

Is tamsulosin effective for the passage of symptomatic ureteral stones

A systematic review and meta-analysis

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Abstract

Background: Some trials have stated that there is no benefit to tamsulosin administration for clearing ureteral stones, which is contrary to previous studies. To confirm the efficacy of tamsulosin for treating symptomatic ureteral stones, we performed this review.

Methods: We searched the PubMed, Embase, and Cochrane Library databases to identify all studied variables, including tamsulosin, urinary stones, expulsion, and side effects. In addition, for all patients and different stone sizes, the treatment efficacy, expulsion rate, and expulsion time were also recorded for this treatment.

Results: Forty-nine studies involving 6436 patients met the inclusion criteria. The data synthesized from these studies indicated that tamsulosin improved the renal stone clearance rate (80.5% vs 70.5%; mean difference (MD), 1.16; 95% confidence interval (CI), 1.13–1.19; $P < .00001$) and reduced the expulsion time (MD, –3.61; 95% CI, –3.77 to –3.46; $P \leq .00001$). Regarding complications, no significant difference was found between the 2 groups in terms of the total side effects (MD, 1.15; 95% CI, 0.97–1.35; $P = .10$) or divided complications, including retrograde ejaculation ($P = .01$), hypotension ($P = .52$), dizziness ($P = .07$), diarrhea ($P = .58$), vomiting ($P = .88$), headache ($P = .84$), nausea ($P = .91$), and fatigue ($P = .10$).

Conclusions: Tamsulosin should be strongly recommended for patients with ureteral stones to increase treatment efficacy. The side effects were not significantly different between the tamsulosin and control treatments.

Abbreviations: CI = confidence interval, CT = computed tomography, MD = mean difference, RCT = randomized controlled trial, RR = relative risk, USD = urinary stone disease.

Keywords: expulsive, side effects, tamsulosin, urinary stone

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YS, G-LL and XW contributed equally to this work and should share the co-first author.

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1. Introduction

The prevalence of urolithiasis, or urinary stone disease (USD), is increasing among adults and children worldwide. Because the most common symptoms of USD include severe flank and abdominal pain, nausea, vomiting and hematuria, patients often present to the emergency department for treatment.^[1] Many clinical studies have been performed.^[2–50] In general, trials have supported the use of tamsulosin to achieve higher stone expulsion rates and lower analgesic requirements. The presumed mechanism of action of α -blockers is inhibition of smooth muscle contraction in the ureter, facilitating passage of the stone into the bladder.^[4] Nevertheless, these guidelines have been called into question by several recently published high-quality randomized controlled trials (RCTs), and the effectiveness of α -blockers has been questioned for the management of ureteral colic.^[4,7–11] For instance, a phase III trial that included multiple centers reported no benefit of tamsulosin for patients with distal ureteral calculi in terms of spontaneous stone passage, time to stone expulsion, or analgesic requirements.^[7] In addition, the results of a 28-day course of tamsulosin showed that this treatment did not increase the overall stone passage rate or improve a wide range of secondary outcomes in patients who presented to the emergency department with symptomatic ureteral stones less than 9 mm in diameter.^[4] The contradictory results provided by several RCTs versus the findings of other studies encouraged us to conduct this meta-analysis to address this issue.

Table 1**Patient's characteristics at baseline.**

	Year	Groups	Mean age	Stone size, mm	Stone <6 mm, %	Stone location left/right, %	Stone location (%)
							Upper/Middle/Renal pelvis
Ye	2018	Tamsulosin	40.1 ± 11.6	5.8 ± 1.9	34.0	44/56	17.2/12.0/1.5
		Placebo	40.7 ± 12.3	5.7 ± 1.8	34.0	46/54	17.6/7.8/4.1
Balci	2018	Tamsulosin	29.5 ± 12.1	7.1 ± 1.5	—	—	—
		Placebo	34.5 ± 10.2	6.4 ± 1.1	—	—	—
Meltzer	2018	Tamsulosin	41.8 ± 13.6	3.8 ± 1.4	95.5	—	—
		Placebo	39.3 ± 12.9	3.7 ± 1.4	95.5	—	—
Nuraj	2017	Tamsulosin	35.5 ± 11.0	6.5 ± 1.6	30.8	48.1/51.9	—
		Placebo	35.4 ± 10.8	6.6 ± 1.5	32.7	44.2/55.8	—
Arda	2017	Tamsulosin	44.61 ± 12.03	5.93 ± 1.07	—	—	—
		Placebo	42.2 ± 11.4	5.96 ± 1.18	—	—	—
Ahmed	2016	Tamsulosin	37.84 ± 11.20	—	—	56.9/43.1	—
		Placebo	38.63 ± 11.30	—	—	46.0/54.0	—
Shahat	2016	Tamsulosin	3.5	12	—	—	—
		Placebo	4	12	—	—	—
Furyk	2016	Tamsulosin	45.4	4.0	—	53.5/46.5	—
		Placebo	46	3.7	—	46.2/53.8	—
Berger	2015	Tamsulosin	40.62	3.98	—	—	—
		Placebo	44.52	3.76	—	—	—
Aldaqaqadossi	2015	Tamsulosin	7.7 ± 3.02	—	29.0	54.8/45.2	—
		Conservative	7.25 ± 2.7	—	21.9	43.7/56.3	—
Pickard	2015	Tamsulosin	43.1 ± 11.5	—	75.0	—	25/10/65
		Placebo	42.8 ± 12.3	—	75.0	—	23/11/66
Lee	2014	Tamsulosin	43.6 ± 12.4	3.41 ± 1.04	—	55.6/44.4	—
		Placebo	47.9 ± 11.4	3.65 ± 1.15	—	40.7/59.3	—
Janane	2014	Tamsulosin	41.2 ± 12.4	9.2 ± 2.8	—	—	16.1/12.4/42.3
		Placebo	43.4 ± 12.2	9.4 ± 3.0	—	—	15.3/11.2/44.1
Alizadeh	2014	Tamsulosin	—	0.93 ± 4.6	—	—	—
		Placebo	—	0.83 ± 4.81	—	—	—
Ketabchi	2014	Tamsulosin	24 ± 6.5	6.6 ± 2.3	—	48.08/51.92	—
		Placebo	27 ± 8.8	6.2 ± 3.2	—	44.0/56.0	—
Qadri	2014	Tamsulosin	39 ± 14.7	1.12 ± 0.31	—	48.3/51.7	3.3/8.3/60
		Placebo	41 ± 13.1	1.05 ± 0.26	—	51.7/48.3	1.7/5.0/71.7
Park	2013	Tamsulosin	46.2	9.2 ± 8.5	—	54.5/45.5	—
		Placebo	47.6	9.6 ± 9.0	—	50.0/50.0	—
Ibrahim	2013	Tamsulosin	38.17 ± 14.54	5.58 ± 0.93	—	—	—
		Placebo	36.71 ± 11.64	5.65 ± 1.25	—	—	—
Mohamed	2013	Tamsulosin	40.1 ± 11.8	—	—	—	39/22/40
		Placebo	43.8 ± 10.4	—	—	—	48/20/32
Cakiroglu	2013	Tamsulosin	44.66 ± 13.25	11.40 ± 3.01	—	—	—
		Placebo	42.19 ± 13.17	10.70 ± 3.20	—	—	—
El-Gamal	2012	Tamsulosin	35.3 ± 5.7	7.9 ± 1.93	—	—	—
		Placebo	36.2 ± 6.0	1.63 ± 7.7	—	—	—
Zaytoun	2012	Tamsulosin	39.4 ± 13.1	16.6 ± 0.4	—	50.0/50.0	26.0/22.0/52.0
		Placebo	40.5 ± 11.2	15.9 ± 0.3	—	50.0/50.0	22.0/34.0/44.0
Mokhless	2012	Tamsulosin	7.3 ± 4.2	8.2 ± 2.3	—	—	—
		Placebo	7.1 ± 3.2	7.8 ± 3.1	—	—	—
Vicentini	2011	Tamsulosin	47.3 ± 11.5	—	—	—	28.9/24.2/36.8
		Placebo	45.7 ± 15.1	—	—	—	18.4/42.1/39.5
Singh	2011	Tamsulosin	32.2 ± 12.22	—	—	—	—
		Placebo	36.0 ± 13.78	—	—	—	—
Gomez	2011	Tamsulosin	38.5 ± 11.3	5.3 ± 0.55	—	62.0/38.0	—
		Placebo	38.2 ± 12.4	5.2 ± 0.39	—	52.0/48.0	—
Al-Ansari	2010	Tamsulosin	37.18 ± 9.38	5.88 ± 2.39	—	32.0/68.0	—
		Placebo	36.13 ± 9.32	6.04 ± 2.5	—	42.0/58.0	—
Falihatkar	2010	Tamsulosin	45.5 ± 14	13.22	—	—	—
		Placebo	47 ± 14	12.88	—	—	—
Wang	2010	Tamsulosin	42.4 ± 12.6	9.3 ± 2.6	—	—	—
		Placebo	40.9 ± 10.3	8.6 ± 3.0	—	—	—
Kaneko	2010	Tamsulosin	50.0 ± 8.8	4.6 ± 1.8	—	64.5/35.5	38.7/6.5/45.2
		Placebo	45.0 ± 8.7	4.8 ± 2.1	—	55.9/44.1	41.2/14.7/44.1
Hussein	2010	Tamsulosin	44	—	—	—	25.4/14.9/59.7
		Placebo	40	—	—	—	—

(continued)

Table 1
(continued).

	Year	Groups	Mean age	Stone size, mm	Stone <6 mm, %	Stone location left/right, %	Stone location (%) Upper/Middle/Renal pelvis
Agrawal	2009	Tamsulosin	31.3	6.17			
		Placebo	35.3	6.35			
Hermanns	2009	Tamsulosin	36	4.1	75.6/24.4	40.0/60.0	—
		Placebo	41	3.8	84.4/15.6	64.4/35.6	—
Fere	2009	Tamsulosin	47 ± 14	3.5 ± 1.2	—	—	—
		Placebo	45 ± 12	3.8 ± 1.0	—	—	—
Naja	2008	Tamsulosin	31.17 ± 12.59	12.12 ± 3.59	—	—	17.6/7.8/74.6
		Placebo	39.44 ± 14.49	13.06 ± 3.49	—	—	10.8/9.2/80.0
Kobayashi	2008	Tamsulosin	56.76 ± 8.69	10.61 ± 4.45	—	42.1/57.9	—
		Placebo	52.29 ± 14.63	9.85 ± 3.13	—	55.9/44.1	—
Wang CJ	2007	Tamsulosin	50.9 ± 9.8	—	—	50.0/50.0	—
		Placebo	51.9 ± 8.9	—	—	55.3/44.7	—
Gravas	2007	Tamsulosin	48.8	8.5	—	—	—
		Placebo	49.2	8.3	—	—	—
Marco	2006	Tamsulosin	46.3 ± 10.9	6.9 ± 1.0	—	—	—
		Conservative	44.5 ± 11.3	6.4 ± 1.3	—	—	—
Bhagat	2006	Tamsulosin	35.9 ± 7.8	—	—	—	17.2/13.8/20.7
		Placebo	42.3 ± 12.3	—	—	—	20.7/6.9/3.1
Resim	2005	Tamsulosin	35.3 ± 10.9	7.8 ± 2.3	—	—	—
		Conservative	33.5 ± 9.7	7.8 ± 2.2	—	—	—
Gravina	2005	Tamsulosin	48.4 ± 14.0	—	—	—	21.5/23.1/55.4
		Conservative	47.9 ± 13.2	—	—	—	18.5/21.5/60
Resim.S	2005	Tamsulosin	39	2.1	—	—	—
		Conservative	37	2.2	—	—	—
Yilmaz	2005	Tamsulosin	40.62 ± 10.27	6.0 ± 1.25	—	44.8/55.2	—
		Placebo	41.6 ± 12.01	6.07 ± 1.41	—	53.6/46.4	—
Propiglia	2004	Tamsulosin	50.5 ± 17	—	—	—	—
		Placebo	42.7 ± 16	—	—	—	—
Kupeli	2004	Tamsulosin	41.9	4.7	—	—	—
		Placebo	43.74	4.9	—	—	—
Dellabella	2003	Tamsulosin	42.3 ± 12.7	6.7 ± 2.1	—	—	—
		Conservative	38.1 ± 10.6	5.8 ± 1.3	—	—	—

2. Methods

A comprehensive search strategy was used to investigate the efficacy of tamsulosin for the treatment of USD and included the PubMed (updated to current), the Embase (updated to current), the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews electronic databases. No ethical review was necessary to conduct this meta-analysis. The initial search process was designed to capture all relevant studies using the following search terms: tamsulosin, urinary colic, and expulsion. The reference lists from the retrieved documents were also searched. In addition, the included patients had to meet the following criteria: adults aged 18 to 60 years; emergency admission for renal colic; presence of a single ureteral stone confirmed by plain abdominal radiography (kidney–ureters–bladder), urinary ultrasonography, and/or non-contrast-enhanced computed tomography (CT). A distal ureteral stone location was defined as a stone located below the level of the sacroiliac joint on CT, stone size was defined by the largest diameter in 3 planes, and all stone were evaluated by the reporting radiologist on CT images. The exclusion criteria were fever; urinary tract infection; severe hydronephrosis; renal insufficiency, which was defined as an estimated glomerular filtration rate of <60 mL/min per 1.73 m²; abnormal anatomy, such as a solitary kidney, horseshoe kidney, or duplex urinary system; urethrostenosis; history of ureteral stricture; diabetes mellitus; current use of α -adrenoceptor antagonists or corticoste-

roids; and known or suspected allergy to the studies medications. The quality of the studies included was determined according to the Cochrane Collaboration Reviewer's Handbook and the Quality of Reporting of Meta-analysis guidelines.^[50,51] The assessment tool contained 6 core items: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. Each study classified as having a low, unclear, or high risk of bias was resolved by a third author. All of the included studies were also evaluated using the Jadad scale, and the trials were considered to be of high quality if the Jadad score was ≥ 3 and low quality if the score was ≤ 2 .^[52]

We divided patients into 2 groups according to the different treatment methods in this meta-analysis. Analysis 1 included patients who were treated with tamsulosin, and analysis 2 included patients who were treated with control treatments, including placebo and conservative treatments. The outcome measures were expulsion rate, expulsion time and side effects. Data were extracted independently by 2 authors using a predesigned data extraction form. Data extraction included the data source, eligibility, methods, participant characteristics, interventions, and results.

Data analysis for this meta-analysis was performed using RevMan 5.1.4. Continuous outcomes are presented as the weighted mean difference (MD) with the 95% confidence interval

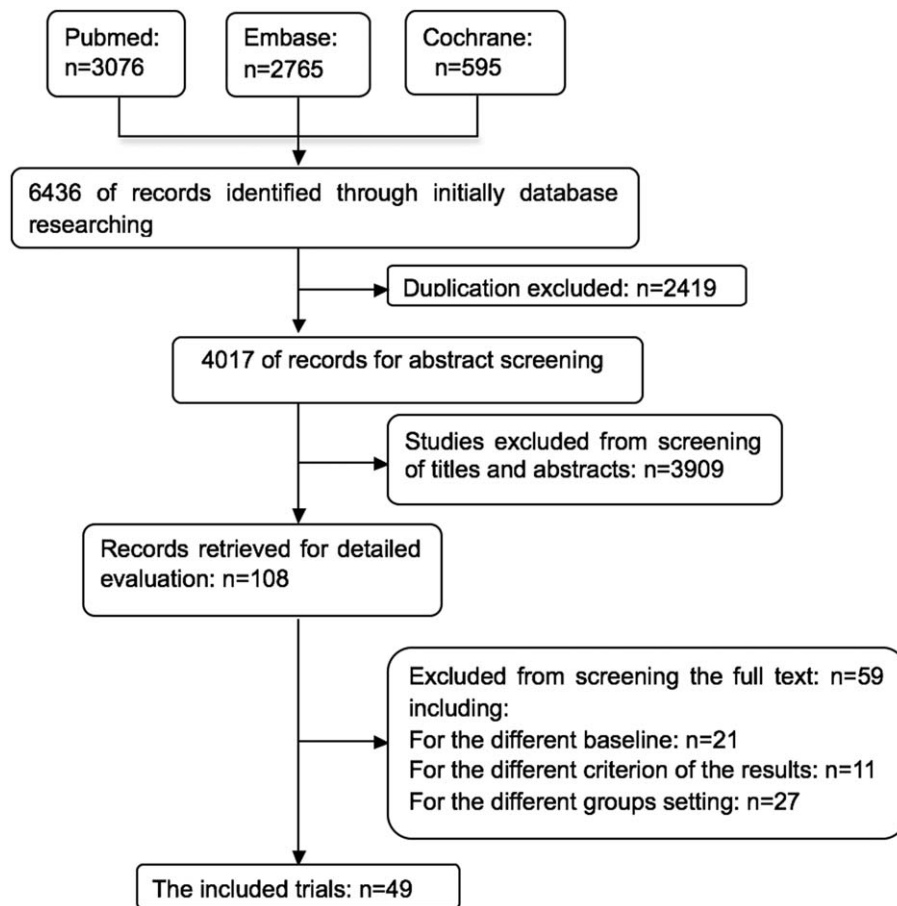


Figure 1. The search flow diagram.

(CI). Dichotomous data are presented as the relative risk (RR) with the 95% CI. A fixed-effects or random-effects method was used to analyze the data. The fixed-effects method was used to combine the results when no significant heterogeneity was present. The random-effects method was applied when heterogeneity was present. Statistical heterogeneity among the trials was evaluated using the I^2 test, with significance set at $P < .05$. Publication bias was evaluated using a funnel plot. In addition, a sensitivity analysis was performed if low-quality trials were included in the analysis.

3. Results

3.1. Description of the included studies

A total of 6436 reports were initially identified from the database and manual search. After removing redundant publications, reviews and meta-analyses, and after scanning titles and abstracts of unrelated records, 6238 reports were excluded from the study. After referring to the full texts, 21 articles with different baselines, 11 articles with different results criteria, and 27 articles with different group settings were excluded. Finally, 49 publications involving 8987 patients were included in this study. The conditions of these studies and the clinical details of the patients are presented in Table 1. The search flow diagram is presented in Figure 1. All of the included trials were assessed by Jadad score

for quality: 45 (91.84%) trials were graded as high quality, and only 4 (8.16%) trials were graded as low quality.

3.2. Comparison of the expulsion rates

The results comparing the efficacy of tamsulosin and the control treatment are presented in Table 2. Forty-six studies compared the expulsion rate between tamsulosin and control treatment. Tamsulosin was better than the control treatment in terms of the expulsion rate (80.5% vs 70.5%; MD, 1.16; 95% CI, 1.13–1.19; $P < .00001$; Fig. 2a). Additionally, 3 studies compared the expulsion rate of stones less than 6 mm (32.9% vs 32.51; MD, 1.02; 95% CI, 0.93–1.12; $P = .62$; Fig. 2b) and more than 6 mm (51.8% vs 44.8%; MD, 1.16; 95% CI, 1.09–1.24; $P < .00001$; Fig. 2c). The expulsion rate of stones less than 6 mm seemed to be similar to the 2 different treatments, but the expulsion rate of stones greater than 6 mm was better with tamsulosin than with the control treatment. The overall expulsion rate was higher with tamsulosin treatment than with the control treatment.

In addition, 20 studies compared the expulsion time between tamsulosin and the control treatment, and tamsulosin treatment had a shorter expulsion time than the control treatment (MD, -3.61 ; 95% CI, -3.77 to -3.46 ; $P < .00001$; Fig. 2d). Only 1 study explored the expulsion time between tamsulosin and the control treatment of stones less than 6 mm (MD, -7.20 ; 95% CI,

Table 2**Patient's outcomes by treatment group.**

	Groups	Expulsion rate, %	Expulsion time, day	Expulsion rate (%) <6 mm/≥6 mm	Expulsion time (%) <6 mm/≥6 mm
Ye	Tamsulosin (1642)	1419 (86)	6.2±2.6	488 (88)/931 (87)	139.9±68.9/152.5±64.3
	Placebo (1654)	1300 (79)	10.4±3.2	486 (87)/814 (75)	147.1±77.5/299.5±79.2
Balci	Tamsulosin (25)	19 (76)	9±3.2	—	—
	Placebo (25)	9 (36)	10.3±6.7	—	—
Meltzer	Tamsulosin (122)	102 (83.6)	—	—	—
	Placebo (116)	90 (77.6)	—	—	—
Nuraj	Tamsulosin (52)	47 (90)	9.6±7.1	25 (89.2)/20 (83.3)	—
	Placebo (52)	37 (71)	13.7±7.3	23 (82.1)/12 (50.0)	—
Arda	Tamsulosin (150)	113 (72.4)	—	—	—
	Placebo (150)	75 (50)	—	—	—
Ahmed	Tamsulosin (123)	96 (78.0)	—	—	—
	Placebo (126)	87 (69.0)	—	—	—
Shahat	Tamsulosin (60)	50 (83.3)	—	—	—
	Placebo (60)	49 (81.7)	—	—	—
Furyk	Tamsulosin (198)	140 (87)	—	110 (88.0)/30 (83.3)	—
	Placebo (195)	127 (81.9)	—	102 (89.5)/25 (61.0)	—
Ahmad	Tamsulosin (49)	42 (85.7)	—	—	—
	Placebo (48)	26 (54.2)	—	—	—
Berge	Tamsulosin (53)	33 (62.1)	—	—	—
	Placebo (47)	26 (54.4)	—	—	—
Aldaqaqadossi	Tamsulosin (31)	27 (87.1)	—	—	—
	Conservative (32)	20 (62.5)	—	—	—
Pickard	Tamsulosin (378)	307 (81.0)	—	—	—
	Placebo (379)	303 (80)	—	—	—
Lee	Tamsulosin (54)	40 (74.1)	14.3±7.9	—	—
	Placebo (54)	25 (46.3)	19.6±8.5	—	—
Janane	Tamsulosin (186)	144 (77.4)	8.4±1.8	—	—
	Placebo (170)	82 (48.2)	10.6±1.6	—	—
Alizadeh	Tamsulosin (50)	41 (82)	3.7±5.07	—	—
	Placebo (46)	30 (62.5)	4.7±8.03	—	—
Ketabchi	Tamsulosin (52)	48 (92.31)	—	—	—
	Placebo (50)	35 (70.0)	—	—	—
Qadri	Tamsulosin (60)	58 (96.7)	—	—	—
	Placebo (60)	48 (80)	—	—	—
Park	Tamsulosin (44)	37 (84.1)	10.0±7.0	—	—
	Placebo (44)	29 (65.9)	13.2±14	—	—
Ibrahim	Tamsulosin (40)	34 (85.0)	—	—	—
	Placebo (32)	14 (44.0)	—	—	—
Mohamed	Tamsulosin (65)	55 (85)	—	—	—
	Placebo (65)	58 (89)	—	—	—
Cakiroglu	Tamsulosin (59)	—	8.34±7.6	—	—
	Placebo (64)	—	12.59±8.63	—	—
El-Gamal	Tamsulosin (48)	33 (68.8)	—	—	—
	Placebo (46)	12 (26.1)	—	—	—
Zaytoun	Tamsulosin (50)	46 (92.0)	5.3±2.6	—	—
	Placebo (50)	42 (84.0)	7.3±2.7	—	—
Mokhless	Tamsulosin (33)	29 (87.8)	8.2±3.4	—	—
	Placebo (28)	18 (64.2)	14.5±4.5	—	—
Vicentini	Tamsulosin (38)	23 (60.5)	15.3±2.1	—	—
	Placebo (35)	17 (48.6)	15.9±2.4	—	—
Singh	Tamsulosin (59)	—	26.78±11.96	—	—
	Placebo (58)	—	31.28±18.31	—	—
Gomez	Tamsulosin (32)	22 (69.0)	—	—	—
	Placebo (33)	23 (70.0)	—	—	—
Al-Ansari	Tamsulosin (50)	41 (82.0)	6.4±2.77	—	—
	Placebo (46)	28 (61.0)	9.87±5.4	—	—
Falihatkar	Tamsulosin (70)	50 (71.4)	—	—	—
	Placebo (61)	43 (61.0)	—	—	—
Wang	Tamsulosin (52)	23 (46.2)	—	—	—
	Placebo (55)	41 (74.5)	—	—	—
Kaneko	Tamsulosin (31)	24 (77.0)	14±8.5	—	—
	Placebo (34)	17 (50.0)	17±11	—	—
Husseini	Tamsulosin (67)	49 (73.0)	—	—	—
	Placebo (69)	38 (55.0)	—	—	—
Agrawal	Tamsulosin (34)	28 (82.3)	12.3±8.3	—	—
	Placebo (34)	12 (35.2)	24.5±5.9	—	—
Hermanns	Tamsulosin (50)	43 (86.0)	—	—	—
	Placebo (50)	44 (88.0)	—	—	—
Fere	Tamsulosin (38)	27 (71.1)	—	—	—

(continued)

Table 2
(continued).

	Groups	Expulsion rate, %	Expulsion time, day	Expulsion rate (%)		Expulsion time (%)	
				<6 mm/≥6 mm	<6 mm/≥6 mm	<6 mm/≥6 mm	<6 mm/≥6 mm
Naja	Placebo (39)	24 (61.5)	—	—	—	—	—
	Tamsulosin (51)	48 (94.1)	—	—	—	—	—
Kobayashi	Placebo (65)	55 (84.6)	—	—	—	—	—
	Tamsulosin (38)	32 (84.1)	15.66 ± 6.14	—	—	—	—
Wang CJ	Placebo (34)	30 (88.24)	35.47 ± 3.7	—	—	—	—
	Tamsulosin (34)	29 (85.0)	6.1 ± 2.3	—	—	—	—
Gravas	Placebo (38)	31 (82.0)	6.5 ± 2.7	—	—	—	—
	Tamsulosin (38)	19 (63.33)	—	—	—	—	—
Marco	Placebo (34)	16 (51.6)	—	—	—	—	—
	Tamsulosin (50)	45 (90)	4.4 ± 2.1	—	—	—	—
Bhagat	Conservative (46)	27 (58.7)	7.5 ± 1.8	—	—	—	—
	Tamsulosin (30)	28 (96.6)	—	—	—	—	—
Resim	Placebo (30)	23 (79.3)	—	—	—	—	—
	Tamsulosin (30)	26 (86.6)	—	—	89.5/89.5	—	—
Gravina	Conservative (30)	22 (73.3)	—	—	70/75	—	—
	Tamsulosin (56)	44 (78.6)	—	—	—	—	—
Yilmaz	Conservative (56)	34 (60.7)	—	—	—	—	—
	Tamsulosin (29)	23 (79.31)	6.31 ± 0.88	—	—	—	—
Propiglia	Placebo (28)	15 (53.57)	10.54 ± 2.12	—	—	—	—
	Tamsulosin (28)	24 (85)	—	—	—	—	—
Kupeli	Placebo (28)	12 (43)	—	—	—	—	—
	Tamsulosin (15)	8 (53.3)	—	—	—	—	—
Dellabella	Placebo (15)	3 (20)	—	—	—	—	—
	Tamsulosin (30)	21 (70)	2.7 ± 2.77	—	—	—	—
Cervenakov	Conservative (30)	30 (100)	4.63 ± 2.73	—	—	—	—
	Tamsulosin (51)	41 (80.4)	—	—	—	—	—
	Conservative (51)	32 (62.7)	—	—	—	—	—

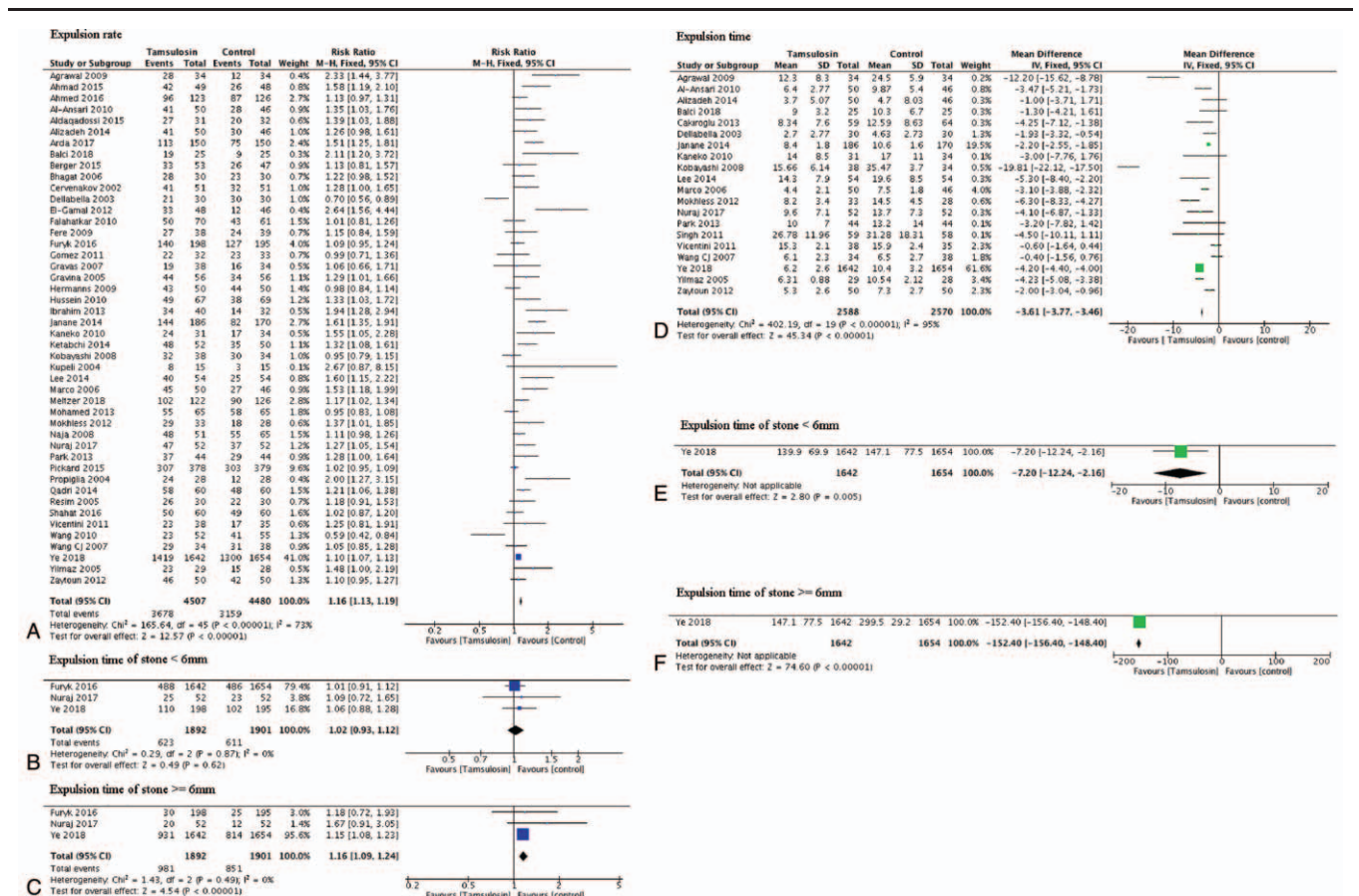


Figure 2. Compare the efficacy of stone expulsion between tamsulosin and the control treatment.

Table 3
Patient's adverse events by treatment group (%).

	Groups	Retrograde ejaculation	Hypotension	Dizziness	Diarrhea	Vomiting	Headache	Nausea	Fatigue	Total
Ye	Tamsulosin (1642)	67 (6.2)	—	52 (3.2)	21 (1.3)	38 (2.3)	41 (2.5)	43 (2.6)	18 (1.1)	92 (5.6)
	Placebo (1654)	48 (4.6)	—	50 (3.0)	17 (1.0)	31 (1.9)	46 (2.8)	41 (2.5)	15 (0.5)	84 (5.1)
Balci	Tamsulosin (25)	—	—	—	—	—	—	—	—	2 (8)
	Placebo (25)	—	—	—	—	—	—	—	—	1 (4)
Meltzer	Tamsulosin (212)	28 (18.2)	—	25 (11.8)	—	50 (23.6)	51 (24.1)	—	—	—
	Placebo (187)	10 (7.4)	—	18 (9.6)	—	46 (24.6)	43 (23.0)	—	—	—
Arda	Tamsulosin (159)	9 (6.0)	10 (6.3)	—	—	—	24 (15.0)	—	—	—
	Placebo (156)	12 (8.0)	9 (6.0)	—	—	—	17 (11.0)	—	—	—
Furyk	Tamsulosin (198)	33 (17.8)	—	41 (22.2)	19 (10.3)	17 (9.2)	40 (21.6)	56 (30.3)	53 (28.7)	57 (28.6)
	Placebo (195)	32 (17.3)	—	35 (18.9)	19 (10.3)	19 (10.3)	54 (29.2)	56 (30.3)	44 (23.8)	59 (30.2)
Ahmed	Tamsulosin (123)	—	—	—	—	—	—	—	—	21 (17.70)
	Placebo (126)	—	—	—	—	—	—	—	—	27 (21.4)
Berger	Tamsulosin (53)	—	—	—	—	—	—	—	—	10 (18.9)
	Placebo (57)	—	—	—	—	—	—	—	—	9 (19.1)
Pickard	Tamsulosin (378)	—	—	—	—	—	—	—	—	0 (0.0)
	Placebo (379)	—	—	—	—	—	—	—	—	1 (0)
Aldaqaqadossi	Tamsulosin (31)	1 (3.23)	—	—	—	—	—	—	—	1
	Conservative (32)	0 (0.0)	—	—	—	—	—	—	—	0
Ahmad	Tamsulosin (49)	—	—	—	—	—	—	—	—	9
	Placebo (48)	—	—	—	—	—	—	—	—	19
Janane	Tamsulosin (186)	—	—	5	—	—	—	—	—	5
	Placebo (170)	—	—	0	—	—	—	—	—	0
Katabchi	Tamsulosin (52)	—	1	1	—	—	—	—	—	3
	Placebo (50)	—	0	0	—	—	—	—	—	5
Park	Tamsulosin (44)	—	—	1	—	—	—	—	—	1
	Placebo (44)	—	—	0	—	—	—	—	—	0
Ibrahim	Tamsulosin (44)	3 (6.8)	2	—	—	—	—	—	—	5
	Placebo (32)	0 (0)	0	—	—	—	—	—	—	0
Zaytoun	Tamsulosin (50)	—	—	—	—	—	—	—	—	16
	Placebo (50)	—	—	—	—	—	—	—	—	0
Gomez	Tamsulosin (32)	—	—	—	—	—	—	—	—	2
	Placebo (33)	—	—	—	—	—	—	—	—	0
Wang	Tamsulosin (55)	—	—	2	—	—	—	—	—	2
	Placebo (52)	—	—	0	—	—	—	—	—	0
Ai-Ansari	Tamsulosin (50)	—	—	—	—	—	—	—	—	9
	Placebo (46)	—	—	—	—	—	—	—	—	5
Agrawal	Tamsulosin (34)	—	0	4	—	—	5	—	2	9
	Placebo (34)	—	0	2	—	—	1	—	1	5
Hermanns	Tamsulosin (50)	2	—	0	—	—	—	—	—	4
	Placebo (50)	0	—	1	—	—	—	—	—	1
Naja	Tamsulosin (51)	—	1	—	—	—	—	—	—	2
	Placebo (65)	—	0	—	—	—	—	—	—	0
Wang CJ	Tamsulosin (34)	—	1	—	—	—	—	—	—	—
	Placebo (38)	—	0	—	—	—	—	—	—	—
Marco	Tamsulosin (50)	—	0	0	1	—	—	—	—	2
	Conservative (46)	—	2	1	0	—	—	—	—	3
Resim	Tamsulosin (30)	0	—	5	0	2	4	—	—	—
	Conservative (30)	1	—	3	1	3	4	—	—	—
Resim.S	Tamsulosin (32)	1	0	4	2	—	5	—	—	—
	Conservative (35)	0	0	0	0	—	2	—	—	—
Propiglia	Tamsulosin (28)	—	—	—	—	—	—	—	—	1
	Conservative (28)	—	—	—	—	—	—	—	—	0

−12.24 to −2.16; $P=.005$; Fig. 2e) and more than 6 mm (MD, −152.40; 95% CI, −156.40 to −148.80; $P<.00001$; Fig. 2f).

3.3. Comparison of side effects between the 2 treatments

The results comparing the side effects of tamsulosin and the control treatment are presented in Table 3. Nine studies showed that the incidence rate of retrograde ejaculation was higher in the tamsulosin group than in the control group (MD, 1.36; 95% CI,

1.07–1.73; $P=.01$; Fig. 3a). Eight studies showed that there was no difference in the occurrence of hypotension between the 2 treatments (MD, 1.26; 95% CI, 0.63–2.52; $P=.52$; Fig. 3b). Eleven studies compared the dizziness rate and found no difference between the 2 groups (MD, 1.25; 95% CI, 0.99–1.58; $P=.07$; Fig. 3c). Five studies compared the diarrhea rate and found no difference between the tamsulosin and control groups (MD, 1.13; 95% CI, 0.74–1.71; $P=.58$; Fig. 3d). Four reviews showed that the rate of vomiting was not different

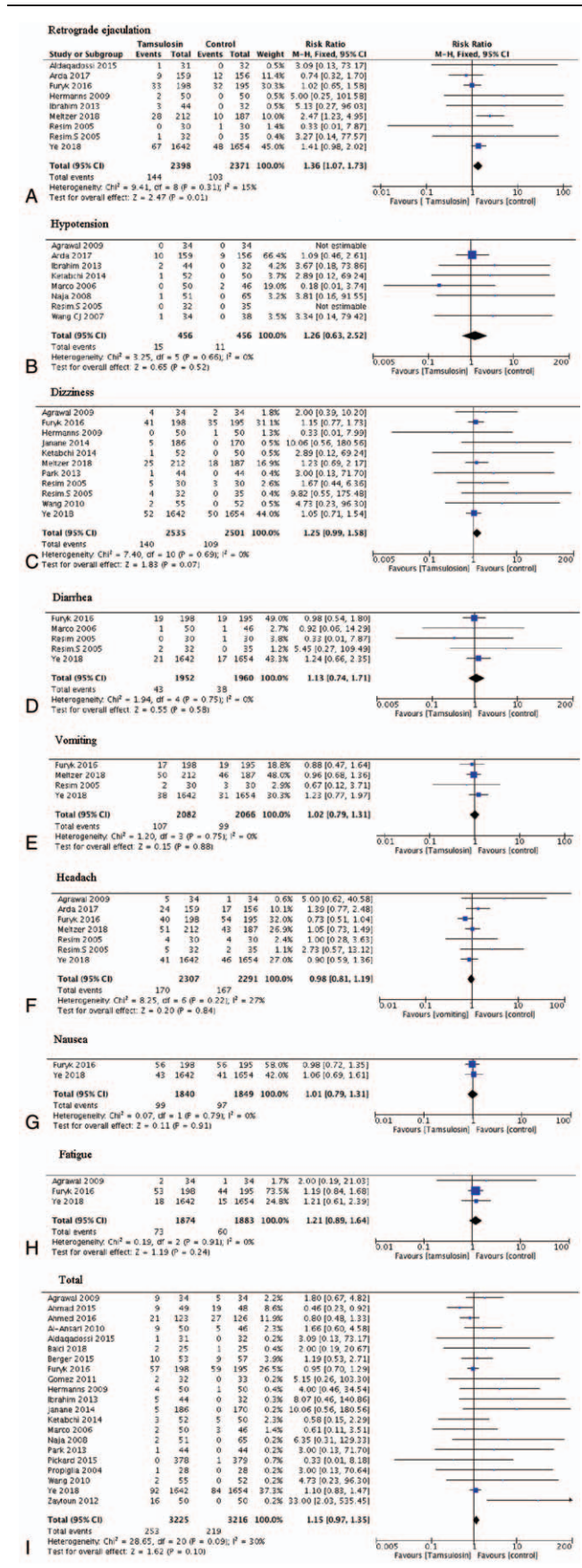


Figure 3. Compare the complications between tamsulosin and the control treatment.

between the 2 treatments (MD, 1.02; 95% CI, 0.79–1.31; $P = .88$; Fig. 3e). Seven studies found that the occurrence of headache was no difference between the 2 groups (MD, 0.98; 95% CI, 0.81–1.19; $P = .84$; Fig. 3f). Only 2 studies included the rate of nausea and found no difference between the 2 groups (MD, 1.01; 95% CI, 0.79–1.31; $P = .91$; Fig. 3g), and only 3 studies evaluated the rate of fatigue (MD, 1.21; 95% CI, 0.89–1.64; $P = .24$; Fig. 3h). The total complication rate was also not significantly different between the 2 groups (MD, 1.15; 95% CI, 0.97–1.35; $P = .10$; Fig. 3i).

3.4. Publication bias

The low risk of publication bias in the outcomes of expulsion rate and complications is shown by the shapes of the inverted funnel plots (Fig. 4).

4. Discussion

The management of ureteral stones has largely evolved from open surgery to minimally invasive methods, such as extracorporeal shockwave lithotripsy (ESWL), ureterorenoscopic removal of stones, or watchful waiting, due to the many advances in endourological techniques and instrumentation. The management of ureteral stones with open surgery has evolved to the use of minimally invasive methods due to advances in endourological techniques and instrumentation. Currently, the most widely accepted therapies for ureteral colic are minimally invasive and are the gold standard treatments. However, these techniques are quite expensive, even though they are associated with decreased risk, and are not widely available in developing countries. A treatment that can aid in the passage of urinary stones without surgery could reduce both patient morbidity and healthcare costs associated with this condition.^[5] Watchful waiting and medical expulsion therapy are the 2 most commonly used conservative methods that have been increasingly more frequently used in the treatment of distal ureteral stones to allow spontaneous stone passage, especially in patients who have less than grade 2 hydronephrosis.^[5,3] Prior published meta-analyses, as well as the current American Urological Association Guidelines on the Surgical Management of Colic, provide a strong recommendation that tamsulosin be used in these patients.^[4] In addition, other types of α -adrenoceptor antagonists, such as nifedipine, have also been suggested to have efficacy in some studies; at the time of the trial design, a trial by Pickard et al showed that the duration of use of agents including nifedipine could increase the rate of spontaneous stone passage and relieve pain.^[11] However, tamsulosin remains the most commonly used pharmaceutical.

Some recently published studies have reported that treatment with tamsulosin does not seem to improve renal stone clearance. Alizadeh et al reported that tamsulosin did not increase the overall stone passage rate compared with placebo, even though this treatment can reduce the duration of expulsion, pain and the need for analgesics and has been found to be beneficial. A study by Katabchi et al also demonstrated that the expulsion time was reduced by tamsulosin.^[16] These studies call into question the therapeutic application of tamsulosin. On the other hand, several published meta-analyses regarding the therapeutic effectiveness of tamsulosin have demonstrated the clinical benefit of this treatment.^[2] However, the evidence from these reviews is limited due to the number of included studies; however, in our review, which contained 49 studies, the level of evidence was stronger than in previous studies due to the large number of patients. In

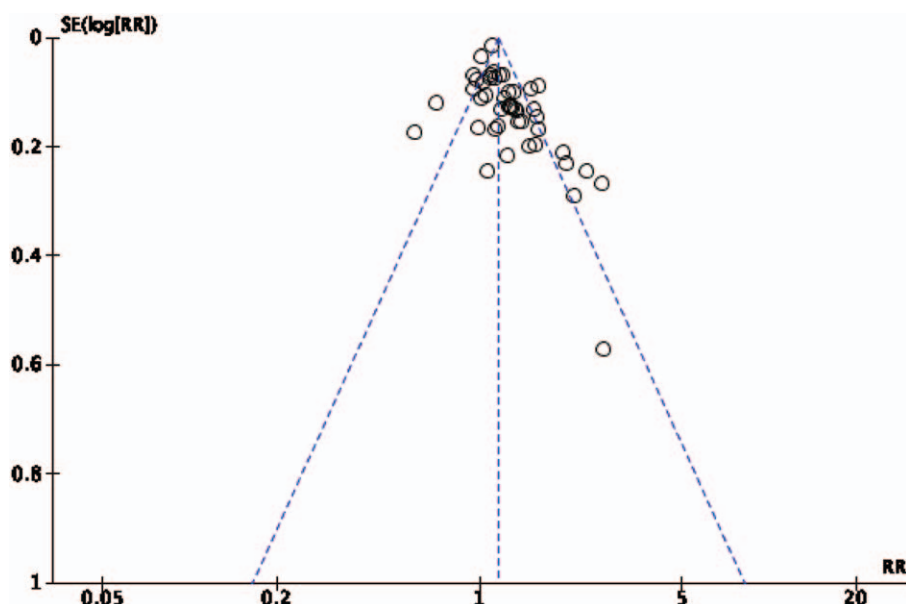


Figure 4. The risk of publication bias.

our study, we found that the use of tamsulosin was safe and clinically effective in patients with ureteral stones and was not associated an increase in side effects. When we performed the subgroup analysis, the results identified a specific clinical benefit of tamsulosin for stones measuring greater than 6 mm. Based on the evidence of many studies, we confirmed that treatment with tamsulosin is better than other conservative treatments, such as watchful waiting and massive intake of water. As a result, the dosages of pain relief medications were also reduced when tamsulosin was used.^[2]

Above all, this review strengthens the evidence that tamsulosin is a useful and promising treatment method for large stones, and this finding is in accordance with the study by Ye et al.^[2] Moreover, some studies have also shown that when α -1-adrenoceptors are applied to the smooth muscle of the ureters to blockade these receptors, they can significantly diminish the transmission of pain signals to the central nervous system.^[2] Ureteral stones are a common, painful disease, and simple treatment may facilitate more efficient and rapid spontaneous stone passage, which is very important for patients. However, different trials have suggested opposing ideas, and a review including a sufficient number of studies for strong evidence is necessary for clinical application. This study provides strong evidence for the use of tamsulosin. However, there are some published reviews about this topic, such as the study performed by Wang et al, which only included 8 studies and the latest research included in this meta-analysis was published in 2015. We included 49 studies in our research, and the latest study was published in 2018.

There are some limitations in this study. First, the control methods used in the included studies were different; some used a placebo, some used watchful waiting, and some used massive intake of water; second, we did not compare tamsulosin with other α -blockers or medicines. Most of the studies focused on stone expulsion, and few explored pain relief, even though this symptom is the most important reason why patients present to emergency clinics. The exploration of pain relief requires further study.

5. Conclusion

Our results show that tamsulosin significantly facilitates the passage of distal ureteral stones. Subgroup analyses provided evidence of a superior expulsion rate for stones measuring greater than 6 mm. In addition, evaluation of complications also showed that this method did not increase the rate of side effects. In summary, tamsulosin is a safe and effective medical expulsion therapy for ureteral stones.

Author contributions

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Supervision: Yi Sun, Qiang Wei.

Validation: Yi Sun, Xin Wei.

Visualization: Yi Sun.

Writing – original draft: Yi Sun, Xin Wei.

Writing – review & editing: Xin Wei.

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