Tamsulosin for Ureteral Stones in the Emergency Department: A Randomized, Controlled Trial

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Study objective: The α-adrenergic antagonist tamsulosin hydrochloride has become an increasingly common adjunct in the treatment of ureteral calculi; however, its efficacy in a general emergency department (ED) population has not been investigated.

Methods: We conducted a randomized, controlled trial of adult ED patients with distal ureteral calculi diagnosed by computed tomography scan. Patients were randomized to receive either a 10-day course of ibuprofen and oxycodone plus tamsulosin or ibuprofen and oxycodone alone. The primary outcome measure was successful spontaneous ureteral stone expulsion at 14 days. Secondary outcomes included time to stone passage, self-reported pain scores, number of colicky pain episodes, unscheduled return ED/primary care visits, number of days of missed work/usual function, amount of analgesic used, and adverse events.

Results: Eighty subjects were enrolled in the study, with 77 completing the trial. Mean stone size was 3.6 mm (95% confidence interval [CI] 3.4 to 3.9). Successful spontaneous stone expulsion at 14 days was similar between the groups, with 27 (77.1%) subjects in the tamsulosin group and 24 (64.9%) subjects in the standard therapy group reporting spontaneous stone passage, a difference of 12% (95% CI −8.4% to 32.8%). At 2-, 5-, and 14-day follow-up, there were no clinically important (or statistically significant) differences between the groups for any secondary outcome measure. No adverse events were reported in either group.

Conclusion: In this cohort of adult ED patients with distal ureteral calculi, treatment with tamsulosin did not substantially improve any of the studied outcome measures compared with treatment with ibuprofen and oxycodone alone. [Ann Emerg Med. 2009;54:432-439.]

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INTRODUCTION

Background and Importance

Flank pain from acute renal colic is a common presenting complaint to emergency departments (ED) that is increasing in frequency.[1] In the United States, approximately 13% of men and 7% of women will be diagnosed with kidney stones at some time in their life.[2] The majority of ureteral stones cause pain that is intense and rapid in onset, causing patients to seek care acutely in an ED or primary care physician's office. In 2000, there were more than 600,000 visits to US EDs and approximately 2 million outpatient visits for ureterolithiasis, with a total health care–related cost of $2.1 billion. The average patient incurred $4,500 of direct health care costs and missed an average of 19 hours of work.[1,3,4]

Several studies, including 2 recent meta-analyses evaluating the use of tamsulosin in a select cohort of patients who had distal ureterolithiasis and were referred to urologists, have demonstrated that tamsulosin hydrochloride, when added to a standardized pain control regimen, increases spontaneous stone passage and decreases the severity of pain and the number of colicky pain episodes compared with that of patients receiving pain medications alone.[5-17] Despite the positive findings of these urology-based studies and the significant numbers of patients diagnosed with ureterolithiasis in EDs, our literature review revealed no published studies evaluating the use of tamsulosin hydrochloride (Flomax; Boehringer Ingelheim, Ingelheim, Germany) in a general ED patient population diagnosed with distal ureterolithiasis. We therefore conducted this study to determine whether the use of tamsulosin would be effective in all patients diagnosed with distal ureterolithiasis in the ED.

Goals of This Investigation

The purpose of this study was to evaluate the efficacy of a 10-day course of tamsulosin in comparison to standard therapy for the treatment of adult ED patients with distal

Editor's Capsule Summary

What is already known on this topic

Patients with ureteral calculi are often prescribed adjunctive treatment with an α-blocking agent to enhance spontaneous stone passage. This practice has not been validated in emergency department (ED) patients.

What question this study addressed

Does the addition of a 10-day course of tamsulosin to standard therapy after discharge from the ED increase the rate of passage of distal ureteral stones?

What this study adds to our knowledge

In this randomized trial of 80 patients, most of whom had stones of 4 mm or less, time to stone passage was similar in tamsulosin and control patients.

How this might change clinical practice

This study does not support the routine use of tamsulosin in ED patients, though it is possible that it would be beneficial in patients with larger stones.

ureterolithiasis. We hypothesized that there would be a greater than or equal to 30% difference at 14 days post–ED visit in the proportion of subjects who reported stone passage in subjects receiving a 10-day course of tamsulosin plus standard pain control therapy compared with those receiving standard pain control therapy alone. Furthermore, we hypothesized that there would be improvement in the tamsulosin group when pain scores, number of colicky pain episodes, time to stone passage, need for opioid analgesia, return ED/unscheduled primary care visits, days of missed work or usual function, and adverse events were compared with those in the standard therapy group.

MATERIALS AND METHODS

Theoretical Model of the Problem

Renal colic is most often caused by stones that are lodged in the ureter, usually in its distal portion.[9] The main factors affecting the retention of ureteral calculi are ureteral muscle spasm, submucosal edema, pain, and infection within the ureter.[9] Obara et al[18] demonstrated that α-1 receptors are predominant in the ureteral smooth muscle and hypothesized that the blockade of these α-adrenergic receptors by a specific antagonist would result in decreased ureteral peristaltic amplitude and frequency, decreasing intraureteral pressure and allowing increased fluid transport to occur.[19] More recently, Sigala et al[20] demonstrated that specific adrenoreceptor subtypes ($\alpha_{1A}$and α_{1D}) are prevalent in the distal part of the ureter. Tamsulosin is a selective $\alpha_{1A}$and α_{1D} adrenoreceptor blocker that is used for the initial treatment of patients with lower urinary tract symptoms suggestive of benign prostatic hypertrophy. The use of tamsulosin or other selective adrenoreceptor blockers in addition to a standardized pain control regimen in patients with distal ureterolithiasis has been called medical expulsive therapy.[12,15] Several studies and 2 meta-analyses have shown that medical expulsive therapy increases the successful passage of distal ureteral stones and decreases the severity of pain and the overall number of colicky pain episodes compared with a standardized pain control regimen alone in patients who have distal ureterolithiasis and are referred to a urologist, thus avoiding the need for surgical removal of the stone.[5,6,11,12,15-17] Referral patterns to urologists for the treatment of distal ureterolithiasis differ greatly among practitioners. We are unaware of any studies evaluating the use of medical expulsive therapy in a nonselect group of patients diagnosed with distal ureterolithiasis in the ED. We therefore conducted this study to evaluate the use of tamsulosin in a nonselect group of patients diagnosed with distal ureterolithiasis in the ED.

STUDY DESIGN

We conducted a randomized, controlled trial comparing treatment with standard analgesic therapies with a combination of tamsulosin and standard therapies. The study was approved by the Maine Medical Center Institutional Review Board and was conducted in accordance with the provisions of the Declaration of Helsinki and Good Clinical Practice guidelines. The study medication was purchased for the subjects from the hospital's pharmacy with grant funds from the Maine Medical Center Mentored Research Committee.

Setting

The study took place in the Department of Emergency Medicine at Maine Medical Center, an academic ED housing an emergency medicine residency program. At the time of the study, the ED census was approximately 52,000 visits per year.

Selection of Participants

Subjects were eligible for study inclusion if they were at least 18 years of age, were able to provide written informed consent, and had a computed tomography (CT)–confirmed diagnosis of a single calculus in the distal third of the ureter (distal to the internal iliac vessels) inconsistent with phleboliths, as determined by a board-certified radiologist. Subjects were excluded for the following criteria: allergy or sensitivity to the study drug (tamsulosin hydrochloride); sulfa/sulfonamide allergy; lithiasis of the ureteral intramural tract; acute or chronic renal failure; fever; presence of multiple ureteral stones; peptic ulcer disease; liver failure; pregnancy; breastfeeding; and a history of urinary surgery, a history of endoscopic treatment, or concomitant treatment with any of the following pharmaceuticals: α-lytic drugs, calcium channel antagonists, nitrates, and vardenafil hydrochloride. Patients with an inability to use the study pain scale or an inability to read, write, and speak the English language were also excluded.

Interventions

From August 2006 to November 2007, we conducted a randomized, controlled trial in which potential subjects were identified on a convenience basis, completed the process of informed consent, and were randomly assigned to one of 2 study groups. As part of the informed consent process, information on the differences between the 2 study groups was provided to patients before their decision about whether or not to participate in the study. Randomization was accomplished by using a table of random numbers to assign sequentially numbered study packets to one of the study groups. The information on group assignment was contained in a sealed envelope within each study packet, and the envelopes were clearly labeled "do not open until informed consent is obtained." On discharge from the ED, patients randomized to the standard therapy group were provided with, and instructed on the use of, standardized doses of ibuprofen (800 mg orally, 3 times a day) and oxycodone (5 to 10 mg orally, every 4 to 6 hours) as needed for pain. Those randomized to the treatment group received tamsulosin hydrochloride 0.4 mg by mouth daily for 10 days in addition to the standard analgesic therapy described above. All subjects also received standard discharge instructions for renal colic and were given a urine strainer and instructions on straining their urine and collecting debris. All patients were instructed to follow up with the hospital's on-call urologist in 10 to 14 days.

Data Collection and Processing

Standardized data collection sheets were completed for all study participants. All subjects were provided with a study follow-up data sheet and were instructed to document events such as medication usage, number of colicky episodes, and spontaneous passage of their renal calculi. Investigators initiated telephone follow-up with all subjects at 2, 5, and 14 days post-discharge from the ED, using a standardized data collection sheet, including scripted questions to be posed to the subjects (Appendix E1, available online at http://www.annemergmed.com). All data elements were entered into a study database by 1 investigator.

Methods of Measurement

The primary outcome measure was the successful spontaneous passage of ureteral calculi at 14 days. Secondary outcomes included the time in days until spontaneous stone expulsion, the number of episodes of colicky pain experienced by the subject, the number of return visits to the ED or unscheduled primary care visits for continued pain, the amount of opioid analgesic used, the number of days of missed work or inability to perform usual functions (household duties, etc, if not working outside the home), the occurrence of adverse events, and self-reported pain scores, as evaluated with the 11-point Numeric Rating Scale.[21] This scale asks patients to choose 1 number, on a scale from 0 (no pain) to 10 (severe pain), corresponding to the intensity of their pain. All outcomes were evaluated at the 2-, 5-, and 14-day telephone follow-up sessions.

Primary Data Analysis

According to a previously reported 30% difference between the study groups in the rate of stone expulsion and an expectation that the proportion of subjects with spontaneous stone expulsion would increase from 65% to 95%, sample size was calculated to achieve a statistical power of 80% at 5% type 1 error, with 34 subjects being required for each group.[6,9,10] An additional 15% was added in anticipation of attrition and subjects lost to follow-up, requiring a total of 80 subjects, with 40 in each treatment group.

Data were analyzed with SPSS for Windows, version 11.0 (SPSS, Inc., Chicago, IL). Primary analyses were performed according to the intention-to-treat principle. Statistical significance was set at an α of less than 0.05. Interim analysis was performed at 50% enrollment to evaluate for the presence of adverse medication–related events by an investigator (T.D.S.) blinded to the study group assignments at the analysis.

We tested the hypothesis that there would be a greater than or equal to 30% difference between our study groups in the proportion of subjects experiencing spontaneous stone expulsion at 14 days. Descriptive statistics were used to describe the study population and examine demographic variables. Univariate analyses were conducted with the independent samples *t* test (to compare means between normally distributed groups), whereas the Mann-Whitney *U* test was used for non-normally distributed variables. Levene's test was used to evaluate for homogeneity of variances between the groups. Nominal parameters were evaluated with Fisher's exact test. Kaplan-Meier analysis was used to examine time to stone expulsion, whereas log-rank analysis was used for the group comparison. Ninety-five percent confidence intervals (CIs) were calculated by the exact method.

Because some subjects in each study group were uncertain about whether they had passed their ureteral stones, sensitivity analyses were conducted to determine the effect of this uncertainty on the primary outcome measure, successful spontaneous stone expulsion at 14 days. Best-case sensitivity (all subjects with unknown status passed their stones), worst-case sensitivity (no subjects with unknown status passed their stones), and midcase sensitivity (3 of 5 standard therapy and 2 of 3 tamsulosin therapy subjects with unknown status passed their stones) analyses were performed. Sensitivity analysis was also calculated for best-case tamsulosin, in which all unknown subjects in the study group passed their stones and no unknown subjects in the control group passed their stones.

RESULTS

Characteristics of Study Subjects

Of 80 patients who were randomized, 77 completed the study protocol. Thirty-nine subjects were randomized to the tamsulosin study group, whereas 41 were randomized to the standard therapy group. One subject in each group chose not to participate in the study after randomization, and 1 subject was found to have a ureteral stone more proximal than allowed by the study protocol and was excluded from further participation.

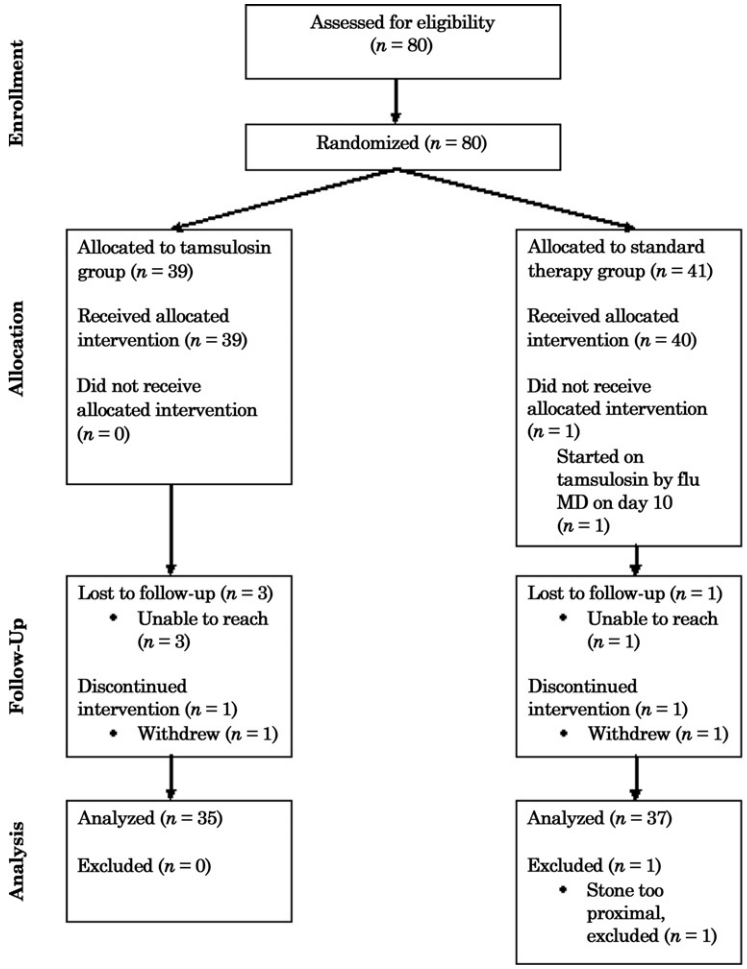

Figure 1. CONSORT diagram.

One subject randomized to the standard therapy group began receiving tamsulosin therapy by her follow-up urologist 10 days after discharge from the ED; the intention-to-treat principle was maintained and the subject's data were analyzed as part of the standard therapy group (Figure 1). This subject's stone was surgically removed on post-ED discharge day 12. Although there were more men in the tamsulosin group (84.2% versus 61.5%), other demographic characteristics were similar in the 2 groups and are presented in Table 1.

Table 1. Demographic characteristics of the study participants.

Characteristic	Tamsulosin Group (n=38)	Standard Therapy Group (n=39)
Male sex, No. (%)	32 (84.2)	24 (61.5)
White race, No. (%)	35 (92.1)	38 (97.4)
Disposition, No. (%), discharged	38 (100.0)	39 (100.0)
Age, y (SD)	47 (14)	45 (12)
Body mass index (SD)	28.1 (4.5)	27.5 (5.2)
Stone size, mm (SD)	3.5 (1.2)	3.8 (1.0)
ED LOS, mm (SD)	242 (77)	269 (105)

LOS, Length of stay.

Main Results

Spontaneous passage of ureteral stones was reported by 27 subjects (77.1%) in the tamsulosin group and by 24 subjects (64.9%) in the standard therapy group, a difference between the groups of 12% (95% CI −8.4% to 32.8%) that was not found to be statistically significant, P=.504. Spontaneous passage of ureteral stones greater than 4.0 mm (n=19), was 50% (4 of 8) in the tamsulosin group and 54.5% (6 of 11) in the standard therapy group, difference between the groups=4.5% (95% CI −50% to 41%), P=.491. Stone disposition at 14-day follow-up is depicted in Table 2.

Time to spontaneous stone expulsion was evaluated with Kaplan-Meier analysis, and the log-rank test was used to assess for group differences. For subjects in the tamsulosin group, the median number of days to stone expulsion was 1 (95% CI 0 to 2 days). The median number of days to stone expulsion for those in the standard therapy group was 3 (95% CI 2 to 4 days).

Table 2. Ureteral stone disposition at 14-day follow-up.

Outcome	Tamsulosin, No (%) (n=38)	Standard Therapy, No (%) (n=39)
Spontaneous passage	27 (71.1)	24 (61.5)
Not passed	2 (5.3)	3 (7.7)
Surgical removal	3 (7.9)	5 (12.8)
Subject uncertain	3 (7.9)	5 (12.8)
Missing data	4 (10.5)	2 (5.1)

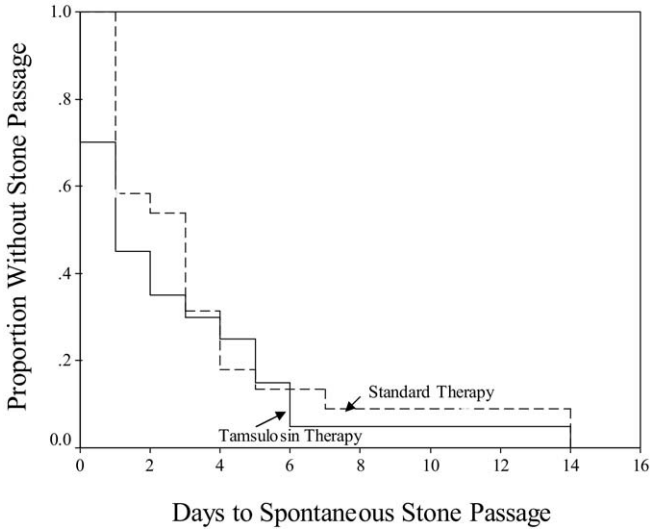

Figure 2. Survival curves for time to spontaneous stone expulsion.

When the number of days to stone passage was compared between the groups, a statistically significant difference was not identified, log-rank $\chi^2=0.92$, $df=1$, $P=.3372$. Figure 2 displays the survival curves for time to spontaneous stone expulsion. Figure E1 depicts days to stone passage by stone size and study group (available online at http://www.annemergmed.com).

During the follow-up period, 6 subjects (17.1%) in the tamsulosin group and 8 subjects (21.6%) in the standard therapy group returned to the ED or had an unscheduled visit with their primary care provider for continued renal colic pain. This represents an intergroup difference of 4.5% (95% CI – 14.1% to 23.1%), $P=.634$.

Other secondary outcomes, including number of colicky pain episodes, self-reported 11-point Numeric Rating Scale pain scores, days missed of work/usual function, and amount of opioid analgesic used, were reported at 2, 5, and 14 days after discharge from the ED. Significant differences between the groups were not observed at any follow-up point or cumulatively throughout the entire follow-up period. Tables 3 and 4 report data on these outcomes.

At each telephone follow-up, subjects were directly questioned about the presence or absence of the following adverse medication effects: nausea, vomiting, dizziness, hypotension, ejaculatory abnormalities, diarrhea, headache, arthralgia, and rash. None of these adverse medication effects were reported in either group.

Sensitivity Analyses

Five subjects in the standard therapy group and 3 subjects in the tamsulosin group were unsure whether or not they had passed their ureteral stones by follow-up at 14 days. For our best-case sensitivity analysis, we assumed that all 8 subjects with unknown stone passage had passed their stones. Under this scenario, 85.7% (n=30) of subjects in the tamsulosin group and 78.4% (n=29) of subjects in the standard therapy group would have experienced successful stone passage, difference between the groups=7.3%, $P=.788$. In our midcase sensitivity analysis, we assumed that 3 of 5 standard therapy and 2 of 3 tamsulosin group subjects with unknown stone passage had passed their stones. Here, 82.9% (n=29) of tamsulosin subjects and 73.0% (n=27) of standard therapy subjects would have passed their stones spontaneously (difference between the groups=9.9%; $P=.625$). Assuming the worst case, that no subject with unknown stone passage had passed their stone, yields a situation in which 69.2% (n=27) of tamsulosin and 64.9% (n=24) of standard therapy subjects would have experienced successful stone expulsion, for a difference of 4.3% between the groups, $P=.821$.

Under the final scenario, we assumed that all subjects taking tamsulosin passed their stone and all subjects in the standard therapy group did not pass their stone. Here 85.7% (n=30) of tamsulosin subjects and 64.9% (n=24) of standard therapy subjects would have experienced spontaneous stone passage, representing a difference of 20.8%, $P=.341$.

In addition to these sensitivity analyses, a per-protocol analysis of the one subject who was randomized to standard therapy but received tamsulosin beginning on day 10 was completed. Because the subject's stone was surgically removed on day 12, the number of subjects experiencing successful spontaneous stone passage is unchanged regardless of whether she is included in the tamsulosin (per-protocol analysis) or standard therapy (intention-to-treat analysis) group; however, the percentage of tamsulosin subjects experiencing spontaneous passage decreases from 77.1% to 75%, whereas the percentage in the standard therapy group increases from 64.9% to 66.7%. The difference between the groups decreases from 12.2% to 8.3%. Under the per-protocol analysis, the number of subjects experiencing surgical stone removal in the tamsulosin group increases by 1, bringing the percentage with this outcome from 8.6% to 11.1%. The corresponding decrease in surgical stone removal for the standard therapy subjects decreases the percentage undergoing surgery from 13.5% to 11.1%, eliminating the 4.9% difference between the groups.

LIMITATIONS

Considering the limitations of this study and its differences from previously published works can assist in placing our results into the context of the current literature. Our investigation was conducted in a single US ED and, despite reaching the enrollment requirements of our sample size calculation, is a relatively small study. Because calculating sample size depends on estimating a clinically important difference between the

Table 3. Mean result for each outcome measure, by treatment.

	Outcome Measure, Study Group											
	Colicky Pain Episodes			11-Point Numeric Rating Scale Pain Scores			Opioid Use (5-mg Tabs)			Days Missed Work/Usual Function		
Follow-up Time, Days	Tams.	Standard	Δ (95% CI)	Tams.	Standard	Δ (95% CI)	Tams.	Standard	Δ (95% CI)	Tams.	Standard	Δ (95% CI)
2	3.2	5.7	2.0 (–0.6 to 4.5)	2.0	3.0	1.1 (–0.5 to 2.6)	3.6	3.2	–0.3 (–2.5 to 1.8)	1.1	1.3	0.2 (–0.3 to 0.6)
5	3.1	2.3	–0.8 (–2.7 to 1.1)	1.3	0.7	–0.6 (–1.6 to 0.4)	4.9	0.6	–3.9 (–7.8 to 0.7)	1.7	1.5	–0.2 (–1.0 to 0.5)
14	1.8	0.9	–0.9 (–2.9 to 1.1)	0.6	0.3	–0.3 (–1.0 to 0.4)	1.6	0.5	–0.6 (–2.7 to 1.5)	2.2	1.9	–0.3 (–1.8 to 1.3)
Cumulative	7.9	7.9	–0.1 (–4.8 to 4.7)	—	—	—	10.2	4.3	–4.9 (–12.0 to 2.2)	—	—	—

Tams., Tamsulosin; –, data not collected.

Table 4. Group differences in outcome measures.

Outcome, Follow-up Time	No.*	Mean Difference (95% CI)
Colicky pain episodes, days		
2	67	1.95 (–0.62 to 4.51)
5	71	–0.78 (–2.65 to 1.09)
14	70	–0.88 (–2.85 to 1.09)
Cumulative	71	–0.05 (–4.81 to 4.70)
11-Point Numeric Rating Scale scores, days		
2	69	1.09 (–0.45 to 2.63)
5	70	–0.57 (–1.58 to 0.44)
14	68	–0.30 (–0.97 to 0.36)
Opioid used, days		
2	69	–0.34 (–2.47 to 1.79)
5	71	–3.86 (–7.78 to 0.68)
14	70	–0.62 (–2.69 to 1.46)
Cumulative	71	–4.94 (–12.04 to 2.15)
Missed work/function, days		
2	71	0.19 (–0.26 to 0.64)
5	71	–0.24 (–0.95 to 0.46)
14	68	–0.27 (–1.81 to 1.27)

*Sample size for individual outcomes may not sum to cohort size because of missing data points.

study groups, we identified a difference of 30% in the rate of stone expulsion as the most commonly reported minimum clinically relevant difference, according to previous literature.[6,9,10] Although a 30% difference between the groups is rather large, when coupled with previous statistically significant results in smaller samples and the expense and time required to adequately power a trial aimed at identifying a smaller difference, we deemed 30% both appropriate to answer our study question and achievable, given our resources.

Also related to additional trial complexity and expense, we chose not to include the provision of a placebo control to those subjects randomized to our control group. We opted instead to standardize the medications received by our subjects by preprinting "to-go" prescriptions for ibuprofen and oxycodone for all subjects while providing prepackaged tamsulosin for those in the intervention group.

Not all subjects were confident of their stone disposition at 14-day follow-up, as shown in Table 2. Three subjects in the intervention group and 5 in the control group reported resolution of their symptoms, yet had not identified a stone while straining their urine. Although it is possible that these subjects had passed their stones, it is also plausible that the stones had not passed and were asymptomatic at follow-up.[1] Additionally, there were more men in the tamsulosin group than in the standard therapy group. Although this may have theoretically affected stone passage rates, we did not find a difference in the rate of stone passage according to sex ($P=.270$).

Finally, although we accounted for attrition in our sample size calculation, complete follow-up data (for all 3 points of 2, 5, and 14 days) were not obtained for all subjects. We attempted to contact all subjects on multiple occasions; however, we were unsuccessful in obtaining complete information about spontaneous stone expulsion in 3 intervention group and 2 standard therapy group subjects.

DISCUSSION

According to studies published in the urologic literature that used a combination of ED and outpatient referral patients, the use of tamsulosin has become increasingly common in the treatment of distal ureterolithiasis in US ED patients. Despite the numerous articles published on this topic, conclusive evidence about whether tamsulosin therapy is efficacious, tolerable, and safe for use in a general ED population remains unproved. In addition, important patient-oriented data such as self-reported and clinically significant pain relief have been limited. We endeavored to fill these gaps in

knowledge with the present trial and have arrived at a conclusion contrary to those of previous reports.

We conducted this randomized, controlled trial and evaluated 8 outcomes in an effort to determine the efficacy of tamsulosin in the treatment of a general adult ED patient population with distal ureterolithiasis. Using previously published studies that showed a large treatment effect, we performed a power calculation with standard α and β values to determine our sample size. In contrast to the previously published literature on the topic, we found no evidence to suggest a benefit for the addition of tamsulosin to standard therapies at the level of treatment effect previously published ($\geq$30%). Although our study showed a trend toward improvement in the success of spontaneous stone passage at 14 days (a 12% difference between the groups) and decreased return ED/unscheduled primary care physician visits in subjects taking tamsulosin, it was not statistically significant. We did observe 25% fewer return ED or primary care physician visits in the tamsulosin group; however, this represented only 2 patients and was not found to be statistically significant (P=.634). We observed no difference in our other 5 outcome variables, including patient-oriented outcomes of overall pain scores, number of colicky pain episodes, amount of opiates used, and days missed of work/usual function. Our results may differ from those of the previously reported randomized trials and 2 meta-analyses for several reasons, including lack of referral bias, smaller mean stone size, and a shorter period of treatment and observation. Several important factors may be implicit in the reasons for these differences.

First, we were interested in studying tamsulosin in a general population of ED patients with uncomplicated distal ureterolithiasis. Previous researchers may have reached different conclusions by virtue of their study populations, consisting of outpatient urology patients referred from other physicians for renal colic. The few studies that enrolled subjects in an emergency setting included patients first referred to a urologist and treated in the ED of a urology department, rather than an inclusive ED population consisting of all subjects diagnosed with ureterolithiasis.[6,8,15]

A second consideration is the relatively small stone size observed in our study population, 3.46 mm in our intervention group and 3.83 mm in our control group. Approximately 25% of our subjects had stones measuring greater than 4.0 mm, with the largest reported measurement being 6.0 mm. It is well established that spontaneous stone passage is directly related to stone size and location, with smaller and more distal stones having a greater likelihood of spontaneous passage.[22] Previous literature examining the utility of tamsulosin has reported mean stone sizes ranging from 4.7 to 7.8 mm, with the majority of studies reporting stone sizes greater than 6.5 mm. Although we were unable to detect a relationship between stone size and successful spontaneous stone passage, it is plausible that the size of the treatment effect of tamsulosin in the other studies was affected by stone size. We were unable to find any studies conducted from US EDs describing the average stone size observed in patients presenting with renal colic; however, 3 studies of patients who had acute renal colic and presented to radiology for emergency CT scans describe mean stone sizes of 3.9 mm, 4.4 mm, and 4.6 mm, respectively, a mean size similar to that observed in our study.[4,23,24]

Although a 0.4 mg/day dose of tamsulosin is standard in the current literature, the duration of treatment has varied. Studies have reported treatment durations between 7 and 28 days, and 2 recent articles failed to report the duration of therapy.[5,14] After consultation about the typical treatment duration prescribed by urologists in our area, we chose to evaluate a 10-day course of tamsulosin because this would likely coincide with the patient's first outpatient urology visit. Standard practice in our region involves surgical stone removal for patients who continue to experience pain and have need for analgesia after 10 to 14 days. Ultimately, we were interested in evaluating the shortest effective treatment duration because the medication is expensive for patients and is not covered by many insurance plans, particularly when prescribed for women.

In addition to the differences noted above, significant limitations exist in the current literature on this topic. Interpretation of a 2002 randomized trial is inhibited by the authors' failure to include their statistical analysis: only raw numbers without point and interval estimates are reported.[5] Additional work from 2003 included few women, used treatment regimens significantly different from those used in the United States, and did not report a power analysis.[6] More recent work from 2004 and 2005 used small samples sizes, included few female subjects, did not evaluate patient-oriented outcomes such as pain or return ED visits, did not report power analyses to support sample sizes, and failed to provide CIs around point estimates.[8-11,13,15] Although every trial will contain its own methodological and statistical imperfections, these methodological flaws limit our ability to interpret and apply this body of literature.

In Retrospect

As with any clinical trial, we learned several important lessons and may have considered some alternatives in designing our project. We were surprised that some subjects were unable to determine whether they had passed their ureteral stones; all were able to determine when they stopped experiencing pain, but many did not recall actually passing a stone. Had we sought approval to obtain follow-up information from our local urologists, we may have had some additional data on whether or not subjects had actually passed their stones. We might have also asked our subjects to return collected stones for analysis, enhancing our ability to say with certainty that these subjects had definitively passed their calculi.

Next, we recognize the potential bias that may have been introduced by our lack of a double-blind, placebo-controlled design. Certainly this would have added strength to our trial, despite the additional cost and complexity.

The relatively small size of the stones observed in our study was also unexpected. In our literature review, we were unable to find information on the "typical" size of ED ureteral stones and therefore chose not to limit study inclusion to only patients with larger stones. In doing so, we may have limited our ability to detect utility for tamsulosin, as it is possible that its effect is greater in those with larger stones. It is possible that a trial including a greater

number of subjects with larger stones would be useful in further elucidating tamsulosin's efficacy in this population.

In conclusion, we were unable to detect a difference greater than or equal to 30% when comparing treatment with a 10-day course of tamsulosin to treatment with ibuprofen and oxycodone alone in a cohort of adult ED patients with distal ureteral calculi.

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APPENDIX E1. The efficacy of tamsulosin in the treatment of ureteral stones in ED patients.*

Patient Label	**Research Office Use** **Study ID:** **Data Entered:** **Initials:**

Follow-Up Time:
☐ 48 Hours ☐ Other: _____
Patient Disposition:
☐ Discharged ☐ Admitted ☐ Other: _____
Discharge Diagnosis:
Pain "On the scale of 0 to 10 we used previously, how much flank pain are you having now?"
NRS Scale:
Episodes of Pain "How many episodes of kidney pain have you had since leaving the emergency department?"
Number:
Kidney Stone "Have you passed your kidney stone?"
☐ Yes ☐ If yes, Date & Time Passed: _____ ☐ No
Missed Work: If you work outside of the home, how many days of work have you missed due to your kidney stone since you left the emergency department? If you do not work outside of the home, how many days have you been unable to complete your usual activities due to kidney stone pain?
Days:
Medication Use: Since leaving the emergency department, how much of your pain medication have you needed to use?

Medication name: Number of doses:	
Return ED Visits: Since leaving the emergency department, have you needed to return to the ED or make an unscheduled visit to your primary care provider?	
☐ Yes ☐ No	If yes, how many times?_____
Side Effects: Have you experienced any of the following?	
Rash	Abnormal Ejaculation
Arthralgia	Orthostatic Hypotension
Headache	Nausea
Dizziness	Vomiting
Diarrhea	Other:

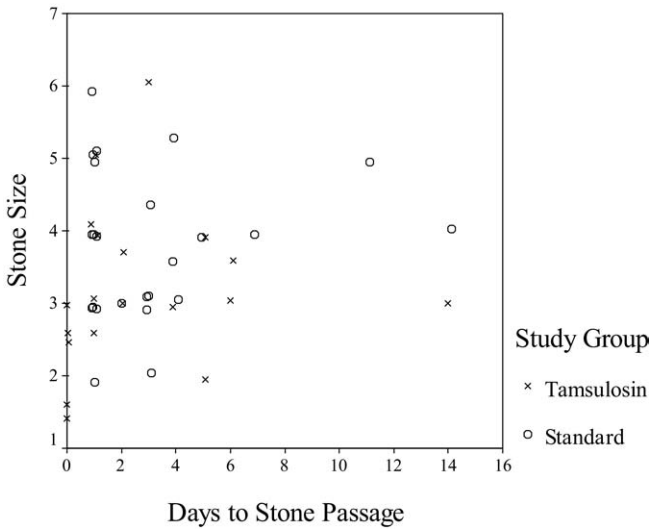

Figure E1 Days to stone passage by stone size and study group.