Effect of Tamsulosin on calculus clearance after extracorporeal shock wave lithotripsy in patients with Renal Stone: a randomized, placebo-controlled study

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Abstract

The prevalence of stone disease has been estimated in Europe and North America, at 5%-10% of the population at least once in their life, and about one half develop recurrent disease, with the probability of having a stone varying according to age, gender, race, and geographic location. A randomized single-blind clinical trial was performed from March to September 2013, in Baghdad, Iraq, Patients who were admitted to undergo extracorporeal shock wave lithotripsy were approached and those with renal pelvis or calyceal calculi sized between 10 mm and 20 mm were selected. The study sample consist of 30 patients enrolled by Simple Randomization, and then subdivided into two groups, 15 patients received starch as placebo supplied in 00 capsules for 12 weeks, and 15 patients received tamsulosin HEXAL (Germany) capsule 0.4 mg/d for 12 weeks. All patients underwent follow-up examinations at 4, 8, and 12 weeks after extracorporeal shock wave lithotripsy, by kidney, ureter, and bladder radiography and ultrasonography. Four weeks following ESWL, 3 (20%) and 4 (26.6%) patients in the Tamsulosin and placebo groups had fragmented calculi without clearance, 10 (66.7%) and 10 (66.7%) had partial stone clearance, and 2 (13.3%) and 1 (6.7%) patients were totally stone free, respectively. Tamsulosin had an insignificant effect on the stone-free rate (P = 0.788). Eight weeks following ESWL, 1 (6.7%) and 3 (20%) patients in the Tamsulosin and placebo groups had fragmented calculi without clearance, 4 (26.6%) and 7 (46.7%) had partial stone clearance, and 10 (66.7%) and 5 (33.3%) patients were totally stone free, respectively. Tamsulosin had an insignificant effect on the stone-free rate (P = 0.175). Twelve weeks following ESWL, 1 (6.7%) and 3 (20%) patients in the Tamsulosin and placebo groups had partial stone clearance, 14 (93.3%) and 12 (80%) patients were totally stone free, respectively. Tamsulosin had an insignificant effect on the stone-free rate (P =

0.299). Overall, Tamsulosin had no significant effect on the stone-free rate. Treatment with tamsulosin after extracorporeal shock wave lithotripsy to assist calculus clearance, is neither effective, nor implying a shorter expulsion time.

Keywords: tamsulosin, extracorporeal shock wave lithotripsy, renal stone.

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Introduction

Urinary stone disease is one of the most common reasons for patients visiting a urology practice, affecting 5–10% of the population [(1)]. An even higher frequency has been reported from other parts of world (so called 'stone belts') and there are only a few geographical areas in which stone disease is rare, e.g. in Greenland and in the coastal areas of Japan [(2)].

Since its introduction in the early 1980s [(3)], extracorporeal shock wave lithotripsy (ESWL) has become the initial treatment for patients with kidney calculi. Even with the refinement of current endourological methods for stone removal, ESWL remains the primary treatment for most patients with uncomplicated calculi [(4)]. ESWL has many advantages, e.g. patients can be treated in an outpatient setting (with no anesthesia), a low morbidity rate, and high patient compliance.

When active removal is necessary, ESWL is the first choice of treatment for most patients, with a reported clearance rate for kidney stones of 66%-99% in patients with stones <20 mm. However, the success rate of ESWL depends on a number of factors, including the location and composition of the stone, the lithotripter used, and the body mass index of the patient [(5)].

Evidence that medical treatment with a α_1-adrenoceptor antagonist or a calcium antagonist could improve the clearance of stone fragments generated with ESWL is growing [(6)]. Thus, medical expulsive therapy adjuvant to ESWL could potentially decrease they costs related to

repeat ESWL or other treatment options such as retrograde ureteroscopic lithotripsy or percutaneous nephrolithotomy.

The aim of the present study is to evaluate the effect of tamsulosin on calculus clearance after extracorporeal shockwave lithotripsy in patients with renal stone.

Patients and Methods

A randomized single-blind clinical trial was performed from March to September 2013, at Ghazy Al-Hariri hospital for surgical specialties in Baghdad, Iraq. Patients who were admitted to undergo ESWL were approached and those with renal pelvis or calyceal calculi sized between 10 mm and 20 mm were selected. From 35 patients, only 30 patients were complete the study. The Ethics Committee of college of pharmacy /Al-Mustansiriyah University approved the study.

Inclusion criteria were adults 18-60 years, 10-20 mm size of the renal stone, without double-J or nephrostomy, no urinary tract infection (UTI), not using α-blocker before and have no contra-indication to tamsulosin.

Patients were evaluated before the procedure as diagnostic methods with urinalysis, intravenous urography (IVU), and ultrasonography. When needed, computed tomography of the urinary tract were performed.

A Modulith SLK-F2 machine equipped with a cylindrical electromagnetic shock wave source (Storz Medical, Tuttlingen, Switzerland) was used to perform lithotripsy. All patients received 3000 shocks with an energy level of 7 kV and a mean frequency of 1.5 Hz with a variable focus. After successful ESWL, the patients were assigned by Simple Randomization. Patients were divided into two groups: group A the control group fifteen patients received starch as placebo supplied in 00 capsules for 12 weeks. group B tamsulosin group fifteen patients received tamsulosin HEXAL (Germany) capsule 0.4 mg/d for 12 weeks.

All patients underwent follow-up examinations at 4, 8, and 12 weeks after ESWL. The primary outcome measurement was the complete stone clearance rate (absence of fragments larger than 4 mm on ultrasonography) after 12 weeks. The main methods of follow-up were diagnostic imaging (kidney, ureter, and bladder radiography and ultrasonography) and structured interviews of the patients. During these interviews, adverse events and tolerance of the medical expulsive therapy were also assessed.

Statistical Analysis Data were analyzed using the SPSS software (Statistical Package for the Social Sciences, version 12.0, SPSS Inc. Chicago, Illinois, USA). ANOVA test was used to compare categorical variables, the chi-square test for continuous ones between the two groups after 4 and 8 weeks, and fisher exact correction after 12 weeks. A *P* value less than 0.05 was considered significant.

Results

The study sample consist of 30 participants enrolled randomly, and then subdivided into two groups tamsulosin and placebo, these subdivision done after completion of matching process for each groups with each other regarding to: age, sex, stone size and stone locations. The intake of the drugs was followed for 12 weeks immediately after extracorporeal shock wave lithotripsy for each sample groups, and there were no missing values among the study sample.

Demographic profile as shown in table (1): males represent 63.33% of the study sample, while female represent 36.67%, mean of age variable among study sample was 42 years old, SD ± 9.334, and age range from 22-60 years old, while according to groups means of the age variable was as follow; 42.47 years and 41.53 years in the tamsulosin group and control group respectively.

Clinical characteristics related to stone size was shown in table (3-1); means of stone size were mean ±SD (14.6±3.312) mm and mean ±SD (14±3.381) mm in tamsulosin and control group respectively,

Clinical characteristics related to stone location among study sample were lie mainly in lower calyx and renal pelvis representing 83.33% of the locations, while the upper and middle calyx representing only 16.67% of the stone locations among study sample.

Four weeks following ESWL, 3 (20%) and 4 (26.6%) patients in the Tamsulosin and placebo groups had fragmented calculi without clearance, 10 (66.7%) and 10 (66.7%) had partial stone clearance, and 2 (13.3%) and 1 (6.7%) patients were totally stone free, respectively.

Table 1: Demographic profile and clinical characteristics among of the study samples

Variable		Tamsulosin group	Control group	Total
Number of patients		15	15	30
Mean of age in year ± SD		42.47 ±7.51	41.53 ±9.54	
sex	Male	9	10	19
	Female	6	5	11
Mean stone size in mm ± SD		14.6 ±3.312	14.0 ±3.381	
Stone location	Upper calyx	1	1	2
	Middle calyx	1	2	3
	Lower calyx	4	6	10
	Renal pelvis	9	6	15

Tamsulosin had an insignificant effect on the stone-free rate (P = 0.788). Eight weeks following ESWL, 1 (6.7%) and 3 (20%) patients in the Tamsulosin and placebo groups had fragmented calculi without clearance, 4 (26.6%) and 7 (46.7%) had partial stone clearance, and 10 (66.7%) and 5 (33.3%) patients were totally stone free, respectively. Tamsulosin had an insignificant effect on the stone-free rate (P = 0.175). Twelve weeks following ESWL, 1 (6.7%) and 3 (20%) patients in the Tamsulosin and placebo groups had partial stone clearance, 14 (93.3%) and 12 (80%) patients were totally stone free, respectively. Tamsulosin had an insignificant effect on the stone-free rate (P = 0.299). Overall, Tamsulosin had no significant effect on the stone-free rate.

There was no statistical significant difference (p value > 0.05) between clinical outcomes obtained from tamsulosin, over placebo groups regarding increased calculus clearance after ESWL. p value = 0.788 at 4 weeks, p value = 0.175 at 8 weeks and p value = 0.299 at 12 weeks as shown 1n figures 1, 2 and 3. But the rate of clearance and complete stone free state were higher in the tamsulosin group comparing to placebo group (93.3% *vs*. 80.0%).

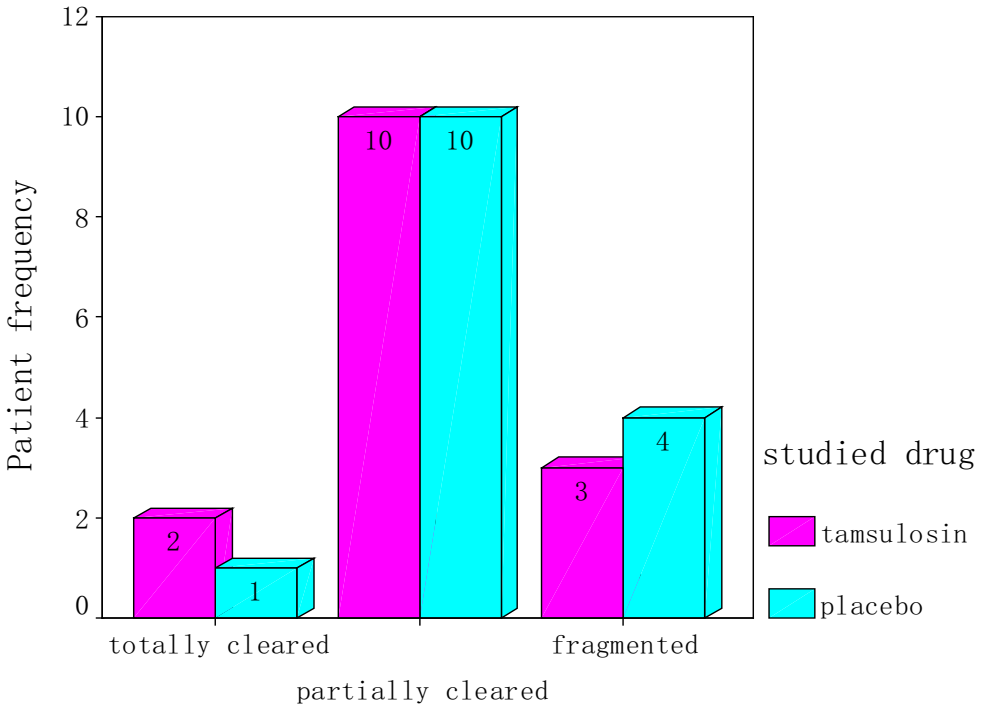

Figure 1: The clinical outcome at 4 weeks from ESWL, and the renal clearance comparing between tamsulosin and control groups.

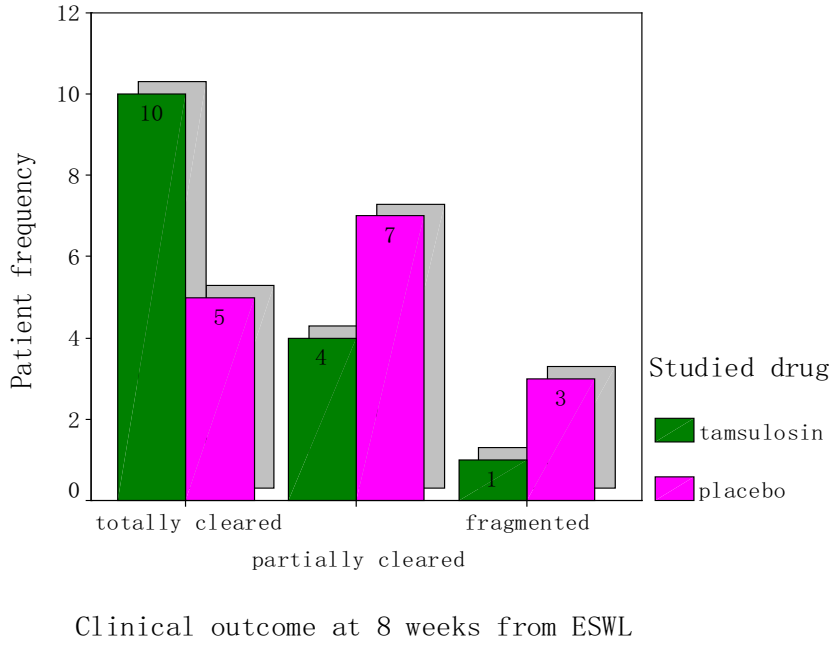

Figure 2: The clinical outcome at 8 weeks from ESWL, and the renal clearance comparing between tamsulosin and control groups.

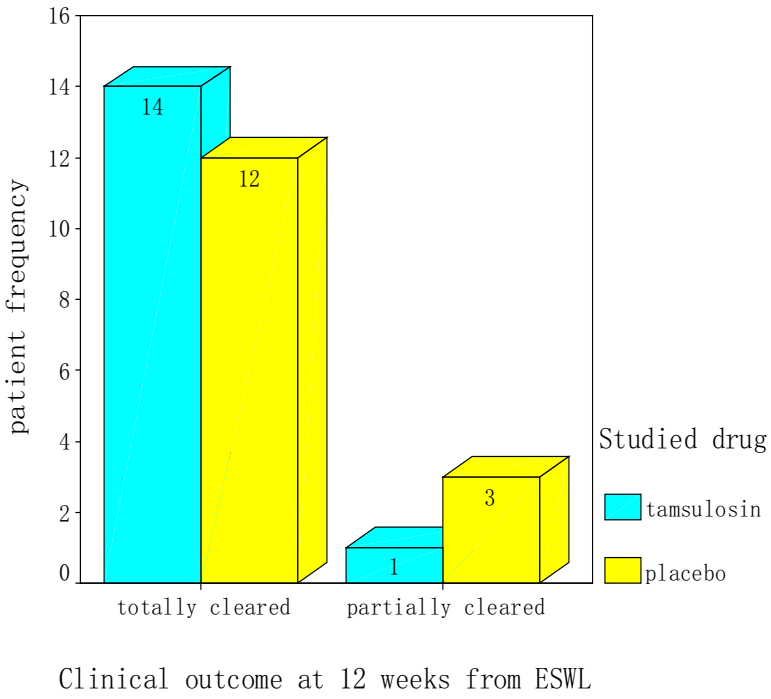

Figure 3: The clinical outcome at 12 weeks from ESWL, and the renal clearance comparing between tamsulosin and control groups.

Discussion

The use of adjuvant drugs, mainly tamsulosin, for ureteral stones has been demonstrated to be effective in several reports. The use of this drugs is associated with a greater likelihood of ureteral stone elimination, less pain, and faster elimination compared with a placebo [(7,8)]. Although the use of tamsulosin for ureteral stones has been widely studied, few reports have studied the use of tamsulosin for the elimination of renal stones after ESWL.

Medical expulsive therapy for urolithiasis has gained increasing attention in the last years [(9)]. Various medications such as nifedipine and corticosteroid agents have been investigated as spasmolytic agents that would promote the expulsion of the ureteral stones, both in watchful, waiting patients and patients with post ESWL [(10,11)].

Stone fragment expulsion after renal ESWL is probably not dissimilar to spontaneous discharge. Several variables play a fundamental role for the migration process of calculi: stone size; configuration and location, smooth muscle spasm, sub-mucosal edema, intrinsic areas of narrowing within the ureter; ureteral peristalsis; and infections [(12)].

Furthermore, α_1-blockers decrease the tension, release the spasm of smooth muscles, and, thus, lessen the obstruction and irritation symptoms in the lower urinary tract [13].

In the present study, the results were insignificant and the differences from other studies due to two main reasons. The first one was that, we included all of the renal stones without exclusion of non-lower pole renal calculi, as this was considered as a cornerstone in some of the researches which had proved a significant effect of tamsulosin on calculus clearance after ESWL [14,15]. Despite they wrote their exclusion of non-lower pole renal stone, they do not mention the exception of non-lower pole renal stone in their conclusions.

On the other hand, the rest of the researches that had proved a significant effect of tamsulosin on calculus clearance after ESWL were included renal and ureteric calculi, which is the second reason [16-20]. They do not explain why they combine renal and ureteric stone in spite of there are an obvious differences among them.

Naja (2008) and Falahatkar (2011) proved earlier clearance for tamsulosin vs. placebo [21,22], whereas Hussein (2010) said that, tamsulosin is insignificant at 2 weeks [23]. In our study, tamsulosin has no earlier clearance.

However, when we approved an insignificant results of tamsulosin on calculus clearance without any bias or unsatisfactory inclusion and exclusion criteria, we shall save millions dollars for the patients worldwide. And this is a good result to the patients in saving their money.

Conclusion

There was no statistical significant difference between clinical outcomes obtained from using tamsulosin, over the using of placebo as to increase calculus clearance after extracorporeal shock wave lithotripsy. So treatment with tamsulosin after ESWL to assist calculus clearance, is neither effective, nor implying a shorter expulsion time.

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