Comparative Study

Tamsulosin vs Naftopidil in Medical Expulsive Therapy for Ureteral Stones — A Randomized Controlled Study

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Abstract

The aim of the present study was to compare the efficacy of naftopidil and tamsulosin in the management of ureteral stones. A total of 92 patients with symptomatic, single ≤ 10 mm ureteral stone, were enrolled in a prospective study and randomized into two groups. Group 1, received 0.4 mg tamsulosin daily, whereas Group 2, received 50 mg naftopidil daily. Patients were followed –up for up to 6 weeks. The primary end point was stone expulsion rate and secondary end points were stone expulsion time , the rate of interventions such as uretero-renoscopy, ureteric stenting and extracorporeal shock wave lithotripsy and side effects. There were no significant differences between the groups with respect to age, sex, stone size and location. Stone expulsion rate were 76% and 56% in the tamsulosin and naftopidil group respectively. No significant difference in the stone expulsion time and the rate of interventions between the two groups. The finding suggest that tamsulosin is superior to naftopidil for stone expulsion therapy.

Introduction

Expectant treatment for ureteral calculi upto 5 mm in size is an accepted mode of treatment, as a large percentage of ureteric stones of this size passes out spontaneously. Medical expulsive therapy using alpha-adrenoceptor antagonists has recently emerged as an alternative strategy for the management of small ureteral stones[1]. Tamsulosin which is a selective α_{1A} adrenoceptor antagonist which have been found to facilitate the spontaneous passage of ureteral stones in many studies[2] . Naftopidil is a relatively selective α_{1D} adrenoceptor antagonist. This study was performed to compare the effects of tamsulosin and naftopidil as medical expulsion therapy to facilitate the passage of ureteral stones.

Methods

This study was conducted in a period of 18 months, from March 2011 to August 2012 and a total of 92 patients were included in this study. The patients were adult males and females, who presented with symptomatic single ureteral stone ≤ 10 mm in size. Patients with urinary tract infection, multiple stones, impacted stone, severe hydronephrosis or non excreting kidney, a solitary kidney, current use of any type of alpha blocker or calium antagonist were excluded from the study. Patients were randomized into two groups using a random number table envelope method. Group 1, received 0.4 mg of Tamsulosin,

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one tablet daily at bed time whereas Group 2, received 50 mg Naftopidil, one tablet in the morning. Patients were evaluated with plain X-Ray KUB, ultrasonography, X-Ray IVP and NCCT KUB or CT urogram when necessary. Stone size was calculated from the plain X-Ray KUB or NCCT. Patients were followed up biweekly with X-Ray KUB and ultrasonography and patients were assessed for their symptoms of pain, urinary tract infection and any adverse events. The indications for intervention were, uncontrollable pain, urinary tract infection or unchanged stone position on follow up. Patients were instructed to record the date and time of stone passage. Patients were followed up until they are rendered stone free by intervention or spontaneous stone expulsion, for a maximum period of 6 weeks. The stone free rate was the end point of the study. The stone expulsion time, defined as the number of days from the start of therapy until stone expulsion. The intervention rate was also evaluated as a secondary end point. Data were analyzed by student's t test and the chi square test as appropriate. All statistical analysis were performed using Microsoft Excel (Microsoft, Redmond, WA, USA) and $p < 0.05$ was considered significant.

Results

Eight patients in group 1 and seven patients in group 2 were lost to follow up, with 77 patients remaining for statistical analysis. There were no significant difference between the two groups with respect to age, sex, stone size or stone location (**Table 1**). Spontaneous stone expulsion was observed in 29 of 38 patients in group 1 (76%) and 22 of 39 patients in group 2 (56%) ($p = 0.04$). There were no significant difference between Tamsulosin and Naftopidil groups with regard to mean stone expulsion time which were 16 ± 14 and 16 ± 12 , respectively ($p = 0.9$). Intervention was required in 9 of 38 in group 1 (24%) and 17 of 39 patients in group 2 (44%), the difference was found to be significant ($p = 0.04$) (**Table 2**). No side effects of the drugs were reported in the groups.

Table 1
Demographic features of the two study groups

Characteristic	Group 1 (Tamsulosin)	Group 2 (Naftopidil)	p-value
Number of patients	38	39	
Age (Mean ± SD) in years	35 ± 13	32 ± 14	0.2
Stone size (Mean ± SD) in mm	5.4 ± 1.4	5.8 ± 1.8	0.4
Sex (Male / Female)	21/17	18/21	0.1
Location of the stone (n)			
Upper ureter	14	13	0.1
Middle ureter	4	6	
Lower Ureter	20	20	
None of the difference were statistically significant			

Table 2
Treatment results

Result	Group 1 (Tamsulosin)	Group 2 (Naftopidil)	p-value
Stone expulsion rate	29/38 (76%)	22/39 (56%)	0.04
Time to expulsion (mean ± SD in days)	16 ± 14	16 ± 12	0.8
Intervention rate	9/38 (24%)	17/39 (44%)	0.04
Interventions included uretero-renoscopy, double J stenting and extra-corporeal shock wave lithotripsy			

Discussion

Alpha and Beta adrenoceptors are distributed through the entire length of human ureter and there is increased tone and frequency of contractions of the ureter when exposed to á- adrenoceptor agonist[3]. Many studies have been published on the presence of $á_1$ adrenoceptors in the human ureter since the first report in 1970. It was found that α_{1D} and α_{1A} adrenoceptors were expressed in significantly larger amounts than α_{1B} adrenoceptors in the human ureter. It was also demonstrated that the distal ureter expressed a greater amount of α_1- adrenoceptor mRNA than the proximal and mid ureter, α_{1D}- adrenoceptor mRNA is more highly expressed than α_{1A}- adrenoceptor mRNA in each region of the ureter[4] but ureteral contraction is mediated mainly by α_{1A}- adrenoceptor, even though α_{1D}- adrenoceptors were more prevalent [5]. Clinical studies have shown the efficacy of α blockers in promoting the passage of distal ureteral stones. Many studies have shown better stone expulsion rate in patients who received 0.4 mg tamsulosin than in controls[6,7,8]. Other α blockers like naftopidil have been used less frequently in clinical studies for stone expulsive therapy[1,9]. Few studies have demonstrated the efficacy of α_1- adrenoceptor antagonists in the management of lower ureteral stone regardless of the type of α – blocker used[7,8,10,11]. Our results suggest that tamsulosin is a better choice in the medical expulsive therapy for ureteral stones compare to Naftopidil. Our results indicate that α_{1A}- adrenoceptor antagonist is more effective than α_{1D}- adrenoceptor antagonist with respect to stone expulsion rate, suggesting more clinical usefulness of α_{1A}- adrenoceptor antagonist. In conclusion, Tamsulosin (as an example of a selective α_{1A}- adrenoceptor antagonist) was more effective than Naftopidil (as an example of a selective α_{1D}- adrenoceptor antagonist) with respect to stone expulsion rate and intervention rate for medical expulsive therapy.

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