Efficacy of Tamsulosin in Expulsion of Lower Ureteric Stone upto 10mm

Pradhan M*, Poudyal S, Chapagain S, Luitel BR, Chalise PR, Sharma UK, and Gyawali PR
Department of Urology and Kidney Transplant Surgery, Tribhuvan University Teaching Hospital, Nepal

Abstract

Background: Amongst numerous treatment modalities available for the lower ureteric calculi, medical expulsion therapy (MET) is the cost effective and popular amongst patient as it avoids invasive surgery. Although the efficacy of Tamsulosin as MET has been well studied in the other countries, in our population it remains unanswered.

Methods: This randomized control trial was done in 70 patients of lower ureteric calculi less than 10 mm in size who presented to the surgical outpatient department or the emergency department of the Tribhuvan University Teaching Hospital, Kathmandu, Nepal over a period of 10 months (From February 2016 to November 2016). Patients were randomized to two groups (Tamsulosin vs. control) using computer generated random number generator. Patients were followed up at one week and three weeks of initial visit to determine the expulsion rate of stone and dose of analgesic use.

Result: Among 70 patients who consented for the trial, 5 were lost to follow up (2 in Tamsulosin and 3 in control group). Among remaining 65, 46 were males and 19 were females. Average stone size was 6.17 mm in Tamsulosin group and 6.03 mm in control group (p=0.724). The expulsion rate was 54.54 % in the Tamsulosin group and 43.75% in the control group (p=0.384). Mean amount of analgesic (Tab. Diclofenac) use was 563.32 mg in the Tamsulosin group and 637.5mg in the control group (p=0.121).

Conclusion: This study shows that medical expulsive therapy using tamsulosin for the lower ureteric stones is not efficacious as thought before.

INTRODUCTION

Urolithiasis is one of the common urological problems in Nepal. The prevalence of this disease varies according to the geography, race/ethnicity, climate, gender, age and occupation [1]. Although the prevalence in our country is yet to be determined, it remains unanswered.

Among the various treatment modalities available, the efficacy of mini-invasive therapies, such as extracorporeal shock wave lithotripsy (ESWL) and ureteroscopic lithotripsy has been proven by several studies [5,6]. Nevertheless these techniques are not risk-free, are problematic and are expensive [7]. A watchful waiting approach can be used in a large number of cases, as demonstrated by several studies that revealed high spontaneous passage rates of small distal ureteral stones [1,8]. Even the simple watchful waiting approach can result in complications, such as infection of the urinary tract, hydronephrosis and impaired renal function [9].

These days, use of the watchful waiting approach has been extended by using pharmacological therapy, which can reduce symptoms and facilitate stone expulsion [10,11].

The therapeutic potential of α-blockers for ureteral stone disease has been recognized after the detection of Alpha receptors in ureteral smooth muscle cells [12]. A1-alpha receptors are known to densely populate in the smooth muscle cells of the distal ureter, bladder and prostatic urethra [13]. Successful medical expulsive therapy (MET) for patients with distal ureteral stones using the nonselective alpha-blocker doxazosin was first reported in the late 1990’s [11]. Since then, numerous clinical trials have been performed to investigate the efficacy of MET using the selective alpha-blocker tamsulosin alone and in combination with other drugs like corticosteroids and antibiotics [14-17].

The joint EAU/AUA Nephrolithiasis Guideline panel have shown efficacy of tamsulosin as a drug for MET for ureteric stone 10mm or less in size [18]. However, the results of various studies done in the different part of the world to evaluate the efficacy of tamsulosin (MET) have been conflicting and there has not been enough studies in Nepal to judge the efficacy of MET using selective a-blocker like tamsulosin. Hence this study aims
to evaluate the efficacy of tamsulosin in expulsion of the lower ureteric stone less than 10 mm.

MATERIALS AND METHODS

This was a randomized control trial conducted in the department of urology and kidney transplant surgery, TUTH, over a period of 10 months (From February 2016 to November 2016) after taking the clearance from the institutional review board. All patients presenting with lower ureteric stone up to 10mm in size, diagnosed by USG abdomen/pelvis or X-ray KUB, were included in the study. Exclusion criteria were: presence of multiple ureteric stones, radiolucent stones, urinary tract infection, pregnancy, pediatric population, patients with a history of ureteral surgery or previous endoscopic procedures and patient requiring emergency intervention.

Informed consent was taken from the patients and randomly allotted to either an intervention group who received the drug Tamsulosin 0.4mg along with an analgesic (Diclofenac 50mg TDS for three days then as per need basis), antispasmodic (Hyoscine butylbromide 10mg along with diclofenac) and proton pump inhibitor (Pantoprazole 40mg once daily), or a control group who received similar medications except for Tamsulosin (Table 1).

The sample size was determined with the formula:

\[ N = \frac{K \times (P_1 - P_2)}{(P_1 - P_2)^2} \]

Where

\[ N = \text{sample size} \]
\[ P_1 = \text{successful passage in conservative group} \]
\[ P_2 = \text{successful passage in tamsulosin group} \]
\[ K = \text{constant which depended on value of } \alpha \text{ and } \beta \text{ as given below:} \]

<table>
<thead>
<tr>
<th>Power</th>
<th>50%</th>
<th>80%</th>
<th>90%</th>
<th>95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \alpha )</td>
<td>( \beta = 0.5 )</td>
<td>( \beta = 0.2 )</td>
<td>( \beta = 0.1 )</td>
<td>( \beta = 0.05 )</td>
</tr>
<tr>
<td>0.10</td>
<td>2.7</td>
<td>6.2</td>
<td>8.6</td>
<td>10.8</td>
</tr>
<tr>
<td>0.05</td>
<td>3.8</td>
<td>7.9</td>
<td>10.5</td>
<td>13.0</td>
</tr>
<tr>
<td>0.02</td>
<td>5.4</td>
<td>10.0</td>
<td>13.0</td>
<td>15.8</td>
</tr>
<tr>
<td>0.01</td>
<td>6.6</td>
<td>11.7</td>
<td>14.9</td>
<td>17.8</td>
</tr>
</tbody>
</table>

Chi-square test was used for analysis of qualitative data like patient sex, location of stone (right vs left), expulsion of stone, Fisher’s exact test was used for analysis of stone expulsion in subgroup with less than 5mm or more than 5mm and t-test was used for continuous variables. \( P \) value of <0.05 was considered statistically significant.

Data analysis was done using Statistical Package for Social Sciences (SPSS) version 17.0.

RESULTS

Among 70 patients who consented for the trial, 5 were lost to follow up (2 in Tamsulosin and 3 in control group). Among remaining 65 (33 in Tamsulosin group and 32 in control group), 46 were males and 19 were females, with M: F ratio of 2.4:1. Average stone size was 6.17 mm in Tamsulosin group and 6.03 mm in control group (\( p = 0.724 \)). The expulsion rate was 54.54% in the Tamsulosin group and 43.75% in the control group (\( p = 0.384 \)). Mean amount of analgesic (Tab. Diclofenac) use was 563.32 mg in the Tamsulosin group and 637.5mg in the control group (\( p = 0.121 \)) (Table 2).

As per the analysis, use of tamsulosin was not significantly associated with higher expulsion rate (\( p = 0.384 \)) or significantly less dose of analgesic use (\( p = 0.121 \)).

Only five patients complained of side effects of tamsulosin, among which one male patient complained of abnormal ejaculation and two patients complained of headache and two other patients complained of dizziness. None of them required stoppage of the drug and symptoms of dizziness improved on its own where as abnormal ejaculation resolved after the course of tamsulosin.

DISCUSSION

Recent advances in the urological procedures and fine instruments have largely diverted the management of ureteral stones to either minimal invasive methods like ESWL and ureteroscopy or to watchful waiting [19]. The minimally invasive therapies for distal ureteral stone are now recommended by recent EAU guidelines, with URS being first choice for stone larger than 10mm and both URS and ESWL for stone smaller than 10mm [20]. Nevertheless, these techniques are not risk free, are quite expensive and are concentrated at tertiary care centers [21]. Moreover, the simple watchful waiting approach, although shown to be effective in some studies, can result in complications, such as infection of the urinary tract, hydronephrosis and impaired renal function [9]. In complete obstruction, the signs of kidney injury appear in 3 to 4 weeks. For this reason the spontaneous passage of the stones can be waited on for 4 weeks [22].

Since 1990s, numerous clinical trials have been performed to investigate the efficacy of MET using the selective alpha-blocker tamsulosin alone and in combination with other drugs like corticosteroids and antibiotics [14-18].

This study investigates the efficacy of the drug Tamsulosin in expulsion of stones in our population. Although the number of stone passers were relatively higher in tamsulosin group as compared to the control group but statistically it was not significant (\( p = 0.384 \)). Similarly, the amount of analgesic use was
Table 1: Demographic data of two groups.

<table>
<thead>
<tr>
<th></th>
<th>Tamsulosin</th>
<th>Control</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Stone size in mm ± SD</td>
<td>6.17 ± 1.8</td>
<td>6.03 ± 1.3</td>
<td>0.724</td>
</tr>
<tr>
<td>Sex ratio (M/F)</td>
<td>24/9</td>
<td>22/10</td>
<td>0.789</td>
</tr>
<tr>
<td>Mean Age in yrs</td>
<td>29.12 ± 9.91</td>
<td>30.13 ± 8.81</td>
<td>0.668</td>
</tr>
<tr>
<td>Stone location (Rt/Lt)</td>
<td>23/11</td>
<td>20/12</td>
<td>0.797</td>
</tr>
</tbody>
</table>

Table 2: Comparison of results in two groups.

<table>
<thead>
<tr>
<th></th>
<th>Tamsulosin</th>
<th>Control</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expulsion rate</td>
<td>54.54% (18/33)</td>
<td>43.75% (14/32)</td>
<td>0.384</td>
</tr>
<tr>
<td>Expulsion rate in &lt;5mm stones</td>
<td>66.66% (8/12)</td>
<td>61.53% (8/13)</td>
<td>0.790</td>
</tr>
<tr>
<td>Expulsion rate in &gt;5mm stones</td>
<td>47.61% (10/21)</td>
<td>31.57% (6/19)</td>
<td>0.301</td>
</tr>
<tr>
<td>Mean analgesic use</td>
<td>563.3 ± 213mg</td>
<td>637.5 ± 166mg</td>
<td>0.121</td>
</tr>
</tbody>
</table>

CONCLUSION

Although the use of Tamsulosin for MET seem to cause more number of stone expulsion, this study could not find the statistical benefit of Tamsulosin in spontaneous passage of lower ureteric stones less than 10 mm in size. More randomized control studies with higher sample size are required to establish Tamsulosin as standard therapy for small distal ureteric stones.

LIMITATION OF THE STUDY

The main limitation of our study was the fact that it was carried out in outpatient basis, hence, we could not follow up the patient for longer period of time. Although, many similar studies have followed up patient for four to six weeks to see the expulsion rate in both the tamsulosin and control group, we could not do so mainly because there would have been higher dropout rate if the study was carried out for longer duration. Also, the fact that patients in our setting already present late for treatment meant that we had to intervene earlier in other to persevere the renal function.

REFERENCES