretics, suggesting the effect is proximal [33]. However, when lower doses of thiazide diuretics were employed in rats, urinary calcium excretion fell and distal nephron calcium transport proteins were upregulated suggesting a distal tubular effect [34]. In addition, micropuncture and microperfusion studies by Costanzo and Windhager showed that when applied to the luminal surface of the distal tubule thiazides do stimulate calcium transport [35]. It is likely that thiazides act to reduce urinary calcium excretion in both the proximal and distal tubule with the proximal tubular effect predominating at higher doses associated with ECF volume contraction.

One trial involving six healthy subjects without hypercalciuria established a dose–response relationship between hydrochlorothiazide and urinary calcium excretion [36]. Each subject was maintained for one week on increasing doses of hydrochlorothiazide daily (12.5, 25, and 50 mg). As dose increased a statistically significant reduction in urinary calcium (dose response) was seen. To our knowledge, similar studies have not been performed in stone formers. Whether the dose response would be quantitatively different between stone formers and normals or even between different phenotypes of idiopathic hypercalciuria (absorptive versus renal leak) is unknown. Six of our patients had 24-h urine collections at baseline and on at least 2 different doses of hydrochlorothiazide (Table 4). In 5 of 6 patients, urinary calcium excretion declined with increasing dose of hydrochlorothiazide. Urinary calcium excretion (mg/day) progressively declined as hydrochlorothiazide dose increased as was observed in normal volunteers from a baseline urine calcium excretion of 306.3 ± 70.9 mg/day, to 261.2 ± 106.1 mg/day at 25 mg, and to 183.3 ± 60.9 mg/day at doses ≥ 50 mg/day. This finding in a small number of stone formers requires verification in a larger group of patients under conditions where dietary intake is controlled.

Conclusions

Our study shows that in the majority of patients treated with hydrochlorothiazide for prevention of recurrence of calcium-containing kidney stones, the drug was not being used in an evidence-based fashion. Sixty-five percent of patients were prescribed a dose that has

not been studied in RCTs. This may be the result of several factors including: trends in hydrochlorothiazide prescribing practices for hypertension that may have carried over into its use for management of kidney stones and/or lack of knowledge of randomized prospective trials. Whether low dose hydrochlorothiazide would be effective in reducing stone recurrence would require a large randomized prospective trial comparing high- and low-dose hydrochlorothiazide versus placebo. In addition, whether supplemental agents such as potassium chloride, potassium citrate, or potassium-magnesium-citrate further reduce stone recurrence needs to be part of such a trial. This will allow determination of the best drug combination to reduce calcium-containing kidney stone recurrence with the smallest amount of long-term risk to the patient. In addition, dose-response studies of hydrochlorothiazide's effect on hypercalciuria are limited and need to be carried out in kidney stone formers under conditions where dietary intake is controlled.

Acknowledgments

This work was supported by the University of Texas Southwestern Medical Center O'Brien Kidney Research Core Center (P30DK079328).

References

1. Jørgensen FS. Effect of thiazide diuretics upon calcium metabolism. *Dan Med Bull.* 1976; 23:223–230. [PubMed: 789016]
2. Beyer KH. The mechanism of action of chlorothiazide. *Ann NY Acad Sci.* 1958; 71:363–379. [PubMed: 13583792]
3. Lamberg BA, Kuhlback B. Effect of hydrochlorothiazide on the excretion of calcium in urine. *Scand J Clin Lab Invest.* 1959; 11:351–357. [PubMed: 14413581]
4. Lichtwitz A, Parlier R, De Seze S, Hioco D, Miravet L. L'effect hypocalcémique des sulfamides diurétiques. *Sem Hôp Paris.* 1961; 37:2350–2362.
5. Yendt ER, Guay GF, Garcia DA. The use of thiazides in the prevention of renal calculi. *Can Med Assoc J.* 1970; 102:614–620. [PubMed: 5437394]
6. Brocks P, Dahl C, Wolf H. Do thiazides prevent recurrent idiopathic renal calcium stones? *Lancet.* 1981; 2:124–125. [PubMed: 6113485]
7. Scholz D, Schwille PO, Sigel A. Double-blind study with thiazides in recurrent calcium lithiasis. *J Urol.* 1982; 128:903–907. [PubMed: 7176047]
8. Laerum E, Larsen S. Thiazide prophylaxis of urolithiasis. *Acta Med Scand.* 1984; 215:383–389. [PubMed: 6375276]
9. Wilson DR, Strauss AL, Manuel MA. Comparison of medical treatment for the prevention of recurrent calcium nephrolithiasis. *Urol Res.* 1984; 12:39–40.
10. Robertson, WG.; Williams, RE.; Hargreaves, TB. A multicenter trial to evaluate three treatments for recurrent idiopathic calcium stone disease- a preliminary report. In: Schwille, PO.; Smith, LH.; Robertson, WG.; Vahlensieck, W., editors. *Urolithiasis and related clinical research.* Plenum Press; New York: 1985. p. 545-548.
11. Mortensen JT, Schultz A, Ostergaard AH. Thiazides in the prophylactic treatment of recurrent idiopathic kidney stones. *Int Urol Nephrol.* 1986; 18:265–269. [PubMed: 3533825]
12. Ettinger B, Citron JT, Livermore B, Dolman LI. Chlorthalidone reduces calcium oxalate calculous recurrence but magnesium hydroxide does not. *J Urol.* 1988; 139:679–684. [PubMed: 3280829]
13. Ohkawa M, Tokunaga S, Nakashima T, Orito M, Hisazumi H. Thiazide treatment for calcium urolithiasis in patients with idiopathic hypercalciuria. *Br J Urol.* 1992; 69:571–576. [PubMed: 1638340]
14. Borghi L, Meschi T, Guerra A, Novarini A. Randomized prospective study of a nonthiazide diuretic, indapamide, in preventing calcium stone recurrences. *J Cardiovasc Pharmacol.* 1993; 22(suppl 6):S78–S86. [PubMed: 7508066]

15. Fernández-Rodríguez A, Arrabal-Martín M, García-Ruiz MJ, Arrabal-Polo MA, Pichardo-Pichardo S, Zuluaga-Gómez A. The role of thiazides in the prophylaxis of recurrent calcium lithiasis. *Actas Urol Esp.* 2006; 30:305–309. [PubMed: 16749588]
16. Flack JM, Cushman WC. Evidence for the efficacy of low-dose diuretic monotherapy. *Am J Med.* 1996; 101(suppl 3A):53S–60S. [PubMed: 8876475]
17. Huen SC, Goldfarb DS. Adverse metabolic side effects of thiazides: implications for patients with calcium nephrolithiasis. *J Urol.* 2007; 177:1238–1243. [PubMed: 17382697]
18. Preminger GM. Renal calculi: pathogenesis, diagnosis, and medical therapy. *Semin Nephrol.* 1992; 12:200–216. [PubMed: 1561497]
19. Pak CYC. Etiology and treatment of urolithiasis. *Am J Kidney Dis.* 1991; 18:624–637. [PubMed: 1962646]
20. Hosking DH, Erickson SB, Van Den Berg CJ, Wilson DM, Smith LH. The stone clinic effect in patients with idiopathic calcium urolithiasis. *J Urol.* 1983; 130:1115–1118. [PubMed: 6644890]
21. Spector R, Park GD. Regression to the mean: a potential source of error in clinical pharmacological studies. *Drug Intell Clin Pharm.* 1985; 19:916–919. [PubMed: 4085350]
22. Ernst ME, Carter BL, Basile GN. All thiazide-like diuretics are not chlorthalidone: putting the ACCOMPLISH study into perspective. *J Clin Hypertens.* 2009; 11:5–10.
23. Berglund G, Andersson O. Low doses of hydrochlorothiazide in hypertension: antihypertensives and metabolic effects. *Eur J Clin Pharmacol.* 1976; 10:177–182.
24. Stein CM, Neill P, Kusemamiwo T. Antihypertensive effects of low doses of hydrochlorothiazide in hypertensive black Zimbabweans. *Int J Cardiol.* 1992; 37:231–235. [PubMed: 1452381]
25. Scholze J, Breitstadt A, Cairns V, Bauer B, Bender N, Priestley C, Moreadith C, Phillips J, Vander Elst E, Koch G. Short report: ramapril and hydrochlorothiazide combination therapy in hypertension: a clinical trial of factorial design The East Germany Collaborative Trial Group. *J Hypertens.* 1993; 11:217–221. [PubMed: 8385183]
26. Canter D, Frank GJ, Knapp LE, Phelps M, Quade M, Texter M. Quinapril and hydrochlorothiazide combination for control of hypertension: assessment by factorial design. *J Hum Hypertens.* 1994; 8:155–162. [PubMed: 8006914]
27. Chrysant SG. Antihypertensive effectiveness of low-dose lisinopril-hydrochlorothiazide combination. *Arch Intern Med.* 1994; 154:737–743. [PubMed: 8147677]
28. Beermann B, Groschinsky-Grind M. Antihypertensive effect of various doses of hydrochlorothiazide and its relation to the plasma level of the drug. *Eur J Clin Pharmacol.* 1978; 13:195–201.
29. Flack JM. Evidence for the efficacy of low-dose diuretic monotherapy. *Am J Med.* 1996; 101(Suppl 3A):53S–60S. [PubMed: 8876475]
30. Suki WN, Hull AR, Rector FC Jr, Seldin DW. Mechanism of the effect of thiazide diuretics on calcium and uric acid. *J Clin Invest.* 1967; 46:1121.
31. Brickman AS, Massry SG, Coburn JW. Changes in serum and urinary calcium during treatment with hydrochlorothiazide: studies on mechanisms. *J Clin Invest.* 1972; 51:945–954. [PubMed: 4552338]
32. Breslau N, Moses AM, Weiner IM. The role of volume contraction in the hypocalciuric action of chlorothiazide. *Kidney Int.* 1976; 10:164–170. [PubMed: 966453]
33. Nijenhuis T, Hoenderop JG, Loffing J, van der Kemp AW, van Os CH, Bindels RJ. Thiazide-induced hypocalciuria is accompanied by a decreased expression of Ca^{2+} transport proteins in kidney. *Kidney Int.* 2003; 64:555–564. [PubMed: 12846750]
34. Lee CT, Shang S, Lai LW, Yong KC, Lien YH. Effect of thiazide on renal gene expression of apical calcium channels and calbindins. *Am J Physiol.* 2004; 287:F1164–F1170.
35. Costanzo LS, Windhager EE. Calcium and sodium transport by the distal convoluted tubule of the rat. *Am J Physiol.* 1978; 235:F492–F506. [PubMed: 727266]
36. Martins MC, Meyers AM, Whalley NA, Margolius LP, Buys ME. Indapamide (Natrlix): the agent of choice in the treatment of recurrent renal calculi associated with idiopathic hypercalciuria. *Br J Urol.* 1996; 78:176–180. [PubMed: 8813907]

Table 1

Demographics

Gender	92.6% male, 7.4% female
Race	86.1% Caucasian, 12.1% AA, 0.9% Asian, 0.9% NA
Age at time of study	61.3 ± 10.7 years
Age range	37–82 years

AA African American; NA Native American

Table 2

Thiazide diuretic use in patients with nephrolithiasis

Drug and dose	Number and %
Hydrochlorothiazide (mg/day)	
6.25	0
12.5	13 (13%)
25	53 (52%)
37.5	0
50	35 (34%)
75	0
100	1 (1%)
Total	102
Indapamide— ≥ 2.5 mg/day	4
Chlorthalidone—25 mg/day	1

mg Milligrams

Table 3

Evidence-based use of thiazide diuretic by clinic

Evidence-based use	Renal	Endocrine	Neither
Yes	31	8	2
No	55	6	5

Table 4

Urinary Ca (mg/24 h)

Patient	Control	25 mg	≥50 mg
1	223	260	160
2	377	406	245
3	368	244	209
4	318	131	72
5	337	358	209
6	215	168	205
Mean ± SD	306.3 ± 70.9	261.2 ± 106.1	183.3 ± 60.9

SD Standard deviation