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Tamsulosin as an Expulsive Therapy for Steinstrasse After Extracorporeal Shock Wave Lithotripsy: A Randomized Controlled Study

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ABSTRACT

INTRODUCTION: Steinstrasse is a well-known complication following extracorporeal shock wave lithotripsy (ESWL). It has been identified in 5-10% of patients with large stone burdens (> 2 cm) and may necessitate surgical intervention if medical treatment fails. The objective of the present study was to evaluate the efficacy of tamsulosin as a conservative management of steinstrasse in a randomized, controlled study.

METHODS: The participants were 88 patients with unilateral steinstrasse who were treated between January 2005 and December 2008. The patients were randomly allocated into 2 equal groups of 44 patients. There were no significant differences between groups for age, sex, stone location, stone length, or stone fragment size ($P > .05$). 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 (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. The data were analyzed using chi-square.

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 ($P = .017$). 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 ($P = .017$).

CONCLUSION: When compared with no treatment, tamsulosin can significantly facilitate expulsion of retained ureteral stone fragments following ESWL with less need for hospitalization.

KEYWORDS: Tamsulosin; Steinstrasse; Extracorporeal shock wave lithotripsy (ESWL)

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Tamsulosin as an Expulsive Therapy for Steinstrasse After Extracorporeal Shock Wave Lithotripsy: A Randomized Controlled Study

INTRODUCTION

In 1982, a new era in stone disease management began when Chaussy et al [1] introduced extra-corporeal shock wave lithotripsy (ESWL). However, successful treatment (defined as stone disintegration and clearance) is influenced by factors such as stone burden, stone type, pelvicalyceal (PC) 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 PC system after ESWL [3]. Such ureteral stone retention can occur in 1-4% of patients with small sized stones [2,4], 5%-10% of patients with large (>2 cm^2) stone burdens [4], and up to 40% of patients with partial or complete staghorn calculi [5].

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 [6]. However, some authors recommend ureteral stenting prior to ESWL for large-sized stones [7]. Spontaneous expulsion of steinstrasse is reported in about 37% of cases; otherwise, ureteroscopy, percutaneous nephrolithotomy (PCN), or additional ESWL treatment will be required [8].

Spontaneous stone expulsion after ESWL can be assisted by calcium channel blockers, prostaglandin synthesis inhibitors, spasmolytic regulators, steroid treatment to relieve edema and, more recently, alpha adrenergic blockers [9,10]. The purpose of the present randomized, controlled study was to evaluate the efficacy of tamsulosin to facilitate expulsion of steinstrasse.

METHODS

Participants

A total of 1564 patients had ESWL with a Siemens Lithostar™ Plus device (Siemens AG, 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.

Figure 1. Kidney, Ureter, Bladder (KUB) Radiograph Showing a Patient With Unilateral Steinstrasse.

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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 stone street and the size of the major (leading) stone fragment were recorded. Patients eligible to be enrolled in the study: (1) were older than 18 years old; (2) had absent clinical and laboratory signs of urinary tract infection (UTI), severe hydronephrosis, alterations in creatininemia, diabetes, ulcer disease, or hypotension; (3) had no concomitant usage of calcium antagonists or distal ureteral surgery. Of the 96 patients with steinstrasse, 88 patients fulfilled the inclusion criteria; 8 patients were excluded due to advanced hydronephrosis (n = 2), UTI (n = 2), and past ureteral surgery (n = 4).

The patients were randomly allocated into 2 equal groups of 44 patients. The mean (standard deviation) patient age was 35.61 (9.95) and 33.86 (9.71) for patients 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 1. There were no significant differences between groups for age, sex, stone location, stone length, or stone fragment size ($P > .05$).

Procedures

The study was performed after obtaining an 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

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Table 1. Mean and Standard Deviation (SD) for Stone Length and Major Stone Fragment Size for Patients in Group 1 (Receiving Tamsulosin) and Group 2 (Control); Probability of Significant Group Differences (N = 88).
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Variable	Group 1 (n = 44)		Group 2 (n = 44)		*P*
	Mean	SD	Mean	SD	
Stone length (cm)	6	1.93	6.25	1.97	.96
Major stone fragment (mm)	6.39	0.99	6.07	1.18	.93

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 L 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.

Statistical Analysis

Data were expressed as the mean, standard deviation (SD), median, and range. Chi-square was performed to compare the measured outcomes using SPSS 16.0 (SPSS Inc, Chicago, IL, USA) software, with $P < .05$ considered statistically significant.

RESULTS

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

Table 2 shows the results of stone expulsion. After 28 days, 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 ($P = .017$). There was no significant difference in the rate of stone expulsion between males and females in either group.

The mean stone expulsion time and number of analgesics used for patients in each group are contained in Table 3. There were no significant differences between groups for either variable.

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 group difference in the number of patients needing hospitalization was statistically significant ($P = .017$).

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

Table 2. Number of Patients With Stone Expulsion in Group 1 (Receiving Tamsulosin) and Group 2 (Control); Probability of Significant Group Differences (N = 88).
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Variable	Group 1			Group 2			*P*
	n	group n	%n	n	group n	%n	
Stone expulsion							
Total	32	44	72.7	25	44	56.8	.017
Males	20	28	71.4	15	27	55.5	
Females	12	16	75.0	10	17	58.8	

Table 3. Mean and Standard Deviation (SD) for Stone Expulsion Time and Number of Analgesics Used for Patients in Group 1 (Receiving Tamsulosin) and Group 2 (Control); Probability of Significant Group Differences (N = 88). doi: 10.3834/uij.1944-5784.2010.02.09t3

Variable	Group 1 (n = 44)		Group 2 (n = 44)		*P*
	Mean	SD	Mean	SD	
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

on the site and size of the leading fragment, the internal anatomical structure of the ureter, and a history of spontaneous expulsion [11,12]. In the absence of UTI and/or complete obstruction, steinstrasse can be managed conservatively with observation and concomitant administration of spasmolytic drugs, antiedemics, nifedipine, and antibiotics; these methods have a reported spontaneous clearance of 60-80% [13-16].

More recently, alpha blockers have been used to manage lower ureteral stones [17], based on the study by Malin et al in 1970 [18]. 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 [19,20]. Tamsulosin 0.4 mg/d, doxazosin 4 mg/d, and terazosin 10 mg/d have all been used to facilitate lower ureteral stone expulsion, with nearly equal efficacy [21]. In the present study, tamsulosin was chosen because it is a combined $alpha_{1A}$ and $alpha_{1D}$-selective adrenergic antagonist, and the existence of both of these adrenoceptor subtypes have been found in the smooth muscle cells of the human ureter [22,23].

Dellabella et al [9] proposed that tamsulosin induces an increase in the intraureteral pressure gradient around the stone by: (1) increasing the urine bolus above it (thus increasing intraureteral pressure above the stone), and (2) 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 [9]. Tamsulosin is well tolerated with minimal side effects on blood pressure [24].

In the present study, there was no statistically significant between-group difference in stone expulsion time or analgesic requirements, probably due to ureteral edema associated with the impacted fragments. Consequently, more time was needed for the edema 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 [25,26]. The higher stone expulsion rate is translated into less need for hospitalization and surgical intervention, with consequent early return to work and positive economic impact. Dellabella and associates [9] 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.

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.

Conflict of Interest: none declared

REFERENCES

[1] Chaussy C, Schmiedt E, Jocham D, Brendel W, Forssmann B, Walther V. First clinical experience with extracorporeally induced destruction of kidney stones by shock waves. *J Urol.* 1982;127(3):417-420.

[2] Madbouly K, Sheir KZ, Elsobky E, Eraky I, Kenawi M. Risk factors for the stone formation of a steinstrasse after extracorporeal shock wave lithotripsy: a statistical model. *J Urol*. 2002;167(3):1239-1242.

[3] Al-Awadi KA, Abdul Halim H, Kehinde EO, Al-Tawheed A. Steinstrasse: a comparison of incidence with and without J stenting and the effect of J stenting on subsequent management. *BJU Int*. 1999;84(6):618-621.

[4] Bierkens AF, Hendrikx AJ, Lemmens WA, Debruyne FM. Extracorporeal shock wave lithotripsy for large renal calculi: the role of ureteral stents. A randomized trial. *J Urol.* 1991;145(4):699-702.

[5] Wirth MP, Theiss M, Frohmuller HG. Primary extracorporeal shockwave lithotripsy of staghorn renal calculi. *Urol Int.* 1992;48(1):71-75.

[6] Concensus Conference. Prevention and treatment of kidney stones. *JAMA*. 1988;260(7):977-981.

[7] Sulaiman MN, Buchholz NP, Clark PB. The role of ureteral stent placement in the prevention of Steinstrasse. *J Endourol*. 1999;13(3):151-155.

[8] Kato Y, Yamaguchi S, Hori J, Okuyama M, Kaneko S, Yachiku S. Utility of ureteral stent for stone street after extracorporeal shock wave lithotripsy [in Japanese]. *Hinyokika Kiyo.* 2005;51(5):309-314.

[9] Dellabella M, Milanese G, Muzzonigro G. Efficacy of tamsulosin in the medical management of juxtavesical ureteral stones. *J Urol*. 2003;170(6 Pt 1):2202-2205.

[10] Resim S, Ekerbicer HC, Ciftci A. Role of tamsulosin in treatment of patients with steinstrasse developing after extracorporeal shock wave lithotripsy. *Urology.* 2005;66(5):945-948.

[11] Miller OF, Kane CJ. Time to stone passage for observed ureteral calculi: a guide for patient education. *J Urol.* 1999;162(3 Pt 1):688-691.

[12] Whitfield HN. The management of ureteric stones. Part II: therapy. *BJU Int.* 1999;84(8):916-921.

[13] Fedullo LM, Pollack HM, Banner MP, Amendola MA, Van Arsdalen KN. The development of steinstrassen after ESWL: frequency, natural history, and radiologic management. *AJR Am J Roentgenol.* 1988;151(6):1145-1147.

[14] 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(4):924-931.

[15] Borghi L, Meschi T, Amato F, et al. Nifedipine and methylprednisolone in facilitating ureteral stone passage: a randomized, double-blind, placebo-controlled study. *J Urol.* 1994;152(4):1095-1098.

[16] Cooper JT, Stack GM, Cooper TP. Intensive medical management of ureteral calculi. *Urology.* 2000;56(4):575-578.

[17] Micali S, Grande M, Sighinolfi MC, De Stefani S, Bianchi G. Efficacy of expulsive therapy using nifedipine or tamsulosin, both associated with ketoprofene, after shock wave lithotripsy of ureteral stones. *Urol Res.* 2007;35(3):133-137.

[18] Malin JM Jr, Deane RF, Boyarsky S. Characterisation of adrenergic receptors in human ureter. *Br J Urol.* 1970;42(2):171-174.

[19] Morita T, Wada I, Suzuki T, Tsuchida S. Characterization of alpha-adrenoreceptor subtypes involved in regulation of ureteral fluid transport. *Tohoku J Exp Med*. 1987;152(2):111-118.

[20] Morita T, Wada I, Saeki H, Tsuchida S, Weiss RM. Ureteral urine transport: changes in bolus volume, peristaltic frequency, intraluminal pressure and volume of flow resulting from autonomic drugs. *J Urol.* 1987;137(1):132-135.

[21] Yilmaz E, Batislam E, Basar MM, Tuglu D, Ferhat M, Basar H. The comparison and efficacy of 3 different alpha1-adrenergic blockers for distal ureteral stones. *J Urol*. 2005;173(6):2010-2012.

[22] Sigala S, Dellabella M, Milanese G, et al. Evidence for the presence of alpha1 adrenoceptor subtypes in the human ureter. *Neurourol Urodyn*. 2005;24(2):142-148.

[23] Obara K, Takeda M, Shimura H, et al. Alpha-1 adrenoreceptor subtypes in the human ureter: characterization by RT-PCR and in situ hybridisation. *J Urol*. 1996;155(suppl 5):Abstract 472.

[24] Chapple CR. A comparison of varying alpha blockers and other pharmacotherapy options for lower urinary tract symptoms. *Rev Urol*. 2005;7(Suppl 4):S22-S30.

[25] Cervenakov I, Fillo J, Mardiak J, Kopecny M, Smirala J, Lepies P. Speedy elimination of ureterolithiasis in lower part of ureters with the alpha1-blocker-- Tamsulosin. *Int Urol Nephrol.* 2002;34(1):25-29.

[26] Gravina GL, Costa AM, Ronchi P, et al. Tamsulosin treatment increases clinical success rate of single extracorporeal shock wave lithotripsy of renal stones. *Urology*. 2005;66(1):24-28.

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