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Original Contribution

Tamsulosin does not increase 1-week passage rate of ureteral stones in ED patients☆,☆☆,★,★★

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ABSTRACT

Objective: The objective of the study is to determine if tamsulosin initiated in the emergency department (ED) decreases the time to ureteral stone passage at 1 week or time to pain resolution, compared to placebo.
Methods: We performed a prospective, randomized, double-blinded, placebo-controlled trial of tamsulosin vs placebo in ED patients with ureterolithiasis on computed tomography. Patients were identified and enrolled between April 2007 and February 2009 and were randomized to either 0.4 mg of tamsulosin or placebo for 1 week. We contacted participants using a telephone survey on post-ED visit days 1, 2, 3, and 7. The primary outcome was time to stone passage, with secondary outcomes being maximum pain score and amount of pain medication required.
Results: Of the 127 patients enrolled during this study, 15 were lost to follow-up, and 12 required surgical interventions before the 7-day mark, leaving 100 patients for analysis. Of the 100 patients, 53 received tamsulosin and 47 received placebo. There was no difference between groups in percentage of male, mean age, initial serum creatinine, average stone size, stone location, and history of prior stone. The probability that the patient did not pass a stone at 7 days was not different between tamsulosin and placebo, 62.1% (95% confidence interval, 49.1%-75.1%) vs 54.4% (95% confidence interval, 40.3%-68.6%; $P = .58$). There was no significant difference in the high pain score ($P = .12$) or hydrocodone/acetaminophen intake ($P = .76$) between treatment groups at any of the time points.
Conclusion: This study reveals no difference in the proportion of stone passage or high pain score and pain medication utilization at 7 days between tamsulosin and placebo.

1. Introduction

Renal colic is a common presenting complaint of patients in an emergency department (ED), and ureterolithiasis is a common diagnosis by emergency physicians. The annual incidence of stones and cost of therapy are increasing, and urolithiasis is reported to create $2.1 billion in health care costs in the United States alone [1]. Prior research demonstrates that most stones will pass spontaneously, and stone passage rates tend to be inversely proportional to stone size. A subset of patients with ureterolithiasis requires operative urologic intervention. This contributes to cost as well as morbidity.

Medical expulsive therapy (MET) has been investigated since the 1960s as an alternative to operative management for ureterolithiasis. Many drugs have been investigated, including steroids, nonsteroidal anti-inflammatory drugs, calcium-channel blockers, and α antagonists. Of these studied MET, α-blocker use is supported by the American Urologic Association for its MET properties in patients with ureteral calculi less than 10 mm [2]. This recommendation is level IV, panel/consensus evidence. The theoretical properties, which may make α-blockers effective for MET, include relaxing ureteral smooth muscle, inhibiting ureteral spasms, and dilating the ureteral lumen, which are postulated to facilitate stone passage [3].

Despite tamsulosin's α-blocking properties, which seem to make it ideal for MET, there are conflicting data in the literature, and only a paucity of studies are prospective or randomized controlled clinical trials. Of the 5 prior studies using α-blocker MET, 1 study that was prospective and randomized, but not double blinded or placebo controlled, did not find any added benefit vs standard analgesics [4]. Al-Ansari et al [5] did find benefit in their prospective, randomized, double-blinded, placebo-controlled investigation of distal-only ureterolithiasis. Further studies also suggest a benefit from tamsulosin, but these studies were not blinded or placebo controlled [6-8].

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These studies are further limited, however, in that 2 [6,7] used MET in combination with corticosteroids and 1 [8] analyzed only distal ureteral stones. To address this question, the aim of this study is to determine if tamsulosin monotherapy initiated in the ED decreases the time to ureteral stone passage compared to placebo. Our secondary objective was to assess whether tamsulosin decreased patient pain severity or medication use during the study period.

2. Materials and methods

We performed a prospective, randomized, double-blinded, placebo-controlled trial of tamsulosin vs placebo in ED patients with ureterolithiasis visualized on computed tomography at our tertiary care hospital using a convenience sample. Our tertiary care center has an associated emergency medicine residency program as well as annual ED volume is more than 120 000 patients per year with a 30% admission rate. This was institutional review board approved, and all patients provided informed consent. Emergency department physicians identified potential patients between April 2007 and February 2009 who were then enrolled by research associates and were randomized to either 0.4 mg daily of tamsulosin or placebo for 7 days, in addition to standard analgesia. Inclusion criteria include age 18 years or older, symptoms of acute renal colic, and confirmation of ureteral stone on computed tomography. Exclusion criteria include patients younger than 18 years of age; stone size greater than 1 cm; infected stones; obstructing stones in solitary kidneys; patients currently on Levitra, Nifedipine, or steroids; patients who required immediate surgical intervention; pregnant patients; and if patients were already on tamsulosin before enrollment. Patients also received standardized and similar-appearing pill bottles of tamsulosin or placebo, pain medication (hydrocodone/acetominophen), and ibuprofen. We contacted participants using a structured telephone survey at days 1, 2, 3, and 7 after the index ED visit. Patients were asked if they had passed a stone in their urine at each telephone call. Patients who had passed stones were called subsequently to assure that no further stones were passed. Pain resolution and the use of pain medications were used as a surrogate measure of stone passage. We queried patients regarding their pain severity each day on a 5-point Likert scale; number of pain and anti-inflammatory pills used since the last telephone calll and other symptoms such as fever, nausea, and vomiting. We based our power analysis on previous reports and assumed a 1-week passage rate with tamsulosin of 85% and placebo of 60%. Based on an α error of .05 and power of 80%, we needed 57 subjects per group.

2.1. Statistical analysis

To identify group differences in terms of demographic and other baseline variables, Pearson χ^2 tests of association, independent-samples *t* tests, and Wilcoxon 2-sample rank sum tests were conducted on the data as was appropriate based on the nature of the variable.

Of primary interest was to determine whether there was a difference between treatment groups in terms of passage of the kidney stone within the first 7 days of follow-up time. A stone collected by the patient on strained urine as well as pain resolution and the use of pain medications was used as surrogates to measure stone passage. The cumulative probability of having passed the kidney stone by follow-up days 1, 2, 3, and 7 was calculated for each of those time points using the life table method for survival analysis. To determine whether the tamsulosin and placebo groups had significantly different probabilities of having passed the kidney stone by day 7, the 95% confidence intervals (CIs) for the cumulative probability of having passed the stone were calculated for each group, and the 2 intervals were compared.

Of secondary interest was to determine whether there were differences between treatment groups in pain severity (high pain score) and/or Vicodin intake over the first 7 days of follow-up time. High pain score over time was compared by treatment group with the use of a means model. Vicodin intake over time was compared by treatment group with the use of a generalized estimating equations model. For both models, the type III statistics was examined to determine whether any statistically significant differences between treatment groups existed. All analyses were conducted using SAS version 9.3 for Windows (Cary, NC) and R version 2.15.1 for Windows.

3. Results

Of the 127 patients enrolled during this study, 15 were lost to follow-up, and 12 received surgical intervention before the 7-day mark, leaving 100 patients for analysis. Of the 100 patients, 53 received tamsulosin and 47 received placebo. As seen in the Table, analysis of demographics between the 2 groups revealed similarity in percentage of male, mean age, initial serum creatinine, average stone size, stone location, and history of prior stone.

3.1. Stone passage

Using the life table (Fig. 1) method for survival analysis, the cumulative probability of having passed the kidney stone by day 7 of follow-up was estimated to be 62.1% for the tamsulosin group (95% CI, 49.1%-75.1%) and 54.4% for the placebo group (95% CI, 40.3%-68.6%; $P = .58$), showing no significant difference in kidney stone passage between tamsulosin and placebo patients (Fig. 1).

3.2. High pain score

Fig. 2 plots the mean high pain score over follow-up time, with separate lines for the 2 treatment groups. The tamsulosin group has a higher mean high pain score at all follow-up times. Both groups show a generally decreasing trend in mean high pain score. An analysis of high pain score over the treatment period identified that there was no significant difference in high pain score between treatment groups at any of the time points ($P = .12$). The interaction term between treatment group and time point was nonsignificant ($P = .35$), indicating that group differences in high pain score over time were not statistically significant.

3.3. Vicodin intake

The median number of Vicodin used was similar for both groups at all periods (days 1, 2, 3, and 7) after the ED visit (Fig. 3). Using the GEE analysis; there was no significant difference in Vicodin use between groups ($P = .76$).

3.4. Adverse effects

Adverse effects temporally related to study drug or placebo were reported in a minority of patients and were not different between groups. Overall, 10 (18.9%) of 53 reported adverse effects in the tamsulosin group, and 9 (19.1%) of 47, in the placebo group. The most common adverse effects reported for tamsulosin vs placebo were dizziness (7.5% vs 10.6%). Other side effects that may or may not be attributable to drug were reported in individual instances (sinus pressure, nosebleed,

Table
Demographics of study groups

Demographics	Placebo	Tamsulosin	*P*
% Male	30 (68.2%)	26 (57.8%)	.31
Mean age	44.52	40.62	.20
Serum creatinine	1.01	1	.76
Average stone size (mm)	3.76	3.98	.55
Distal stone	27 (64.3%)	26 (63.4%)	.93
Prior stone	15 (35.7%)	17 (37.8%)	.84
Stone collected by 7 d	18 (46.2%)	21 (53.9%)	.58