



European Association of Urology



Platinum Priority – Stone Disease

Editorial by Gianluca Giannarini and Riccardo Autorino on pp. 413–415 of this issue

Is There a Role for Tamsulosin in the Treatment of Distal Ureteral Stones of 7 mm or Less? Results of a Randomised, Double-Blind, Placebo-Controlled Trial

Thomas Hermanns^{a,1}, Peter Sauer mann^{a,1}, Kaspar Rufibach^b, Thomas Frauenfelder^c,
Tullio Sulser^a, Rät o T. Strebel^{a,d,*}

^a Department of Urology, University of Zürich, University Hospital, Zürich, Switzerland

^b Institute for Social- and Preventive Medicine, Biostatistics Unit, University of Zürich, Zürich, Switzerland

^c Institute for Diagnostic Radiology, University of Zürich, University Hospital, Zürich, Switzerland

^d Department of Urology, Kantonsspital Graubünden, Chur, Switzerland

Article info

Article history:

Accepted March 24, 2009

Published online ahead of
print on April 3, 2009

Keywords:

Adrenergic alpha antagonists
Drug therapy
Tamsulosin
Ureter
Ureteral calculi



www.eu-acme.org/
[europeanurology](http://europeanurology.com)

Please visit

[www.eu-acme.org/](http://www.eu-acme.org/europeanurology)
[europeanurology](http://europeanurology.com) to read and
answer questions on-line.

The EU-ACME credits will
then be attributed
automatically.

Abstract

Background: Numerous randomised trials have confirmed the efficacy of medical expulsive therapy with tamsulosin in patients with distal ureteral stones; however, to date, no randomised, double-blind, placebo-controlled trials have been performed.

Objective: The objective of this trial was to evaluate the efficacy of medical expulsive therapy with tamsulosin in a randomised, double-blind, placebo-controlled setting.

Design, setting, and participants: Patients presenting with single distal ureteral stones ≤ 7 mm were included in this trial.

Intervention: Patients were randomised in a double-blind fashion to receive either tamsulosin or placebo for 21 d. The medication was discontinued after either stone expulsion or intervention. Abdominal computed tomography was performed to assess the initial and final stone status.

Measurements and limitations: The primary end point was the stone expulsion rate. Secondary end points were time to stone passage, the amount of analgesic required, the maximum daily pain score, safety of the therapy, and the intervention rate.

Results: Ten of 100 randomised patients were excluded from the analysis. No statistically significant differences in patient characteristics and stone size (median: 4.1 mm [tamsulosin arm] vs 3.8 mm [placebo arm], $p = 0.3$) were found between the two treatment arms. The stone expulsion rate was not significantly different between the tamsulosin arm (86.7%) and the placebo arm (88.9%; $p = 1.0$). Median time to stone passage was 7 d in the tamsulosin arm and 10 d in the placebo arm (log-rank test, $p = 0.36$). Patients in the tamsulosin arm required significantly fewer analgesics than patients in the placebo arm (median: 3 vs 7, $p = 0.011$). A caveat is that the exact time of stone passage was missing for 29 patients.

Conclusions: Tamsulosin treatment does not improve the stone expulsion rate in patients with distal ureteral stones ≤ 7 mm. Nevertheless, patients may benefit from a supportive analgesic effect.

Clinicaltrials.gov: NCT00831701.

© 2009 European Association of Urology. Published by Elsevier B.V. All rights reserved.

¹Both authors contributed equally to this work.

* Corresponding author. Department of Urology, Kantonsspital Graubünden, Loesstr. 170, 7000 Chur, Switzerland. Tel. +41 81 2566237; Fax: +41 81 2566665.

E-mail address: Raeto.Strebel@ksgr.ch (R.T. Strebel).

1. Introduction

Current therapeutic options for ureteral stones include active intervention as well as conservative *watch and wait* approaches. Endoscopic treatment of ureteral stones has a high success rate and reliably results in immediate stone removal [1,2]; however, surgical as well as anaesthetic risks are not negligible, and serious complications, although rare, are possible [3]. Thus, for many patients, a conservative treatment without invasive procedures is an appealing option. Watchful waiting, however, does not always result in stone clearance and may be associated with recurrent renal colic [4]. Once a conservative approach proves to be unsuccessful, interventional treatment becomes necessary. After a period of conservative treatment, however, intervention is often inefficient or has a higher risk for complications due to stone impaction and the associated inflammatory reaction of the ureter [5,6].

The therapeutic potential of α -blockers for ureteral stone disease has been investigated, prompted by the detection of α -receptors in ureteral smooth muscle cells [7]. Successful medical expulsive therapy (MET) for patients with distal ureteral stones using the nonselective α -blocker doxazosine was first reported in the late 1990 s [8]. Since then, numerous clinical trials have been performed to investigate the efficacy of MET using the 1A/D selective α -blocker tamsulosin alone and in combination with other drugs like corticosteroids and antibiotics [9–18]. Most of these studies were randomised and revealed that tamsulosin treatment significantly improves the expulsion rate of medium-sized (3–10 mm) distal ureteral stones. Thus, tamsulosin represents a noninvasive and cost-effective alternative to interventional approaches [19]. None of the studies, however, was performed in a double-blind, placebo-controlled fashion.

The objective of this trial was to evaluate the efficacy of MET with tamsulosin for ureteral stones ≤ 7 mm in a randomised, double-blind, placebo-controlled setting.

2. Materials and methods

2.1. Participants

This randomised, double-blind, placebo-controlled trial was performed in the Department of Urology at the University Hospital of Zürich with subjects in an outpatient setting. All male and female patients ≥ 18 yr presenting with acute renal colic were evaluated for study participation. Patients with a single ureteral stone ≤ 7 mm below the common iliac vessels, as assessed on non-contrast-enhanced abdominal computed tomography (CT), were eligible for the study. Exclusion criteria were the presence of multiple ureteral stones, renal insufficiency (estimated glomerular filtration rate < 60 ml/min per 1.73 m²), urinary tract infection, a solitary kidney, or pregnancy. Patients with a history of ureteral surgery or previous endoscopic procedures; hypersensitivity to tamsulosin; or current α -blocker, calcium-antagonist, or corticosteroid medication were also excluded. Patient enrolment was performed by the attending urologist.

2.2. Study design

Enrolled patients underwent randomisation in a 1:1 fashion in blocks of 10 to receive either a daily single dose of tamsulosin (0.4 mg) or

placebo. The sequence of randomisation was computer generated and was performed by the university hospital pharmacy using DatInf Randlist software v.1.0 (DatInf GmbH, Tübingen, Germany). Randomisation data were kept strictly confidential in sealed envelopes, accessible only to the primary and senior investigator. Tamsulosin and placebo were provided by the university hospital pharmacy as gelatine capsules of identical appearance and taste and were presented in identical bottles. The patient, the attending urologist, and the investigators were not aware of study arm assignments until the final assessment of outcome.

Sample-size calculation was performed based on previous reports of spontaneous stone expulsion and assumed a clinically relevant difference in expulsion rate of 25% [13,16,17,20]. The stone expulsion rate was estimated to be 90% and 65% for patients with and without tamsulosin medication, respectively. A two-group χ^2 test with a two-sided significance level of 0.05 will have 80% power to detect the difference between a group 1 proportion of 0.65 and a group 2 proportion of 0.90 when the sample size in each group is 43. Fifty patients per group were finally randomised, which allowed for a maximum drop-out rate of 14%.

The study protocol was approved by the local ethics committee, and the study was performed in accordance with the Declaration of Helsinki. All enrolled patients provided written informed consent.

2.3. Intervention

Patients were requested to take the study medication once at the same time each day and to strain their urine. Furthermore, they kept a diary to record the required amount of analgesic, the score of every painful episode on a 10-cm visual analogue scale, the date and time of stone passage, and the presence and type of side-effects thought to be related to the medication. The study medication was discontinued after spontaneous stone expulsion, intervention, or at the end of the study (ie, after day 21). After initial analgesia for acute pain management, no regular analgesic medication was maintained. Oral diclophenac (up to 3×50 mg) as first-line and oral metamizole (up to 4×1 g) as second-line on-demand analgesics were prescribed.

Follow-up was performed weekly with urinalysis, serum creatinine measurement, abdominal ultrasonography, and, in radiopaque stones, plain abdominal x-ray. Low-dose abdominal CT was performed without knowledge of the treatment allocation to assess the stone status at the end of the study. For patients with a stone-free ureter on final abdominal CT but unnoticed stone expulsion, the date of last positive stone status was recorded. Absence of stone expulsion after day 21 was considered failed therapy. In these cases, continued watchful waiting, ureterorenoscopy (URS), or extracorporeal shock-wave lithotripsy (ESWL) was performed. Discontinuation of study medication and intervention before the end of the study due to uncontrollable pain, adverse events, urinary tract infections, acute renal failure, or the patient's desire for stone removal were also considered failed therapy. These patients were included in the final analysis on an intention-to-treat basis. Patients who experienced stone expulsion before first medication, who withdrew their consent, or who were lost to follow-up were excluded from the analysis.

2.4. End points

The primary end point was the proportion of patients experiencing stone expulsion until day 21, as confirmed by low-dose abdominal CT. Secondary end points were time to stone passage, the required total amount of analgesic, the reported maximum daily pain score until stone expulsion, and the intervention rate, as well as the safety of the therapy. Additionally, factors influencing these end points were assessed.

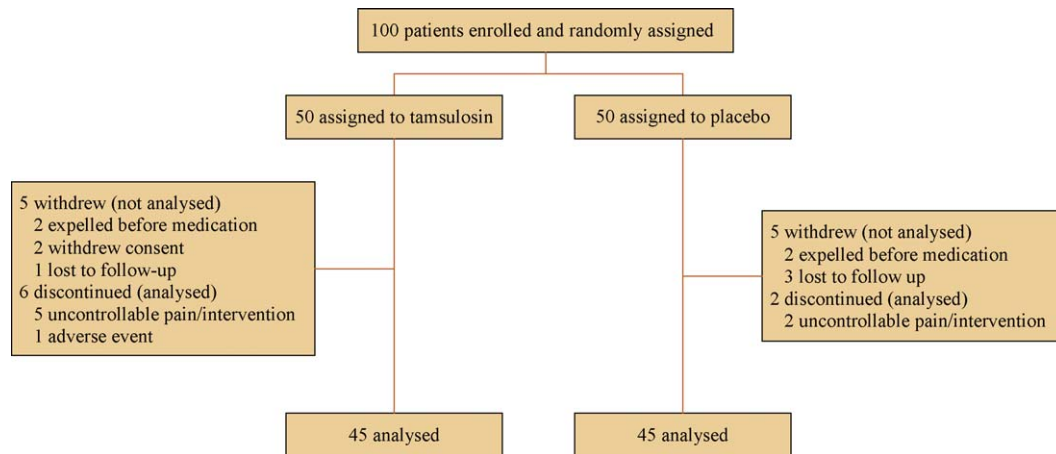


Fig. 1 – Trial profile.

2.5. Statistical analysis

Statistical analysis was performed using R statistical software (R Foundation for Statistical Computing, Vienna, Austria). The Fisher exact test was used to compare nominal variables, and the Mann-Whitney U-test was used to compare continuous variables between the two treatment arms. Kaplan-Meier estimates were computed for time to stone passage and were compared between the two treatment arms using the log-rank test. The patient-defined time of stone expulsion was considered the event for time to stone passage. Patients with unnoticed stone expulsion were censored at the date of last positive stone status, and those who discontinued the therapy were censored at the date of last medication intake. Patients without stone expulsion were censored at day 21. A multiple Cox proportional hazards regression model was generated to jointly assess the predictive value of stone size and location and the prognostic value of therapy. The significance level in the test for the primary end point was set to 0.05. In the exploratory analysis of the secondary end points, all p values <0.05 were considered significant and no correction for multiple testing was performed.

3. Results

From September 2006 to September 2008, a total of 100 patients was randomly assigned to the two treatment arms. Overall, 10 patients were excluded from the final analysis (Fig. 1). In eight cases, treatment was discontinued due to adverse events or uncontrollable pain with subsequent intervention (URS or ESWL).

No statistically significant differences in age, gender, stone size, and stone location were found between the two treatment arms (Table 1). Median stone size in the entire population was 3.9 mm (interquartile range [IQR]: 3.5–4.8 mm).

The spontaneous stone expulsion rate within 21 d was not significantly different between the tamsulosin arm (86.7%) and the placebo arm (88.9%; $p = 1.0$). Univariate analyses revealed that neither the patient's gender and age nor the left/right location of the stone were predictive factors for stone expulsion. The stone location in the ureter, however, had a predictive impact on the stone expulsion rate. The spontaneous expulsion of stones at the ureter-

ovesical junction was significantly higher than of stones in the distal part of the ureter ($p = 0.006$). All 11 stones which did not pass spontaneously or required treatment before the end of the study were located in the distal part of the ureter. Furthermore, stone size was significantly smaller in the group of patients with spontaneous stone expulsion ($p = 0.039$). The stone expulsion rate was significantly higher for patients with stones ≤ 5 mm compared with patients with stones > 5 mm ($p = 0.048$). The expulsion rate, however, was not significantly different between the treatment arms for patients with stones ≤ 5 mm ($p = 1.00$) or for those with larger stones ($p = 1.00$).

The Kaplan-Meier estimates for time to stone passage are shown in Fig. 2. A total of 50 patients (56%) were able to define the time of stone expulsion by collecting the stone after urine filtration. Twenty-nine patients (32%) had unnoticed stone expulsion, eight patients (9%) discontinued

Table 1 – Baseline characteristics of 45 patients treated with tamsulosin and 45 patients treated with placebo*

	Tamsulosin	Placebo	p value
Age, yr	36 (30–44)	41 (33–54)	0.07
Sex			0.57
Male	39 (86.7%)	36 (80%)	
Female	6 (13.3%)	9 (20%)	
Stone size, mm	4.1 (3.5–4.9)	3.8 (3.4–4.3)	0.3
Size distribution			0.43
< 5 mm	34 (75.6%)	38 (84.4%)	
≥ 5 mm	11 (24.4%)	7 (15.6%)	
Side			0.034**
Left	18 (40%)	29 (64.4%)	
Right	27 (60%)	16 (35.6%)	
Stone location			0.66
Distal	27 (60%)	30 (66.7%)	
Ureterovesical junction	18 (40%)	15 (33.3%)	

* Data are presented as median (interquartile range) or number (proportion within treatment arm).

** Indicates a significant difference between the treatment arms.

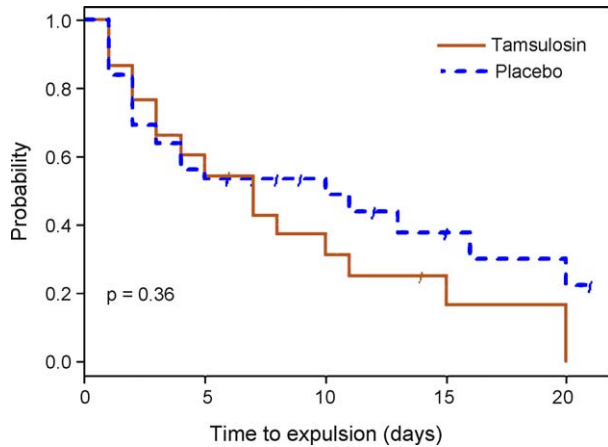


Fig. 2 – Kaplan Meier estimates for time to stone passage for the two treatment arms.

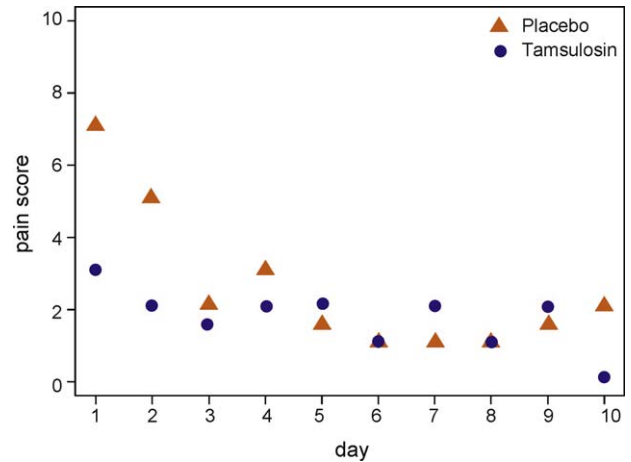


Fig. 3 – Median maximum daily pain-score in the two treatment arms. The pain intensity was slightly higher in the placebo arm until day 4. After the fourth day of treatment, the differences were marginal.

the therapy, and three patients (3%) were not stone free at the end of the study. Median time to stone passage was 7 d (95% confidence interval [CI]: 4–13) for patients overall, 7 d (95% CI: 3–10) in the tamsulosin arm, and 10 d (95% CI: 3–20) in the placebo arm. The difference between the treatment arms was nonsignificant (log-rank test, $p = 0.36$). A multiple Cox regression model to analyse predictive factors for time to stone passage revealed only stone location, and not medical therapy or stone size, as a predictive factor (Table 2). The hazard of expulsion at any time was 3-fold higher for stones located at the ureterovesical junction than in the distal part of the ureter.

The required total amount of analgesic until stone expulsion was significantly different between the two treatment arms ($p = 0.012$). Patients in the tamsulosin arm consumed a median number of three analgesics (IQR: 1–9.8) until stone expulsion, and patients in the placebo arm consumed a median number of seven analgesics (IQR: 4–16) until stone expulsion. Fig. 3 shows the course of the medians of the most painful episodes per day. Only the first 10 d were analysed due to the low number of patients who were at risk after that day.

No severe complications were recorded. Hospital readmissions with consecutive intervention and discontinuation of the medication were due to uncontrollable pain (seven patients) or side-effects (one patient). Six patients (13.3%) in the tamsulosin arm (URS: 4; ESWL: 2) and two patients (4.4%) in the placebo arm (URS: 1; ESWL: 1) required intervention before the end of the study. This difference was statistically nonsignificant

($p = 0.27$). None of the patients treated with tamsulosin and three patients (6.7%) treated with placebo failed to expel their stone until day 21. The overall intervention rate was 13.3% in the tamsulosin arm and 8.9% in the placebo arm ($p = 0.74$).

Four patients (8.9%) in the tamsulosin arm reported minor side-effects. One patient discontinued therapy due to diarrhoea and subsequently was treated by ESWL. One patient with a mild cutaneous reaction and two patients with retrograde ejaculation continued therapy. In the placebo arm, one patient (2.2%) reported dizziness and inappetence but continued therapy.

4. Discussion

This first randomised, double-blind, and placebo-controlled trial investigating the efficacy of MET revealed that tamsulosin treatment did not improve the spontaneous expulsion rate of single distal ureteral stones ≤ 7 mm. The proportion of patients experiencing stone expulsion within 21 d was slightly but not significantly lower in the tamsulosin arm than in the placebo arm. This finding contrasts with the results of previous clinical trials, which have reported significant improvements in the stone expulsion rate with use of tamsulosin [10–12,15]. Two possible reasons that should be highlighted in this context are the actual stone size and the differences in study design between this trial and the previous trials.

Stone size has been identified as an important predictive factor for ureteral stone expulsion [20–22]. The probability for distal ureteral stones to pass spontaneously is as high as 71–98% for stones ≤ 5 mm and only 25–51% for stones > 5 mm [20,23,24]. Approximately 80% of the stones in the present trial were ≤ 5 mm. The actual stone size may be a reason for the high stone expulsion rate in the placebo arm. It remains unclear, however, if the lack of improvement of the stone expulsion rate in the tamsulosin arm is also

Table 2 – Multiple Cox regression analysis for predictive factors for the secondary end point of time to stone passage

Variables	<i>p</i> value	Hazard ratio	95% confidence interval
Therapy	0.97	0.99	0.55–1.79
Stone location	0.0005	3.17	1.66–6.05
Stone size	0.42	0.89	0.66–1.19

attributable to the present stone size. The majority of stones in the trials reporting a beneficial effect of tamsulosin on the stone expulsion rate were >5 mm [10,12,15,18]. It is reasonable to assume that the efficacy of MET will be relatively greater for larger stones, as smaller stones are more likely to pass without any treatment. Currently, it is not known whether a potential α -blocker effect on stone expulsion depends on ureteral stone size. In the present trial, patients with stones >5 mm had less chance of passing the stone spontaneously but tamsulosin treatment did not improve the expulsion rate of these stones. Admittedly, the study was not powered for this subgroup analysis; therefore, the value of this analysis is limited.

Three meta-analyses have confirmed a positive effect of α -blocker therapy on the stone expulsion rate [25–27]; however, important potential confounders have also been pointed out which may affect the validity of the results and may lead to an overestimation of the identified treatment effect [25–28]. Although most of the published studies were randomised, reporting of randomisation methods was often unclear or even absent, as were placebo treatment and blinding to treatment generally. Furthermore, determination of the stone status by abdominal CT at the end of the study was not performed in most of the previous studies. The differences in study design between the present trial and previous trials may be an additional factor contributing to the different outcomes. Interestingly, in accordance with the results of the present study, the only other double-blind, placebo-controlled study for α -blocker therapy of distal ureteral stones also revealed no improvement in the stone expulsion rate [29]. In that study, the mean stone size was <5 mm, but the non-subtype-selective α -1-receptor blocker alfuzosin was investigated.

The decision for a conservative medical treatment or an active interventional treatment is not based only on the overall probability of stone expulsion. For many patients, factors like time to convalescence or reexposure to dreaded colics during conservative treatment have a considerable impact on the decision to opt for an interventional treatment.

A faster and less painful stone expulsion, regardless of stone size, has constantly been reported with MET [10,13,16]. In the present trial, median time to stone passage was 3 d shorter for patients who were treated with tamsulosin than for patients who were treated with placebo. Although this difference may be clinically meaningful, it was statistically nonsignificant.

The secondary end point of total intake of analgesics, however, was significantly different between the treatment arms. Patients in the tamsulosin arm required fewer analgesics until stone expulsion than patients in the placebo arm. This difference may be attributable to the accelerated stone expulsion with a consecutive shorter time at risk for painful events. Additionally, a true analgesic effect of tamsulosin has been reported [30]. The lower maximum pain scores in the tamsulosin arm during the first days support the existence of such an effect. Thus, pain modulation seems to be an important feature of MET with tamsulosin in patients with stones ≤ 7 mm.

No serious complications were recorded in either treatment arm. Adverse events of tamsulosin treatment were mild and led to therapy discontinuation in only one patient.

Some limitations of the present trial deserve mention. The smaller stone size in the present trial compared with previous trials makes it difficult to directly compare the results of the different trials. Furthermore, for 32% of the patients, the exact time of stone passage was not available. Thus, these patients needed to be censored at the last known date of stone presence. The secondary end point of time to stone passage is based on Kaplan-Meier estimation.

5. Conclusions

Patients with single distal ureteral stones ≤ 7 mm do not benefit from MET with tamsulosin in terms of an improved expulsion rate. Nevertheless, the generally well-tolerated treatment may be beneficial for these patients due to an analgesic effect and, thus, a reduced need of analgesics until stone expulsion.

Author contributions: Rätö T. Strebel had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Strebel, Sauerermann, Hermanns, Frauenfelder.

Acquisition of data: Sauerermann, Hermanns, Frauenfelder.

Analysis and interpretation of data: Hermanns, Sauerermann, Strebel, Rufibach.

Drafting of the manuscript: Hermanns, Strebel.

Critical revision of the manuscript for important intellectual content: Sulser, Frauenfelder, Strebel.

Statistical analysis: Rufibach.

Obtaining funding: None.

Administrative, technical, or material support: None.

Supervision: Strebel, Sulser.

Other (specify): None.

Financial disclosures: I certify that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

Funding/Support and role of the sponsor: None.

Acknowledgment statement: The authors acknowledge Ms. Alexandra Veloudios for the excellent organisation of the patient care during the trial as well as Ms. Damina Balmer and Dr. Gary A. Brook for their assistance in the preparation of the manuscript.

References

- [1] Strohmaier WL, Schubert G, Rosenkranz T, Weigl A. Comparison of extracorporeal shock wave lithotripsy and ureteroscopy in the treatment of ureteral calculi: a prospective study. *Eur Urol* 1999;36:376–9.
- [2] Osorio L, Lima E, Soares J, et al. Emergency ureteroscopic management of ureteral stones: why not? *Urology* 2007;69:27–31.
- [3] Preminger GM, Tiselius H-G, Assimos DG, et al. 2007 guideline for the management of ureteral calculi. *Eur Urol* 2007;52:1610–31.

- [4] Shokeir AA. Renal colic: pathophysiology, diagnosis and treatment. *Eur Urol* 2001;39:241–9.
- [5] Farsi HM, Mosli HA, Alzimaity M, Bahnassay AA, Ibrahim MA. In situ extracorporeal shock wave lithotripsy for primary ureteric calculi. *Urology* 1994;43:776–81.
- [6] Seitz C, Tanovic E, Kikic Z, Fajkovic H. Impact of stone size, location, composition, impaction, and hydronephrosis on the efficacy of holmium:YAG-laser ureterolithotripsy. *Eur Urol* 2007;52:1751–9.
- [7] Malin Jr JM, Deane RF, Boyarsky S. Characterisation of adrenergic receptors in human ureter. *Br J Urol* 1970;42:171–4.
- [8] Ukhal M, Malomuzh O, Strashny V. Administration of doxazosine for speedy elimination of stones from lower part of ureter. *Eur Urol* 1999;35(Suppl 2):4.
- [9] Cervenakov I, Fillo J, Mardiak J, et al. Speedy elimination of ureterolithiasis in lower part of ureters with the alpha 1-blocker-tamsulosin. *Int Urol Nephrol* 2002;34:25–9.
- [10] Yilmaz E, Batislam E, Basar MM, et al. The comparison and efficacy of 3 different alpha1-adrenergic blockers for distal ureteral stones. *J Urol* 2005;173:2010–2.
- [11] Wang CJ, Huang SW, Chang CH. Efficacy of an alpha1 blocker in expulsive therapy of lower ureteral stones. *J Endourol* 2008;22:41–6.
- [12] Porpiglia F, Vaccino D, Billia M, et al. Corticosteroids and tamsulosin in the medical expulsive therapy for symptomatic distal ureter stones: single drug or association? *Eur Urol* 2006;50:339–44.
- [13] Porpiglia F, Ghignone G, Fiori C, Fontana D, Scarpa RM. Nifedipine versus tamsulosin for the management of lower ureteral stones. *J Urol* 2004;172:568–71.
- [14] Erturhan S, Erbagci A, Yagci F, et al. Comparative evaluation of efficacy of use of tamsulosin and/or tolterodine for medical treatment of distal ureteral stones. *Urology* 2007;69:633–6.
- [15] Dellabella M, Milanese G, Muzzonigro G. Randomized trial of the efficacy of tamsulosin, nifedipine and phloroglucinol in medical expulsive therapy for distal ureteral calculi. *J Urol* 2005;174:167–72.
- [16] Dellabella M, Milanese G, Muzzonigro G. Efficacy of tamsulosin in the medical management of juxtavesical ureteral stones. *J Urol* 2003;170:2202–5.
- [17] De Sio M, Autorino R, Di Lorenzo G, et al. Medical expulsive treatment of distal-ureteral stones using tamsulosin: a single-center experience. *J Endourol* 2006;20:12–6.
- [18] Autorino R, De Sio M, Damiano R, et al. The use of tamsulosin in the medical treatment of ureteral calculi: where do we stand? *Urol Res* 2005;33:460–4.
- [19] Bensalah K, Pearle M, Lotan Y. Cost-effectiveness of medical expulsive therapy using alpha-blockers for the treatment of distal ureteral stones. *Eur Urol* 2008;53:411–9.
- [20] Kinder RB, Osborn DE, Flynn JT, Smart JG. Ureteroscopy and ureteric calculi: how useful? *Br J Urol* 1987;60:506–8.
- [21] Miller OF, Kane CJ. Time to stone passage for observed ureteral calculi: a guide for patient education. *J Urol* 1999;162:688–90.
- [22] Hubner WA, Irby P, Stoller ML. Natural history and current concepts for the treatment of small ureteral calculi. *Eur Urol* 1993;24:172–6.
- [23] Ueno A, Kawamura T, Ogawa A, Takayasu H. Relation of spontaneous passage of ureteral calculi to size. *Urology* 1977;10:544–6.
- [24] Segura JW, Preminger GM, Assimos DG, et al. Ureteral Stones Clinical Guidelines Panel summary report on the management of ureteral calculi. The American Urological Association. *J Urol* 1997;158:1915–21.
- [25] Singh A, Alter HJ, Littlepage A. A systematic review of medical therapy to facilitate passage of ureteral calculi. *Ann Emerg Med* 2007;50:552–63.
- [26] Parsons JK, Hergan LA, Sakamoto K, Lakin C. Efficacy of alpha-blockers for the treatment of ureteral stones. *J Urol* 2007;177:983–7.
- [27] Hollingsworth JM, Rogers MA, Kaufman SR, et al. Medical therapy to facilitate urinary stone passage: a meta-analysis. *Lancet* 2006;368:1171–9.
- [28] Michel MC, de la Rosette JJMCH. α -blocker treatment of urolithiasis. *Eur Urol* 2006;50:213–4.
- [29] Pedro RN, Hinck B, Hendlin K, et al. Alfuzosin stone expulsion therapy for distal ureteral calculi: a double-blind, placebo controlled study. *J Urol* 2008;179:2244–7.
- [30] Kubacz GJ, Catchpole BN. The role of adrenergic blockade in the treatment of ureteral colic. *J Urol* 1972;107:949–51.