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UROLOGY – ORIGINAL PAPER

Evaluation of the efficiency of tamsulosin and Rowatinex in patients with distal ureteral stones: a prospective, randomized, controlled study

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Abstract
Purpose To compare the efficiency and spontaneous expulsion rates of tamsulosin and Rowatinex in patients with distal ureteral stones.
Methods Between March and July 2009, 90 patients with distal ureteral stones <10 mm in size were included in the study. Patients were randomized in 3 groups: Group 1 ($n = 31$, those received 0.4 mg tamsulosin once daily), Group 2 ($n = 30$, those received 100 mg Rowatinex capsules 3 times a day), and Group 3 ($n = 29$, those received diclofenac 100 mg once daily). All patients were followed up for 10 days.
Results and conclusions Mean age of the patients was 42.4 ± 16.1 (range, 22–75), 46.5 ± 16.5 (range, 22–76), and 43.5 ± 16.6 (range, 18–71) years in Groups 1–3, respectively. On admission, 37.8% had hematuria and 78.9% had lower urinary tract symptoms (LUTS). No statistically significant differences were detected between the three groups regarding patient age, gender, mean stone size, stone location, stone site, additional analgesic requirement, number of ureteral colics during the treatment, and upper urinary tract dilation. The mean stone expulsion time was 3.5 days in Group 1, 6 days in Group 2, and 7 days in Group 3 ($P = 0.02$). Stone expulsion rate was significantly high in Group 1 compared to Group 2 ($P = 0.002$). Similarly, stone expulsion rate was significantly high in Group 1 compared to Group 3 ($P = 0.001$). Medical treatment with tamsulosin seems to be effective in patients with distal ureteral stones <10 mm in size. However, use of Rowatinex does not seem to have any significant effect on clearance rate of distal ureteral calculi.

Keywords Distal ureteric stones · Medical treatment · Tamsulosin · Rowatinex · Diclofenac

Abbreviations

LUTS	Lower urinary tract symptoms
KUB	Kidney, ureter, and bladder plain X-ray graphs
US	Ultrasound of the urinary tract
CT	Non-contrast computed tomography

Introduction

Several treatment options exist regarding the treatment of lower ureteral stones related to stone site, stone size and upper urinary tract status. Due to the presence of alpha-1 adrenergic receptors in the ureteral smooth muscle cells, agents blocking these receptors have been used in this setting [1].

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It has been demonstrated that alpha-1A and alpha-1D receptors are present in the distal ureter [2–5]. Therefore, previous studies reported successful use of tamsulosin in the conservative management of distal ureteral stones, which blocks both of these receptors [2–4]. Tamsulosin decreases amplitude and frequency of ureteral peristalsis leading to interureteral pressure decrease and increased fluid transport in the ureter [6].

Rowatinex is an essential oil preparation of terpenic type composed of pinene (3%), camphene (15%), borneol (10%), anethol (4%), and cineol (3%) in olive oil, which has been suggested for the treatment of urolithiasis, nephrolithiasis, and renal colic due to urinary tract stone disease [7–9].

Herein, we performed a prospective, randomized, controlled study comparing the use of tamsulosin and Rowatinex in the management of distal ureteral stones and their effect on the spontaneous expulsion rate of these stones.

Materials and methods

Between March and July, 2009, 90 patients presenting with stones <10 mm in size located in the distal ureter were included in our study.

Patients were randomized in 3 groups: Group 1 ($n = 31$, those received 0.4 mg tamsulosin once daily), Group 2 ($n = 30$, those received 100 mg Rowatinex capsules, Rowa Pharmaceuticals, Cork, Ireland, 3 times a day), and Group 3 ($n = 29$, those received diclofenac 100 mg once daily). Group 3 was regarded as the control group, and all patients in this group had access to diclofenac. However, patients in Groups 1 and 2 whose pain did not subside following tamsulosin or Rowatinex administration, they received diclofenac when needed. All patients were followed up for 10 days.

Criteria for inclusion were as follows: male or female older than 17 years of age, stones located in the distal ureter with a size of <10 mm in largest diameter.

The exclusion criteria were as follows: presence of urinary tract infection, solitary kidney, severe hydroureteronephrosis, renal insufficiency, diabetes mellitus, multiple stones, bilateral stones, hypotension, pregnancy, previous spontaneous stone expulsion, previous distal ureteral surgery, and history of intake of nifedipine, alpha-adrenergic blockers, calcium antagonist, and steroids.

All patients underwent physical examination and routine urine analysis. Serum creatinine and serum uric acid were measured. Patients also had kidney, ureter, and bladder (KUB) plain X-ray graphs, ultrasound (US) of the urinary tract and non-contrast computed tomography (CT) in selected patients.

All patients were suggested to drink at least 2 l of drinking water daily. For additional pain relief, diclofenac (100 mg/daily) on demand was recommended. Patients filtered their urine and were asked to inform us as soon as they pass their stones and stop the suggested medication. All patients were followed up for 10 days. At the end of the 10th day of follow-up all patients had KUB graphs, US, and when required CT in selected patients.

We compared the effectiveness of tamsulosin and Rowatinex in the treatment of distal ureteral stones.

Statistical analyses

SPSS version 11.5 software (Chicago, Illinois, USA) was used for data analysis. The chi-square test was used to compare categorical variables. Student t test was used to compare continuous variables between the groups. For all groups, one-way ANOVA test was used in order to compare parametric variables. P values less than 0.05 were considered significant.

Results

Mean age of the patients was 42.4 ± 16.1 (range, 22–75), 46.5 ± 16.5 (range, 22–76), and 43.5 ± 16.6 (range, 18–71) years in Groups 1–3, respectively. Mean stone size was 6.7 ± 1.7 mm (range, 4–10) in Group 1, 6.8 ± 2 mm (range, 3–10) in Group 2 and 6.6 ± 1.7 mm (range, 4–10) in Group 3, respectively. No significant difference was detected in terms of mean stone size between the groups ($P = 0.91$). On admission, 37.8% had hematuria, and 78.9% had lower urinary tract symptoms (LUTS).

The mean stone expulsion time was 3.5 days in Group 1, 6 days in Group 2, and 7 days in Group 3 ($P = 0.02$). No statistically significant differences were detected between the three groups regarding patient age, gender, mean stone size, stone location, stone site, additional analgesic requirement, number

Table 1 Characteristics of the groups and outcomes of the evaluated parameters

	Group 1 Tamsulosin	Group 2 Rowatinex	Group 3 Diclofenac	*P*
Patients (*n*)	31	30	29	
Age (y) Mean ± SD (range)	42.4 ± 16.1 (22–75)	46.5 ± 16.5 (22–76)	43.5 ± 16.6 (18–71)	0.607**
Gender n (%)				
Male	22 (71)	17 (56.7)	19 (65.5)	0.501*
Female	9 (29)	13 (43.3)	10 (34.5)	
Stone size(mm) Mean ± SD (range)	6.7 ± 1.7 (4–10)	6.8 ± 2(3–10)	6.6 ± 1.7 (4–10)	0.902**
Side n(%)				
Right	23 (74.2)	15 (50)	14 (43.8)	0.073*
Left	8 (25.8)	15 (50)	15 (51.7)	
Stone location *n* (%)				
Upper distal ureter	12 (38.7)	5 (16.7)	5 (17.2)	0.074*
Lower distal ureter	19(61.3)	25 (83.3)	24 (82.8)	
Incidence of ureteral colic *n* (%)	20 (64.5)	23 (76.7)	23 (79.3)	0.380*
Upper urinary tract dilation *n* (%)	21 (67.7)	19 (63.3)	21 (72.4)	0.757*
Additional analgesic requirement n (%)	10 (32.3)	15 (50)	18 (62.1)	0.066*

* Chi-square test was used in order to compare Groups 1–3

** ANOVA test was used in order to compare Groups 1–3

of ureteral colics during the treatment, and upper urinary tract dilation.

The number of patients requiring additional analgesic was lower in Group 1 compared to Groups 2 and 3, which was not statistically significant (Table 1).

Stone expulsion rate was significantly high in Group 1 (80.6%) compared to Group 2 (43.3%) ($P = 0.002$). Similarly, stone expulsion rate was significantly high in Group 1 compared to Group 3 (37.9%) ($P = 0.001$). No significant difference was detected when Group 2 and Group 3 were compared in terms of stone expulsion rates ($P = 0.67$).

No significant adverse effect was observed with the use of the 3 agents throughout the study.

At the end of the 10th day of our study, patients who were not able to pass their stones underwent ureterorenoscopy and stone removal with complete success.

Discussion

Although Rowatinex was used in patients with urinary tract stone disease [7–9], to the best of our knowledge, no study exists comparing the use of tamsulosin versus Rowatinex in patients with distal ureteric stones in the English literature by using PubMed/Medline.

It has been shown that alpha-1 adrenergic receptors predominate in the human ureter; therefore, the use of alpha-receptor-blocking agents is advocated in the management of ureteral colic secondary to ureteral stones [1]. It was suggested that the blockage of alpha-1 adrenergic receptors in the ureter leads to decreased ureteral peristaltic activity with a consequent loss of interureteral pressure and an increase in fluid transport ability [5, 6]. Morita et al. demonstrated that selective alpha-blocking agents increase interureteral pressure gradient around the obstructed ureter by increasing the bolus of urine above the stone and decreasing the interureteral pressure below the stone [10]. This might facilitate stone passage by increased urine flow. In addition, alpha-receptor-blocking agents seem to decrease the frequency of phasic peristaltic contractions in the ureter and decrease the frequency of ureteral colic, leading to decreased analgesic requirement and use [3, 11].

Several publications exist in the literature regarding the successful use of tamsulosin in patients with urinary tract stone disease. Dellabella et al. reported a 100% spontaneous stone passage rate with decreased

expulsion time, decreased need for hospitalization, and endoscopic procedures with good pain control in a series of 30 patients [4]. De Sio et al. compared the use of diclofenac (100 mg) ($n = 46$) daily plus aescin (80 mg) daily and same treatment plus tamsulosin (0.4 mg) ($n = 50$) daily for a maximum of 2 weeks in patients with distal ureteral stones. Patients in the tamsulosin group had significantly higher rates of stone passage (90% vs 58.7%) over a shorter time period (4.4 vs 7.5 days) with lower analgesic use [12]. Recent research and literature related with the treatment of distal ureteral stones of <10 mm in size with tamsulosin 0.4 mg, once daily suggest that, stone expulsion rate has been reported to be significantly higher compared to the control groups (>80%) in most studies [13–16]. Additionally, the number of pain episodes and expulsion time were also reported to be lower in the tamsulosin group [13–16]. In our study, stone expulsion rate was 80.6% in the tamsulosin group, 43.3% in the Rowatinex group, and 37.9% in the diclofenac group, which was similar to the published literature. Therefore, use of tamsulosin seems to be superior to Rowatinex and diclofenac in our study in terms of pain relief and stone passage rate (Table 1). Although the number of patients with distal ureteric stones located in the upper part of the distal ureter was greater in number, successful outcomes were achieved with the use of tamsulosin treatment. On the other hand, no significant difference was detected in terms of the incidence of renal or ureteral colic between the 3 groups (Table 1).

Rowatinex is an essential oil preparation of terpenic type composed of pinene (3%), camphene (15%), borneol (10%), anethol (4%), and cineol (3%) in olive oil, which has been suggested for the treatment of urolithiasis, nephrolithiasis, and renal colic [7–9]. Miller et al. reported a 65% success rate in spontaneous stone passage rate including 40 patients with urolithiasis who received Rowatinex [17]. Rowatinex is suggested to increase renal blood flow thus facilitating urine excretion leading to stone passage with additional antispasmodic effects [7–9]. Djaladat et al. reported that stone-free rate was significantly higher in patient who used Rowatinex for 2 weeks compared to controls undergoing extracorporeal shockwave lithotripsy [18]. However, they concluded that although Rowatinex might accelerate stone passage, it does not seem to affect the overall outcome [18]. Similarly, Mukamel et al. reported a significantly increased stone expulsion rate in the Rowatinex group compared to controls without any serious side effects in patients with renal colic [8]. In our study, we did not detect any significant difference in terms of stone expulsion rate and mean stone expulsion time in the Rowatinex group compared to the diclofenac group (Table 1). Although the number of patients who required additional analgesic treatment was larger in the diclofenac group, this was not statistically significant.

Conclusion

Our results suggest that the use of tamsulosin as an alpha-adrenergic receptor-blocking agent seems to be effective in the management of distal ureteral stones <10 mm in size provided that there is no contraindication such as infection or severe obstruction. Rowatinex does not seem to have a significant effect on stone clearance rate of distal ureteral calculi.

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