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ORIGINAL ARTICLE

Tamsulosin as an expulsive therapy for steinstrasse after extracorporeal shock wave lithotripsy: a randomized controlled study

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Abstract

Objective. Steinstrasse is a well-known complication following extracorporeal shockwave lithotripsy (ESWL). The objective of this study was to evaluate the efficacy of tamsulosin as a management of steinstrasse. *Material and methods.* 88 patients with unilateral steinstrasse were treated between January 2005 and December 2008. The patients were randomly allocated into two equal groups. There were no significant differences between groups for age, gender, stone location, stone length or stone fragment size ($p > 0.05$). Patients in group 1 (study group) received a single daily morning dose of tamsulosin (0.4 mg) for a maximum of 4 weeks, in addition to pain-relieving therapy. Patients in group 2 (control group) received only the pain-relieving therapy. All patients were checked weekly with a plain X-ray of the urinary tract, urinary ultrasonography, urine analysis and serum creatinine. Pain episodes, day of spontaneous stone expulsion, total analgesic dosage and drug side-effects were recorded. *Results.* Stone expulsion occurred in 32 of the 44 patients (72.7%) receiving tamsulosin and in 25 of the 44 patients (56.8%) in the control group. Patients receiving tamsulosin had a significantly higher stone expulsion rate ($p = 0.017$). There were no significant differences between groups for mean stone expulsion time or number of analgesics used. Twelve patients (27.3%) in the group receiving tamsulosin and 19 patients (43.3%) in the control group needed hospitalization; the group difference was statistically significant ($p = 0.017$). *Conclusions.* When compared with no treatment, tamsulosin can significantly facilitate expulsion of retained ureteral stone fragments following ESWL.

Key Words: *Extracorporeal shock wave lithotripsy, steinstrasse, tamsulosin*

Introduction

In 1982, a new era in stone disease management began when Chaussy et al. [1] introduced extracorporeal shock wave lithotripsy (ESWL). However, successful treatment (defined as stone disintegration and clearance) is influenced by factors such as stone burden, stone type, pelvicalyceal anatomy and shock-wave energy [2]. Steinstrasse (stone street) is defined as a column of stone fragments retained in the ureteral lumen that obstructs the pelvi-calyceal system after ESWL [3]. Such ureteral stone retention can occur in 1–4% of patients with small stones [2,4], 5–10% of patients with large (>2cm^2) stone burdens [4] and up to 40% of patients with partial or complete staghorn calculi [5]. Based on the size of stone fragments, steinstrasse is classified into three types, with type 1 composed of fine particles of 2 mm, type 2 with leading fragments of 4–5 mm and type 3 composed of large fragments [6].

To decrease the incidence of steinstrasse, guidelines from a National Institutes of Health (NIH) consensus conference recommended that patients with stones >2 cm should be managed initially with percutaneous nephrolithotripsy (PNL) followed, if needed, by ESWL [7]. However, some authors recommend ureteral stenting before ESWL for large stones [8]. Spontaneous expulsion of steinstrasse is reported in about 37% of cases; otherwise, ureteroscopy, percutaneous nephrolithotomy (PCN) or additional ESWL treatment will be required [9]. Spontaneous stone expulsion after ESWL can be assisted by calcium channel blockers, prostaglandin synthesis inhibitors, spasmolytic regulators, steroid treatment to relieve oedema and, more

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recently, α-adrenergic blockers [10,11]. The purpose of the present randomized, controlled study was to evaluate the efficacy of tamsulosin to facilitate the expulsion of steinstrasse.

Material and methods

Participants

A total of 1564 patients underwent ESWL with a Siemens Lithostar™ Plus device (Siemens, Berlin, Germany) between January 2005 and December 2008. Kidney–bladder–ureter (KUB) radiographs showed that 96 (6.1%) of these patients had unilateral steinstrasse. An example is shown in Figure 1.

The 96 patients with steinstrasse were assessed with a plain X-ray of the urinary tract (PUT), urinary ultrasonography, urine analysis and serum creatinine level. The level and length of the steinstrasse and the size of the major (leading) stone fragment were recorded. Patients eligible to be enrolled in the study: (i) were older than 18 years old; (ii) had absent clinical and laboratory signs of urinary tract infection (UTI), severe hydronephrosis, alterations in creatininaemia, diabetes, ulcer disease or hypotension; and (iii) had no concomitant usage of calcium antagonists or distal ureteral surgery. Of the 96 patients with steinstrasse, 88 patients fulfilled the inclusion criteria; eight patients were excluded owing to advanced hydronephrosis ($n = 2$), UTI ($n = 2$) and past ureteral surgery ($n = 4$).

Figure 1. Plain X-ray of the urinary tract showing a patient with unilateral steinstrasse.

Using computer-generated random numbers, the patients were randomly allocated into two equal groups of 44 patients. The mean ± standard deviation (SD) age of patients was 35.6 ± 9.95 and 33.9 ± 9.71 in groups 1 and 2, respectively. The male:female ratio was 28:16 and 27:17 for patients in groups 1 and 2, respectively. The stone location was on the right side for 24 of the patients in group 1 and 21 of the patients in group 2. The mean stone length and mean size of the major stone fragments are contained in Table I. There were no significant differences between groups for age, gender, stone location, stone length or stone fragment size ($p > 0.05$).

Procedures

The study was performed after obtaining informed patient consent, in accordance with the Declaration of Helsinki.

Patients in group 1 (study group) received a single daily morning dose of tamsulosin (0.4 mg) for a maximum of 4 weeks, in addition to pain-relieving therapy. Patients in group 2 (control group) received only the pain-relieving therapy. The recommended analgesic for all patients was 100 mg indomethacin suppositories, administered on demand. All patients were encouraged to drink a minimum of 2.5 litres of water daily and advised to filter their urine to detect stone passage.

Evaluation of outcome

All patients were checked weekly with PUT, urinary ultrasonography, urine analysis and serum creatinine level. Pain episodes, day of spontaneous stone expulsion, total analgesic dosage and drug side-effects were recorded.

Patients with unsuccessful stone expulsion within the study period of 28 days were hospitalized. This included patients with uncontrollable pain, fever, severe hydronephrosis or an increased creatinine level (>2 mg/dl).

Stone expulsion time was defined as the number of days from the beginning of assigned oral therapy to stone expulsion. Analgesic requirement was defined as the number of suppositories used throughout the study period.

Table I. Stone length and major stone fragment size for patients in group 1 (receiving tamsulosin) and group 2 (control).

Variable	Group 1 (n = 4)		Group 2 (n = 44)		p^a
Stone length (cm)	6	1.93	6.25	1.97	0.96
Largest steinstrasse transverse diameter (mm)	7.6	1.22	7.3	1.43	0.84
Major stone fragment width × length (mm)	3.1 ±.85 × 6.39 ± 0.99		3 ±.92 × 6.07 ± 1.18		>0.05

Data are shown as mean ± SD.
[a]Probability of significant group differences (n = 88).

Statistical analysis

Data were expressed as the mean, SD, median and range. Chi-squared tests were performed to compare the measured outcomes using SPSS 16.0 (SPSS, Chicago, IL, USA) software, with $p < 0.05$ considered statistically significant.

Results

This prospective, randomized controlled study involved 88 adult patients with steinstrasse following ESWL.

Table II shows the results of stone expulsion. Stone expulsion occurred in 32 of the 44 patients (72.7%) receiving tamsulosin and in 25 of the 44 patients (56.8%) in the control group. Patients receiving tamsulosin had a significantly higher stone expulsion rate than controls (p = 0.017). There was no significant difference in the rate of stone expulsion between males and females in either group (Figure 2).

The mean stone expulsion time and number of analgesics used for patients in each group are contained in Table III. There were no significant differences between groups for either variable.

Each group was further subdivided into two subgroups with a leading fragment size smaller and larger than 5 mm. There was no significant difference in subgroup distribution, with 27 and 30 patients having a leading fragment <5 mm in the study and control groups, respectively (p = 0.3).

Table II. Number of patients with stone expulsion in group 1 (receiving tamsulosin) and group 2 (control); probability of significant group differences (N = 88).

Variable	Group 1			Group 2			
	n	Group n	% n	n	Group n	% n	p^a
Stone expulsion							0.017
Total	32	44	72.7	25	44	56.8	
Males	20	28	71.4	15	27	55.5	
Females	12	16	75.0	10	17	58.8	

[a]Probability of significant group differences (n = 88).

A significantly higher expulsion rate occurred with leading fragments smaller than 5 mm within each group (Table IV). The mean size of the expelled fragments was 5.7 ± 1.1 mm and 5.1 ± 0.92 mm for the study and control groups, respectively, being

Figure 2. Plain X-ray of the urinary tract showing no steinstrasse after tamsulosin therapy.

Table III. Stone expulsion time and number of analgesics used for patients in group 1 (receiving tamsulosin) and group 2 (control).

Variable	Group 1 (n = 44)	Group 2 (n = 44)	p^a
Stone expulsion time (days)	12.67 ± 2.29	15.07 ± 3.55	.53
Analgesics used (number)	4.39 ± 2.42	6.11 ± 3.1	.51

Data are shown as mean ± SD.
[a]Probability of significant group differences (n = 88).

Table IV. Patient distribution according to leading fragment size with stone expulsion within each subgroup.

	All	Expulsion	No expulsion	p^a
(a) Group 1 (receiving tamsulosin)				
<5 mm	27 (61.4)	25 (92.5)	2 (7.5)	<0.05
>5 mm	17 (38.6)	7 (41)	10 (59)	
Total	44	32 (72.7)	12 (17.8)	
(b) Group 1 (control)				
<5 mm	30 (68)	22 (73.3)	8 (26.7)	<0.05
>5 mm	14 (32)	3 (21.4)	11 (78.6)	
Total	44	25 (56.8)	19 (43.4)	

Data are shown as *n* (%).
[a]Probability of significant group differences (*n* = 88).

larger in the study group, but the difference was not statistically significant ($p > 0.71$).

Twelve patients (27.3%) in the group receiving tamsulosin needed hospitalization for unsuccessful stone expulsion. Ureteroscopy was performed. Nineteen patients (43.3%) in the control group needed hospitalization because of uncontrollable pain during therapy ($n = 2$), unsuccessful expulsion after 4 weeks of treatment ($n = 16$) or an infected obstructed kidney ($n = 1$). All patients had ureteroscopy except for the patient with the infected kidney, who was managed with PCN. The number of patients needing hospitalization was statistically significant between groups ($p = 0.017$).

Drug tolerance was excellent, with no drug side-effects necessitating treatment discontinuation in either group. However, patients in the group receiving tamsulosin reported anejaculation ($n = 6$) and headache ($n = 4$).

Discussion

Steinstrasse is a well-known complication following ESWL. It occurs in 5–10% of patients with large stone burdens (>2 cm^2) [4]. The likelihood of spontaneous passage depends mainly on the site and size of the leading fragment, the internal anatomical structure of the ureter, and a history of spontaneous expulsion [12,13]. In the absence of UTI and/or complete obstruction, steinstrasse can be managed conservatively with observation and concomitant administration of spasmolytic drugs, antioedemics, nifedipine and antibiotics; these methods have a reported spontaneous clearance of 60–80% [14–17].

More recently, α-blockers have been used to manage lower ureteral stones [18], based on the study by Malin et al. in 1970 [19]. Malin et al. demonstrated the presence of α- and β-adrenergic receptors in the human ureter, with α-adrenergic receptors predominating.

Blockade of the α-adrenergic receptor by a specific antagonist results in decreased ureteral peristaltic amplitude and frequency, with a subsequent loss of intraureteral pressure. Therefore, there is an increase in fluid transportability [20,21]. Tamsulosin 0.4 mg/day, doxazosin 4 mg/day and terazosin 10 mg/day have all been used to facilitate lower ureteral stone expulsion, with nearly equal efficacy [22]. In the present study, tamsulosin was chosen because it is a combined α_{1A} and α_{1D}-selective adrenergic antagonist, and both of these adrenoceptor subtypes have been found in the smooth-muscle cells of the human ureter [23,24].

Dellabella et al. [10] proposed that tamsulosin induces an increase in the intraureteral pressure gradient around the stone by: (i) increasing the urine bolus above it (thus increasing intraureteral pressure above the stone), and (ii) decreasing peristalsis below the ureter (thus decreasing intraureteral pressure below the stone). These actions are in addition to a decrease in basal and micturition pressures. As a result, there is a stronger urge to expel the stone [10]. Tamsulosin is well tolerated with minimal side-effects on blood pressure [25].

In the present study, there was no statistically significant between-group difference in stone expulsion time or analgesic requirements, probably due to ureteral oedema associated with the impacted fragments. Consequently, more time was needed for the oedema to be resolved.

The use of tamsulosin was associated with a significantly higher stone expulsion rate in the present study, which agrees with the findings reported by other authors [26,27]. The higher stone expulsion rate translates into less need for hospitalization and surgical intervention, with consequent early return to work and positive economic impact. Dellabella et al. [10] reported that tamsulosin prevented hospitalization in 33% and ureteroscopy in 30% of the cases studied, providing an advantage in terms of cost. In the present study, hospitalization was prevented in 32 of the 44 patients (72.7%) receiving tamsulosin.

In agreement with other studies [28,29], these results demonstrate that the size of the leading fragment correlated negatively with spontaneous expulsion, with more need for intervention as the size increases. Tamsulosin facilitated the expulsion of larger fragments, but the size difference was not significant.

In conclusion, in the absence of infection, impaired renal function or intractable pain, tamsulosin can significantly facilitate expulsion of retained ureteral stone fragments following ESWL. Patients receiving tamsulosin have less need for hospitalization than patients receiving no active treatment.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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