

Comparative effects of Tamsulosin alone and in combination with Ketorolac on urinary symptoms in patients with ureteral stones: A double-blind trial

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ABSTRACT

Background: One of usual problems is ureteral stones that needs care practice. Some pharmacological agents are used for treatment of ureteral stones. Alpha-blockers, i.e., tamsulosin, are extensively used for treatment of ureteral stones.

Aim: To compare the effects of Tamsulosin alone and in combination with Ketorolac on urinary symptoms in patients with ureteral stones.

Methods: This randomized clinical study was conducted between December 2016 and February 2016. A total number of 100 adult patients (>17 years of age) and with distal ureteric stones in size of 6–10 mm were assigned into 2 treatments including those intravenously received 0.4 mg Tamsulosin+30 mg Ketorolac (combination group) daily and other group was treated with 0.4mg tamsulosin daily. Urinary symptoms including dysuria and frequent urination were recorded. Pain changes were evaluated by Visual Analog Scale (VAS). Statistical analyses were conducted by Chi-square test.

Results: The results showed that VAS was significantly reduced in patients that received combination treatment compared to those received Tamsulosin alone ($P<0.05$), but dysuria and frequent urination was not different among groups ($P>0.05$).

Conclusion: A combination of α -blockers and non-steroidal anti-inflammatory drugs can have better efficiency compared to α -blocker agent.

Keywords: Dysuria, Frequent urination, Ketorolac, Medical therapy, Tamsulosin

INTRODUCTION

Kidney stones are one of usual and growing challenges in all over world. It is believed that 11% of men and 7% of women will suffer kidney stone during their lifetime. Some risk factors influence on kidney stones such as male gender, obesity, diabetes, gout, and low income (Koski and Zufall, 2018). Renal colic is acute pain in the flanks that are due to the passage of a stone from the ureter (Golzari et al., 2014). Specific ureteric stone-related symptoms are including acute ureteric colic, acute or chronic flank, abdominal or groin pain, hematuria, dysuria, anuria, or urinary tract infection (Marchini et al., 2012). A study reported frequency of ureteric stones in patients with non-specific symptoms by 0.7% (Wimpissinger et al., 2014). Ureteral stones reduce quality of life because these stones cause severe urologic disorders (Kumar et al., 2010). Formation of urinary stone lasts during long time that may be related to a mild to severe symptoms in patients (Wimpissinger et al., 2007). Presence of a dam in the ureter increases ureteric and renal pelvic pressure that result in severe hydronephrosis in along to decreasing glomerular filtration rate, tubular activity, and blood flow of the kidney (Teichman, 2004).

The different procedures are used for management of ureteral stones including medical expulsive treatment (MET), extracorporeal shock wave lithotripsy, ureterorenoscopic lithotripsy, open ureterolithotomy and laparoscopic ureterolithotomy (Hsu et al., 2018). Some pharmacological agents are applied in MET, such as α -blockers, calcium channel antagonists, phosphodiesterase

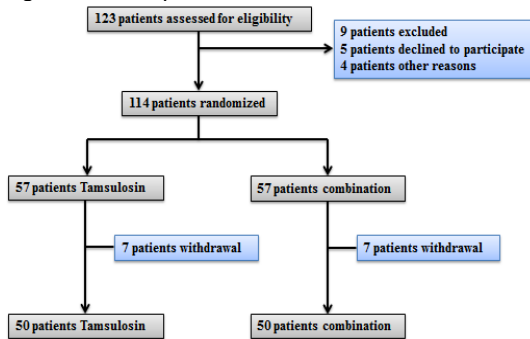
preventors, and corticosteroids. The agents cause to facilitate ureteral stone passage. Among agents used, α -blockers and especially tamsulosin are (Sridharan and Sivaramakrishnan, 2017). Alpha adrenergic receptors are significantly positioned in the smooth muscles of ureter. These are mostly found in bladder outlet, prostate, and proximal urethra, however, α -1d receptors are observed in lower ureter and detrussor muscle of bladder (Cervenakov et al., 2002). The drugs could prevent these receptors relax smooth muscle and prevent peristalsis and relieves spasm (Barnela et al., 2012). Tamsulosin is an efficient agent in expulsion therapy, because it increases the passage rate and decreases the passage time for stones by 10 mm (De Sio et al., 2006). A study showed that use of tamsulosin in renal colic could improve passage rate by 100%, while it was 70% in the control group. This study also showed that mean expulsion time in the treatment group was 65.7 h compared to 111.1 h for the control group (Dellabella et al., 2003). So far, any study has not been conducted to compare the effects of Tamsulosin alone and in combination with Ketorolac on urinary symptoms in patients with ureteral stones. This study, for first time, was conducted to compare the effects of Tamsulosin alone and in combination with Ketorolac on urinary symptoms in patients with ureteral stones.

MATERIALS AND METHODS

Study design and participants: A double-blind, randomized study was conducted in Department of Emergency of Shahid Mohammadi, Bandar Abbas from

December 2016 and February 2016. A total of 100 eligible patients were randomly selected from patients referred to Department of Emergency of Shahid Mohammadi, Bandar Abbas, using the following inclusion criteria: adults, 17–55 year; emergency admission for renal colic; presence of a single ureteral stone confirmed by plain abdominal radiography (kidney–ureters–bladder), urinary ultrasonography, a stone in the distal ureter in range from 4 to 6 mm; and a unilateral presentation. Of the 100 patients, 50 patients were assigned to the Tamsulosin group and the rest patients to Tamsulosin+Ketorolac (combination group). In the current study, 123 patients were initially selected and 23 patients withdrew during the trial, as illustrated in Figure 1.

Figure 1: Trial profile.



Randomization and masking: Patients were randomly allocated into a 1:1 ratio for receiving Tamsulosin or a combination of Tamsulosin+Ketorolac. Randomization and double blinding were conducted on the basis of randomization Table. In the current study, the investigator, participants, care providers, and those assessing outcomes

were blinded for treating during trial. Only researcher informed drugs. Patients were divided into 2 groups including those intravenously received 0.4 mg Tamsulosin+30 mg Ketorolac (combination group) daily and other group was treated with 0.4mg tamsulosin daily. All descriptive variables severity of symptoms, dysuria and frequent urination were registered. Pain changes were evaluated by Visual Analog Scale (VAS).

Statistical analysis: The variables were reported as number (%) and continuous variable as a mean (standard deviation). The Chi-square test in SPSS software (version 21) was used to analyze the data.

RESULTS

Demographics characteristics of the study participants are shown in Table 1. The results showed that these characteristics were similar between groups.

Table 1: Demographics characteristics of study participants

Variable	Combination (n=50)	Tamsulosin (n=50)
Age (year)	33.75±9.05	33.46±8.05
Gender		
Male	46%	
Female	44%	56%

The results showed that the mean for showing symptoms between groups was different (P<0.05) in combination group, so that it was 128.40±35.80 and 23.60±11.40 in pre and post treatment, respectively. However, the data was not different in pre and post-test in Tamsulosin group (P>0.05) (135.06±55.30 vs 28.80±10.90) (P=0.165). The data also showed that only VAS was reduced in combination group (P<0.05) (Table 2)

Table 2: Effects of Tamsulosin alone and in combination with Ketorolac on urinary symptoms in patients with ureteral stones

Variable	Tamsulosin (n=50)	Combination (n=50)	P-value
Dysuria			
Before	15 (40.5%)	22 (59.5%)	0.147
After	5 (38.5%)	8 (61.5%)	0.393
Frequent			
Before	27 (56.3%)	21 (43.7%)	0.230
After	6 (42.9%)	8 (57.1%)	0.564
VAS			
Before	7.4±1.9	6.8±2.20	0.083
After	7.1±1.3	4.0±2.80	0.001

DISCUSSION

To the best of our knowledge, the present study, for first time, was conducted to compare effects of Tamsulosin alone and in combination with Ketorolac on urinary symptoms in patients with ureteral stones. Our findings showed that a combination of Ketorolac and Tamsulosin could decrease the mean for showing symptoms and VAS, but this combination did not have significant effect on dysuria and frequent urination compared to Tamsulosin. The efficiency of MET in reducing pain were evaluated on the basis of presence of the dominance of α-1-adrenoceptors in the smooth muscle of ureters. Blocking these receptors can transmit pain signals into central nervous system (Vo et al., 2016; Shokeir, 2001). A study

showed that administration of tamsulosin significantly decreased renal colic especially in patients with ureteral stones compared to placebo group (Ye et al., 2017). The benefits of MET for stone passage are thought to be mediated by a relaxation of the smooth muscles of the ureter via blockade of α-adrenergic receptors (Morita et al., 1987; Aldaqadossi et al., 2015; Hollingsworth et al., 2010). The α-blockers, i.e. Tamsulosin, prevent α-1-adrenergic receptors, relax smooth muscle and prevent peristalsis and relieves spasm (Barnela et al., 2012). The most concentration of α-1-adrenergic receptors is placed in the distal segment of the ureter. Pickard et al., (2015) evaluated the effectiveness of tamsulosin, nifedipine, and placebo on the rate of expulsion for 4 weeks after treatment initiation and showed effectiveness of agents for stones <5

mm, but could not show effectiveness for stones >5mm. Furyk et al., (2016) did not observe beneficial effects of Tamsulosin for patients with distal ureteric stones <10 mm. Parallel to our findings, Furyk et al (2016) showed a beneficial effects of MET for a stone size of >5 mm but in stones <5 mm. In the current study, a combination of Ketorolac and Tamsulosin could have significant efficiency. Ketorolac belongs to non steroidal anti-inflammatory drugs (NSAIDs). In a review article, Cohen et al. compared the effect of Diclofenac and Ketorolac for the treatment of renal colic and did not show significant difference in efficacy in the groups compared (Cohen et al., 1998). Parallel to our findings, Larkin et al. (1999) showed that Ketorolac has better effectiveness for decreasing patients' renal colic pain compared to meperidine. In addition, when administered together, intravenous morphine and ketorolac reduce pain better than either drug does alone (Safdar et al., 2006). The NSAIDs drugs are involved in auto-regulating renal blood flow system and reducing renal blood flow. The effects of NSAIDs drugs in healthy individuals is known, but in patients with renal colic is unknown. Prostaglandins increase vasodilation in the afferent glomerular arteries and can have a key role in normal glomerular perfusion and glomerular filtration rates. The NSAID drugs prevent the production of prostaglandins and cause to create a contraction in afferent arteries and decrease renal perfusion pressure.

CONCLUSION

This study was conducted to evaluate the comparative effects of Tamsulosin alone and in combination with Ketorolac on urinary symptoms in patients with ureteral stones. These findings showed that a combination of α -blockers and NSAIDs can have better efficiency compared to α -blocker agent. It means a synergism interaction effects between α -blockers and NSAIDs for decreasing urinary symptoms in patients with ureteral stones. A combination of Tamsulosin and Ketorolac can be used in patients with ureteral stones.

Conflict of interest: None.

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