BRIEF ORIGINAL

Effectiveness of medical expulsive therapy with the α-adrenergic blocker tamsulosin for distal ureterolithiasis in adults attended in an emergency department in Chile

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Objective. To assess the effectiveness of medical expulsive therapy with tamsulosin.

Methods. Randomized double-blind controlled trial in an emergency department. We enrolled adults with uncomplicated distal ureterolithiasis and no other complaint. Patients were randomized to take either tamsulosin (0.4 mg/d) plus a nonsteroidal anti-inflammatory drug (NSAID) or placebo plus the NSAID for 21 days.

Results. The stone expulsion rate did not differ statistically between the 2 groups (*P*=.29). Time until expulsion was also similar (*P*=.91).

Conclusion. Medical expulsive therapy with tamsulosin does not improve the rate of distal ureteral stone expulsion.

Keywords: Ureterolithiasis. Tamsulosin. Calculi, urinary tract. α-adrenergic receptor blockers.

Efectividad del tratamiento médico expulsivo con el bloqueador alfa tamsulosina en pacientes adultos que consultan por cálculo ureteral distal en un servicio de urgencias chileno

Objetivo. Evaluar la efectividad del tratamiento médico expulsivo con tamsulosina.

Método. Ensayo clínico prospectivo aleatorizado doble ciego realizado en un servicio de urgencias. Se incluyen adultos con ureterolitiasis distal única no complicada, que fueron asignados aleatoriamente a tamsulosina 0,4 mg/día más antiinflamatorio no esteroideo (AINE) (grupo A), o con placebo más AINE (grupo B), durante 21 días.

Resultados. No se observaron diferencias estadísticamente significativas en la tasa de expulsión de litiasis entre ambos grupos (p = 0,29) ni en el tiempo de expulsión de esta (p = 0,91).

Conclusiones. La terapia expulsiva con tamsulosina no se asocia a una mayor tasa de expulsión de litiasis ureteral.

Palabras clave: Ureterolitiasis. Tamsulosina. Cálculo urinario. Antagonista alfa-adrenérgico.

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Introduction

Urolithiasis has a prevalence of 10-12% in the United States[1] and 5% in South American countries[2]. An important increase in urolithiasis has also been reported in European countries, such as Germany[3]. An episode of renoureteral colic (RUC) is painful and often needs to be treated in an emergency department (ED). Consultation rates for RUC in the United States increased from 178/100,000 in 1992 to 340/100,000 episodes in 2009[4].

The first course of treatment for distal RUC in the absence of complications is medical expulsive therapy (MET). This consists of analgesia plus tamsulosin during an observation period[5]. However, in recent years several recently published studies have not confirmed the effectiveness of MET with tamsulosin[6-9]. The objective of this study is to determine the effectiveness of tamsulosin in the management of patients with single distal ureterolithiasis regarding the expulsion of lithiasis.

Method

A prospective double-blind randomized clinical trial was conducted in the ED of our hospital (from December 2016 to February 2018). After approval by the ethics committee, a consecutive sample of adult patients (18 to 65 years) with a diagnosis of single distal ureterolithiasis objectified by computed tomography (CT) 3 to 8 mm in diameter was offered to participate and selected. Patients who did not have CT scans in the ED were not included in the study. Those who agreed to participate were randomly assigned to one of these two groups: 1) group A, who were treated for 21 days with tamsulosin 0.4 mg/day plus paracetamol 1 g orally/8 hours and ketorolac 10 mg orally/8 hours for three days, and subsequently, if necessary, as a rescue; 2) group B, who received a placebo instead of tamsulosin together with the same analgesic schedule as group A (paracetamol 1 g orally/8 hours and ketorolac 10 mg orally/8 hours) for three days and subsequently, if necessary, as a rescue.

Patients with refractory pain or complicated RUC were excluded. In order to maintain the blinding of patients and clinicians who attended them, the medications were rewrapped and identified with the letter corresponding to the study group. These were not disclosed to the study groups, nor was the treatment assignment sequence, which was done by computer.

Sociodemographic variables, comorbidities and characteristics of lithiasis, as well as outcome variables were collected. Weekly controls were conducted for 21 days. Drug tolerance, presence of adverse effects, additional analgesia, fever and lithiasis expulsion were recorded. The second control was by telephone, and the third week control was in person, and the same parameters were evaluated.

The sample size was calculated for 25% difference in effect (power of 80% and type 1 error of 5%), resulting in 43 patients per branch. Statistical analysis was performed using the Student t test or the sum of Wilcoxon ranges depending on whether the distribution was normal or not in continuous variables. The chi-square test was used for categorical variables.

Results

During the study period, 199 patients attended the ED for single distal RUC. Out of these, 153 met the inclusion criteria and 86 agreed to participate in the study: 40 patients assigned to group A and 37 to group B completed the follow-up period (Figure 1). Both study groups were similar in their general characteristics. There were also no differences in the characteristics of lithiasis or in the time of pre-consultation evaluation (Table 1).

The treatment was effective in 32 patients in group A and 36 in group B (p = 0.03). When applying the intention to treat, assuming the failure of all those who did not complete the study, no difference was observed between the two groups (p = 0.29). There was also no difference in the time of expulsion of lithiasis (16.9 days for group A and 16.5 days for group B, p = 0.91).

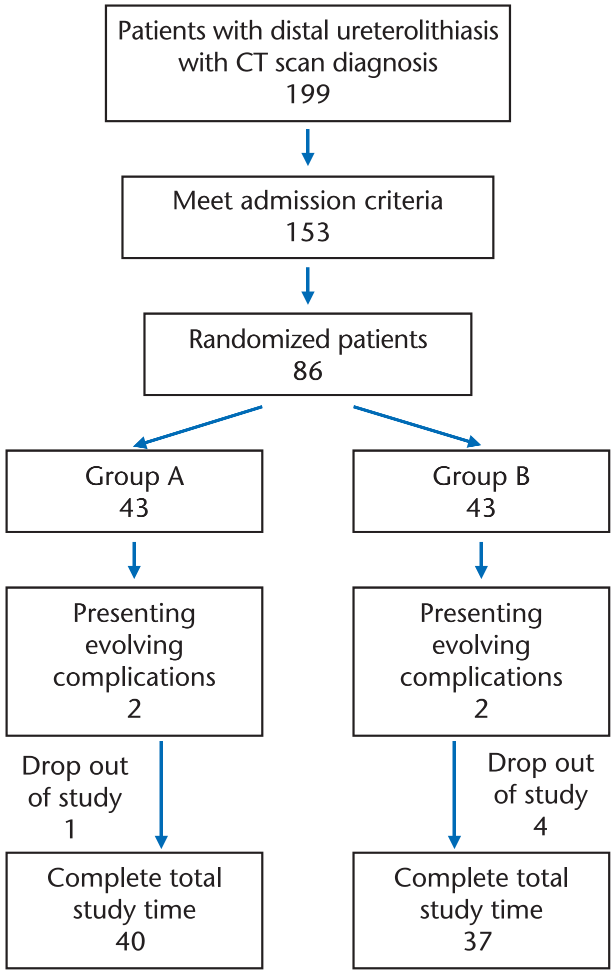

Figure 1. Study patient flowchart. CT: computerized tomography.

Nine patients in group A and four patients in group B had adverse drug reactions (p = 0.17). Twenty-five patients in group A and 18 patients in group B required extra rescue analgesia (p = 0.22). Table 2 shows the clinical and lithiasis expulsion results obtained in the study.

Table 1. General characteristics of the population studied

	Group A	Group B	p
Age in years [mean (SD)]	44.6 (11.0)	42.3 (13.6)	0.39
Male	30 (69.8)	28 (65.1)	0.65
Body Mass Index [mean (SD)]	27.65 (4.09)	27.72 (4.35)	0.94
Diabetes mellitus	0 (0%)	1 (2.33)	0.31
High blood pressure	8 (18.6)	7 (16.28)	0.78
History of urolithiasis	10 (23.3)	13 (30.2)	0.47
History of expulsion lithiasis	10 (23.3)	9 (21)	0.79
Time of evolution in hours [mean (SD)]	12.0 (17.8)	12.7 (17.1)	0.85
Lithium size mm [mean (SD)]	4.3 (1.2)	3.9 (1.0)	0.10
Location of lithiasis			0.52
Right	20 (46.5)	23 (53.5)	
Left	23 (53.5)	20 (46.5)	
Presence of hydronephrosis	42 (97.7)	41 (95.3)	0.56

SD: standard deviation.

Table 2. Summary of clinical outcomes and expulsion of lithiasis in study patients

	Group A (tamsulosin) n (%)	Group B (placebo) n (%)	p
Need for extra analgesia	25 (62.5)	18 (48.6)	0.22
Adverse drug effect	9 (22.5)	4 (10.8)	0.17
Orthotics	7	4	
Retrograde ejaculation	4	0	
Allergy to painkillers	0	1	
Expulsion of lithiasis in the total period	32 (80)	36 (97.3)	0.03
Expulsion with intent to treat	32 (74.4)	36 (83.7)	0.29

Discussion

The effectiveness of MET with tamsulosin in the management of ureterolithiasis has been in discussion since the study by Hermanns et al.[6], which could not demonstrate a higher expulsion rate in patients exposed to the drug. Despite this and other studies, the American and European clinical guidelines still recommend its use, based on studies that do support its efficacy[10,11].

In our sample, both groups were comparable in terms of demographics and characteristics of lithiasis, an important fact since there is evidence showing a relationship between characteristics of lithiasis and expulsion rates[12]. A total of 76% of the patients in group A expelled their lithiasis and 92.3% in group B. When applying intention-to-treat, 74.4 and 83.7% of patients expelled their lithiasis in groups A and B, respectively (p = 0.29). The percentage of expulsion in our series is similar to that reported by Portis et al.[12]. and higher than that published by Meltzer et al. and Sahin et al., who confirm figures close to 50%[13,14]. When analyzing our data, as in recent published series, MET with tamsulosin was not associated with a higher rate of expulsion of lithiasis, and therefore lacks relevant clinical effect[9,13,14]. These results may differ from previous publications due to some methodological aspects, such as lack of placebo control or masking. When compared with the study by Ye et al.[15], it should be noted that these authors found no difference in the expulsion of lithiasis smaller than 5 mm, but did find differences in larger lithiasis. Therefore, due to the size of the lithiasis included in our study, we believe that these may differ from other results.

There are some limitations to our study that we must consider. This is a unicenter study with a small number of patients, so it has no external validity. This number is based on the calculation of the sample size, which considered a clinically significant difference of 25% greater effectiveness of the drug against the placebo, thus justifying potential adverse effects.

Thus, considering our results together with those of other recent studies, and lacking a significant clinical effect, MET with tamsulosin would not be justified due to costs and potential adverse effects (22.5% in our series). Therefore, in conclusion, we estimate that MET with tamsulosin is not associated with a higher rate of expulsion of distal ureteral lithiasis of 3 to 8 mm within three weeks. No increased rate of lithiasis expulsion or associated reduced analgesia requirement was demonstrated.

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