

Comparison between Rowatinex and Tamsulosin as a Medical Expulsion Therapy for Ureteral Stone

Ghassan S.Ahmed^{*}, Kassim J. Al-Shamma^{**1} and Majeed M.Asghar^{***}

^{*}Department of Pharmaceutics and Clinical Pharmacy, College of Pharmacy, Basra University, Basra, Iraq.

^{**}Department of Clinical Pharmacy, College of Pharmacy, Baghdad University, Baghdad, Iraq.

^{***}Department of Clinical Urology, College of Medicine, Basra University, Basra, Iraq.

Abstract

The objective of this study is to evaluate the efficacy and safety of rowatinex and tamsulosin in the treatment of patients with ureteric stone.

Forty patients with ureteric stone ranged (4- 12) mm, were included in this study. They were randomized into two groups where the first group includes twenty patients treated with Rowatinex three times daily (Group 1), and the second group includes twenty patients treated with tamsulosin 0.4mg/day (Group 2). All patients were randomly assigned to receive the designed standard medical therapy for a maximum of 3 weeks.

Each group was given an antibiotic as prophylaxis and an injectable non-steroidal anti-inflammatory drug used on demand. At the outpatient clinic all subjects were assessed by CT-scan at baseline and evaluated every 7 days by physical examination, plain abdominal X-ray (KUB), and abdominal ultrasonography. Data were analyzed by using Student t-test method to compare the results; differences in the success rate between treatments were compared with the chi-square test for 2× 2 tables.

The results showed that tamsulosin significantly increases the expulsion rate, and reduce expulsion time of ureteric stone when compared with rowatinex group. Tamsulosin results in a better control of renal colic pain, and decreases in endoscopic procedures performed to remove the stone.

Key words: Ureteric stone, Tamsulosin, Rowatinex, Medical expulsion therapy.

تأثيرات التامسولوسين ، الفارديلافيل والراواتنكس كعلاج طبي طارد لحصوات الحالب

غسان صلاح احمد^{*}، قاسم جليل الشماخ^{**1} و ماجد محمد اصغر^{***}

^{*} فرع الصيدلانيات والصيدلة السريرية ، كلية الصيدلة ، جامعة البصرة ، بصرة ، العراق .

^{**} فرع الصيدلة السريرية ، كلية الصيدلة ، جامعة بغداد ، بغداد ، العراق .

^{***} فرع الجراحة البولية ، كلية الطب ، جامعة البصرة ، بصرة ، العراق .

الخلاصة

إن الهدف من هذه الدراسة هو تقييم فعالية وسلامة الرواتنكس والتامسولوسين في علاج المرضى الذين يعانون من حصاة الحالب. أربعون من المرضى الذين يعانون من حصاة الحالب التي تراوح حجمها (4-12) ملم قد شاركوا في هذه الدراسة. لقد تم توزيعهم بصورة عشوائية إلى مجموعتين حيث تضم المجموعة الأولى 20 مريضاً عولجوا بالرواتنكس ثلاث مرات يومياً (المجموعة الأولى)، وتضم المجموعة الثانية 20 مريضاً عولجوا بالتامسولوسين 0.4 ملغم باليوم (المجموعة الثانية). تم توزيع كل المرضى عشوائياً لتلقي العلاج لمدة ثلاثة أسابيع كحد أقصى.

أعطيت كل مجموعة المضادات الحيوية كوقاية وأدوية مضادة للالتهاب غير ستيروئيدية كمسكن عند الحاجة. تم تقييم جميع المرضى في العيادة الخارجية بواسطة التصوير الم قطع المحسوب في بداية الدراسة، وتم تقييم المرضى كل 7 أيام بواسطة الفحص البدني والأشعة السينية للبطن والموجات فوق صوتية للبطن.

أظهرت النتائج ان التامسولوسين أحدث زيادة معنوية في معدل طرد حصاة الحالب وتقليل الوقت اللازم لطرد الحصاة عند مقارنتها مع المجموعة التي عولجت بالرواتنكس. فضلاً عن تحسين السيطرة على آلام المغص الكلوي، وانخفاض في تنفيذ العمليات المنظارية لإزالة الحصاة.

الكلمات المفتاحية: تامسولوسين، فارديلافيل، رواتنكس.

Introduction

Urolithiasis is a common disease worldwide and its incidence in Western countries is growing⁽¹⁾. Urolithiasis has been considered as a significant source of morbidity, affecting all

geographical, cultural, and racial groups. The risk of developing urolithiasis throughout lifetime is about 10 – 15% in the developed countries, but can be as high as 20 – 25% in the Middle East.

¹Corresponding author E-mail: drkassim_alshamaa@yahoo.com.

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The increased risk of dehydration in hot climates, coupled with a diet that is 50% lower in calcium and 250% higher in oxalates compared to Western diets, accounts for the higher net risk in the Middle East⁽²⁾. Stones <3 mm in diameter have a better chance to pass spontaneously in the majority of cases, whereas stones >6 mm in the ureter are unlikely to pass in most situations⁽³⁾.

Many factors are involved in the interaction between the ureter and stones, therefore it is useful to understand mechanisms involved in the contraction and relaxation of the ureter. These mechanisms would possibly lead to discovery of new drugs that might facilitate stone passage, relieve symptoms and act as an adjunctive treatment to existing conventional modalities⁽⁴⁾.

Minimal invasive treatment strategies such as extracorporeal shockwave lithotripsy and ureteroscopy are frequently applied procedures in ureteral stone disease. However, indications for watchful waiting might be extended by addition of so-called 'medical expulsive therapy' (MET).

MET developed from several physiologic and pathophysiologic premises. Alpha 1 adrenoceptors (AR) have also been reported to mediate contractile responses in the ureter, and there is evidence that α -1 receptors predominate in ureteral smooth muscle^(5,6).

Alpha-adrenoceptors (AR) -1A, -1B and -1D subtypes were found to be localized in human ureter irrespective of location⁽⁷⁾. Sympathetic nerve bundles were distributed throughout the entire ureter. Therefore, α 1-adrenergic receptor antagonists may act on the entire ureter, reducing its tonus. As a result, these antagonists may be useful for improving the stone freeing rate and inhibiting pain attacks⁽⁸⁾.

Several studies have demonstrated that lower tract ureteral stones can be treated efficiently with different types of α 1-blockers with a low incidence of side effects⁽⁹⁾. Of the available α 1-blockers, we chose tamsulosin because it is a combined α 1A and α 1D-selective adrenergic antagonist and the existence of α 1A and α 1D-adrenoceptor subtypes have been demonstrated in the smooth muscle cells of the human ureter⁽¹⁰⁾.

Rowatinex is a special terpenes combination and is considered to have diuretic, anti-inflammatory and analgesic properties. In a randomized clinical trial, Rowatinex improved stone-free rates and reduced symptoms during stone passage⁽¹¹⁾. Rowatinex is considered to be a traditional therapy for ureteral stones, and

selected to be used in this study as comparative drug. This study was conducted to evaluate the efficacy and safety rowatinex and tamsulosin in the treatment of patients with ureteric stone.

Patients and Methods

This study was conducted prospectively at Al- Basra General Hospital from October 2011 till the end of April 2012. Forty Patients with ureteric stone ranged from 4mm to 12mm (mean 8 ± 2.3), were randomized into 2 groups. patients age ranged from 18 to 65 year (mean 35.27 ± 14.7), of which 31 patients (77.5%) were males and 9 patients (22.5%) were females. The first group (Group 1) was treated with rowatinex three times daily for 3 weeks, and the second group (Group 2) was treated with tamsulosin 0.4 mg once daily for 3 weeks. In the first group the percentage of the proximal, middle, and distal ureteric stones were found to be 45%, 30%, and 25% respectively, while, in the second group they were found to be 55%, 30%, and 15% respectively.

Both groups were given an antibiotic as prophylaxis during the medical expulsive therapy period and an injectable nonsteroidal anti-inflammatory drug used on demand. At the outpatient clinic all subjects were assessed by CT-scan at baseline and evaluated every 7 days by physical examination, plane abdominal X-ray (KUB), and abdominal ultrasonography. Data were analyzed by using Student t-test method used to compare the results and these data were represented as mean \pm standard error of the mean (SE), differences in the success rate between treatments were compared with the chi-square test for 2×2 tables.

Results

The data in table (1) showed that expulsion rate in patients treated with tamsulosin (group 2) was significantly higher ($p < 0.05$) than that of patients treated with rowatinex (group 1) for the same course time.

Table 1: The effects of rowatinex and tamsulosin on the expulsion rate of ureteric stone.

Groups	Number of subjects	Expulsion Rate
Group 1 (Rowatinex)	20	40
Group 2 (Tamsulosin)	20	85*

* Significantly different at ($p < 0.05$)

Significant reduction ($p < 0.05$) in expulsion time was obtained from treatment with tamsulosin when compared with results of treatment with rowatinex as shown in table (2).

Table 2: The effects of rowatinex and tamsulosin on expulsion time of ureteric stone.

Groups	Number of subjects	Expulsion Time (days) \pm SEM
Group 1 (Rowatinex)	20	12.13 \pm 1.94
Group 2 (Tamsulosin)	20	7.69* \pm 1.02

Values expressed as mean \pm standard error of mean.

* Significantly different at ($p < 0.05$).

As shown in table (3), the percent of patient experience colic episode was significantly lower ($p < 0.05$) in patients treated with tamsulosin when compared to the percent of patient experience colic episode in patients treated with rowatinex. At the same time, the total number of colic episodes in the group of patients treated with tamsulosin was significantly lower ($p < 0.05$) than that of patients treated with rowatinex.

Table 3: The effects of rowatinex and tamsulosin on the incidence of colic episodes in patients with ureteric stone.

Groups	Number of subjects	% of patient experience colic episode	No. of colic episode
Group 1 (Rowatinex)	20	35	14
Group 2 (Tamsulosin)	20	10*	4*

* Significantly different at ($p < 0.05$).

* Significantly different at ($p < 0.05$).

Table (4) represents the total number of ureteroscopic (URS) procedures performed to remove the stone, the data showed that the total number of ureteroscopy in the group treated with

rowatinex was significantly higher ($p < 0.05$) as compared to those of group treated with tamsulosin.

Table 4: Effect of treatment with rowatinex and tamsulosin on the total number of ureteroscopic procedures performed to remove the ureteral stone.

Groups	Number of subjects	Total No. Of ureteroscopy (%)
Group 1 (Rowatinex)	20	9 (45)
Group 2 (Tamsulosin)	20	2 (10)*

* Significantly different at ($p < 0.05$).

Discussion

Tamsulosin, a selective α -1A-, α -1D adrenergic antagonist, which has been recently used to treat ureteral stones, achieving unexpected and startling results. The rationale for its use for this pathological condition was taken from several studies. Sympathetic nerve fibers seem to be distributed throughout the entire ureter, and therefore, α -1-blockers would seem to be effective for elimination of ureteral stones irrespective to their locations^(7,12,13).

In this study, tamsulosin 0.4mg/d shows a significant advantage on the expulsion rate of ureteric stone over rowatinex. The data in table (1) showed that expulsion rate in patients treated with tamsulosin was significantly higher ($p < 0.05$) than that of patients treated with rowatinex for the same course time.

The results also demonstrated that patients treated with tamsulosin were associated with a greater tendency to reduce the expulsion time when compared with rowatinex.

These results were consistency with those obtained by M. Dellabella et.al.⁽¹⁴⁾ who found that, the use of tamsulosin in treatment regimen produced stone expulsion in almost all cases in a short time, allowing complete home patient treatment.

Tables (3,4), represent that patients treated with tamsulosin showed better control of renal colic pain as well as demonstrated by the fact that less patients in this group was urgently hospitalized during the study period. The causes of pain related to ureteral colic are the strain on muscular nerve endings and mucosa, which is caused by the increase in ureteral intraluminal pressure resulting from lithic obstruction and the production of lactic acid due to smooth muscle spasm. The stimulus is transferred to the spinal

cord through type A slow fibers and type C fast fibers, and then to the cerebral centers. α -1 receptor blockade results in the reduction of visceral pain and it has been assumed that this α -adrenergic blockade occurs in C-fibers^(15,16).

Therefore, according to our clinical results it would be possible to suppose a double action of tamsulosin on the control of pain associated with ureteral colic, that is a first action on smooth muscles, preventing spasm, and a second action on C-fibers or sympathetic postganglionic neurons, which also blocks pain conduction to the central nervous system.

Our results clinically supporting the validity of the hypothesis of the role of α -adrenergic receptors in the physiology of ureteral motility and the pathophysiology of renal colic^(17,18).

References

1. Pak CYC: Kidney stones. Lancet 1998; 51:1797–1801s.
2. Reilly Jr. RF. Nephrolithiasis 2005; Chapter 13: pp. 192–207.
3. Simon J, Roumeguere T, Vaessen C, Schulman CC: Conservative management of ureteric stones. Acta Urol Belg 1997; 65: 7–9.
4. Davenport K, Timoney A, Keeley FX. A comparative in vitro study to determine the beneficial effect of calcium-channel and alpha (1) - adrenoceptor antagonism on human ureteric activity. BJU Int 2006; 98:651–5.
5. Obara K, Takeda M, Shimura H, Kanai T, Tsutsui T, Komeyama T Alpha-1 adrenoceptor subtypes in the human ureter: characterization by RT-PCR and in situ hybridization. J Urol 1996;155(Suppl):472A
6. Hernandez M, Prieto D, Simonsen U, Rivera L, Barahona MV, Garcia-Sacristan A. Noradrenaline modulates smooth muscle activity of the isolated intravesical ureter of the pig through different types of adrenoceptors. Br J Pharmacol 1992, 107:924
7. Hyoung Keun Park · Eun Young Choi , Byoung Chang Jeong · Hyeon Hoe Kim, Byoung Kwon Kim. Localizations and expressions of α -1A, α -1B and α -1D adrenoceptors in human ureter. Urol Res 2007; 35:325–329.
8. Kazunari Ohki, Yoshihiro Ohno , Kazuhiro Suzuki. The investigation of ureteral sympathetic innervation, using semi-serial sections: why does the α 1-adrenergic receptor antagonist work well for ureteral stones? Int Urol Nephrol ;2010; 42:113–117.
9. Dellabella M, Milanese G, and Muzzonigro G: Efficacy of tamsulosin in the medical management of juxtavesical ureteral stones. J Urol 2003; 170: 2202–2205.
10. Sigala S, Dellabella M, Milanese G, et al: Alpha1 adrenoceptor subtypes in men juxtavesical ureters: molecular and pharmacological characterization. Eur Urol 2004; Suppl 3: 119.
11. Djaladat H, Mahouri K, Khalifeh Shoostary F, Ahmadi A. Effect of Rowatinex on calculus clearance after extracorporeal shock wave lithotripsy. Urol J 2009;6:9–13.
12. Dellabella, M., Milanese, G. and Muzzonigro, G.: Efficacy of tamsulosin in the medical management of juxtavesical ureteral stones. J Urol (2003);170: 2202.
13. Rang HP, Dale MM, Ritter JM, Flower RJ 2007. "Ch. 11", Rang and Dale's Pharmacology. Elsevier Churchill Livingstone, pp179-180.
14. Marco Dellabella, Giulio Milanese and Giovanni Muzzonigro. Randomized trial of the efficacy of tamsulosin, nifedipine and phloroglucinol in medical expulsive therapy for distal ureteral calculi. J Urol 2005;174, 167–172.
15. Ishigooka, I., Nakada, T., Hashimoto, T., Iijima, Y. and Yaguchi, H.: Spinal substance P immunoreactivity is enhanced by acute chemical stimulation of the rat prostate. Urology 2002; 59: 139.
16. Kinnman, E., Nygard, E. B. and Hansson, P.: Peripheral alpha adrenoceptors are involved in the development of capsaicin induced ongoing and stimulus evoked pain in humans. Pain 1997; 69: 79,
17. Hernandez, M., Prieto, D., Simonsen, U., Rivera, L., Barahona, M. V. and Garcia-Sacristan, A.: Noradrenaline modulates smooth muscle activity of the isolated intravesical ureter of the pig through different type of adrenoceptors. Br J Pharmacol 1992; 107: 924.
18. Morita, T., Ando, M., Kihara, K. and Oshima, H.: Function and distribution of autonomic receptors in canine ureteral smooth muscle. NeuroUrol Urodyn 1994; 13: 315.