Efficacy and Safety of Alpha-Blockers for Kidney Stones in Adults

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Abstract

Objective: To review the literature for α -blocker treatment of kidney stones. **Data Sources:** PubMed search performed November 15, 2017, using the following search terms: alpha-blocker, alfuzosin, silodosin, or tamsulosin AND kidney or ureteral stones. Additional studies found through references of primary and tertiary literature. Inclusion criteria included English language, randomized controlled trials (not included in meta-analyses), and meta-analyses evaluating US available alpha-blockers as medical expulsive therapy with or without lithotripsy in adults with renal or ureteral stones, and no date limits. **Study Selection and Data Extraction:** Seven randomized controlled trials (RCTs), 1 case-control trial, and 6 meta-analyses were found and included in this review. Two RCTs and 4 meta-analyses evaluated alpha-blockers without lithotripsy. Five RCTs, 1 case-control trial, and 2 meta-analyses evaluated their use post-lithotripsy. The primary endpoint was stone clearance rate in most studies. **Data Synthesis:** For ureteral stones ≤ 10 mm treated without lithotripsy, alpha-blockers increased clearance in all meta-analyses and one RCT versus control. For ureteral or renal stones treated with lithotripsy, 4 RCTs and all meta-analyses found benefit with alpha-blockers compared with control. When results were stratified by stone size, alpha-blockers performed better for stones 10 to 20 mm, while there was no difference for stones < 10 mm. **Conclusion:** Alpha-blockers are beneficial without lithotripsy for ureteral stones 5 to 10 mm. They are beneficial post-lithotripsy for renal or ureteral stones > 10 mm. They can be considered post-lithotripsy for stones 5 to 10 mm, but little benefit may be seen. Although all uroselective alpha-blockers have been found to be effective, most data are with tamsulosin 0.4 mg daily.

Keywords

alpha-blocker, alfuzosin, silodosin, tamsulosin, kidney stone, ureteral stone, nephrolithiasis

Background

Kidney stones are a common and growing problem in the United States. A recent survey found that 11% of men and 7% of women will experience at least one kidney stone in their lifetime. Recurrence is estimated to be $\leq 50\%$ at 5 years. Risk factors include male gender, obesity, diabetes, gout, and income less than \$75 000. Noncontrast computed tomography imaging is typically used to confirm diagnosis and estimate stone size. Pain is the most common symptom and occurs when the stone attempts to pass through the ureter. Kidney stones are often asymptomatic while growing and may take up to several months to grow to a detectable size.¹⁻³

Treatment of kidney stones depends on factors such as stone size and symptoms. Waiting for a stone to pass spontaneously is the recommended treatment for stones < 5 mm with little to no pain. Management options for larger and painful stones include shockwave lithotripsy (SWL), ureteroscopy, surgical removal, and pharmacologic therapy. While the traditional role of pharmacologic therapy is for

symptomatic relief or to prevent recurrence, some studies suggest using medications to promote the passage of stones and shorten the time it takes to pass the stone spontaneously. This is referred to as medical expulsive therapy (MET) and is where the use of alpha-blockers has been studied. MET can be used as monotherapy, post-lithotripsy, or with additional pharmacologic therapy.² A 2002 to 2009 survey found that MET use was infrequent before 2007, and from 2007 to 2009, it was prescribed in 14% of emergency department urolithiasis visits.³ This article compiles and briefly reviews the studies, including meta-analyses, that examined the efficacy and safety of alpha-blockers as MET in the treatment of kidney stones.

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Table 1. Comparison of Alpha-Blockers.^{23,24}

Generic Name	Trade Name	Dose Forms and Strengths	Average Wholesale Price per Unit	Generic	Specific to Urinary System
Alfuzosin	Uroxatral	Extended-release tablets: 10mg	10 mg: \$4.21	Yes	Yes
Doxazosin	Cardura	Immediate-release tablets: 1 mg, 2 mg, 4 mg, 8 mg	1 mg, 2mg: \$1.35 4 mg: \$1.41 8 mg: \$1.49	Yes	No
		Extended-release tablets: 4 mg, 8 mg	4 mg: \$6.17 8 mg: \$5.87	No	
Prazosin	Minipress	Capsules: 1 mg, 2 mg, 5 mg	1 mg: \$0.90 2 mg: \$1.27 5 mg: \$2.18	Yes	No
Silodosin	Rapaflo	Capsules: 4 mg, 8 mg	4 mg, 8 mg: \$9.11	No	Yes
Tamsulosin	Flomax	Capsules: 0.4 mg	0.4 mg: \$4.21	Yes	Yes
Terazosin	Hytrin	Capsules: 1 mg, 2 mg, 5 mg, 10 mg	1 mg, 2 mg: \$1.56 5 mg, 10 mg: \$1.60	Yes	No

Alpha-blockers, or alpha-1 antagonists, act by preventing adrenergic agonists, like norepinephrine, from stimulating the smooth muscles that regulate the diameter of smaller veins and arteries and the urinary system. This increased dilation of the urinary system is thought to allow kidney stones to pass more quickly out of the body.⁴ Alpha-blockers are approved for benign prostatic hyperplasia and hypertension. They have an off-label use in the management of kidney stones. Agents selective to the prostate have less systemic adverse effects than nonselective agents. A summary of available alpha-blockers can be found in Table 1.

The 2014 American Urological Association (AUA) guidelines for management of urolithiasis focus on stone prevention with diet and medications. Recurrent calcium stones can be prevented with thiazide diuretics or potassium citrate, while urate-containing stones can be prevented with allopurinol. Dietary recommendations include drinking plenty of water, limiting sodium intake, and reducing consumption of animal protein.⁵ The 2016 European Association of Urology (EAU) guidelines on conservative management of urolithiasis recommend alpha-blockers with nonsteroidal anti-inflammatory drugs for recurrent renal colic, for facilitating passage of debris from lithotripsy, and as MET (without lithotripsy) for uncomplicated stones. The EAU makes no recommendation on choice of alpha-blocker. Though many stones <6 mm in diameter pass spontaneously, patients who choose observation or MET should return for follow-up within 2 weeks to assess for hydronephrosis and stone position.⁶ This approach is also recommended by the 2016 AUA guidelines for surgical management of stones, which recommend offering MET with alpha-blocker therapy to patients with distal ureteral stones ≤10 mm (Grade B recommendation). They performed a meta-analysis of 24 studies and found a 73% versus 54% stone-free rate for patients with <10 mm distal ureteral stones treated with

MET versus placebo or no treatment. They recommend a more definitive stone treatment (eg, SWL) if MET is not successful in 4 to 6 weeks. These guidelines do not recommend a specific alpha-blocker or dose, but they acknowledge that their recommendation was heavily influenced by studies using tamsulosin 0.4 mg daily. They also recommend alpha-blockers to help relieve stent discomfort and to facilitate passage of stone fragments following SWL.⁷

Data Sources

A PubMed search was performed on November 15, 2017, using the search terms alpha-blocker, alfuzosin, silodosin, or tamsulosin AND kidney or ureteral stones. Additional studies were found through references of primary and tertiary literature. Inclusion criteria included English language, randomized controlled trials (RCTs; not included in meta-analyses), and meta-analyses evaluating US available alpha-blockers as MET with or without lithotripsy in adults with renal or ureteral stones, and no date limits.

Summary of Studies

Fourteen studies, including 6 meta-analyses, 7 RCTs (not included in meta-analyses), and 1 case-control study (not included in meta-analyses) examined the efficacy and safety of alpha-blockers as MET for renal or ureteral stones. Agents studied include alfuzosin, doxazosin, naftopidil, silodosin, tamsulosin, terazosin, and urapidil. Naftopidil, an uroselective alpha-blocker, and urapidil, a nonselective alpha-blocker, are not available in the United States. Studies had similar inclusion criteria, including age greater than 18 years and presence of a single symptomatic and trackable kidney stone located in the ureter, renal pelvis, or renal calyx. Exclusion criteria included presence of more than

one stone, urinary tract infection, and renal colic lasting more than a day. Study durations varied between 2 weeks and 6 months. The most commonly studied primary endpoint was clearance or expulsion rate, which was successful passing of the stone.⁸⁻²¹ A summary of studies can be found in Table 2.

Four meta-analyses and 2 other (RCTs) evaluated alpha-blockers compared with placebo or other pharmacologic therapy without lithotripsy for management of ureteral stones ≤ 10 mm in diameter.⁸⁻¹³ In a Japanese study, there was no difference in clearance rate between tamsulosin 0.2 mg daily and conservative treatment. The authors acknowledged that 0.4 mg is the accepted tamsulosin MET dose, but only the 0.2 mg for benign prostatic hyperplasia is covered by the Japanese health insurance system.⁸ A Chinese study found both tamsulosin 0.4 mg (82.2%) daily and naftopidil (72.1%) to be more effective than placebo (30.2%) at clearing stones.⁹ There are published meta-analyses for each of the selective alpha-blockers (alfuzosin, silodosin, tamsulosin) and one that evaluated all alpha-blockers (selective and nonselective).¹⁰⁻¹³ The tamsulosin meta-analysis included more than 2700 patients from 29 trials and found a 33% improvement in clearance rate with tamsulosin (0.2 mg and 0.4 mg daily) compared with control. Tamsulosin cleared stones more than calcium channel blockers (6 studies). Tamsulosin 0.4 mg daily was shown to be equally effective to tamsulosin 0.2 mg daily (small study). There was no difference in expulsion rate between tamsulosin and lithotripsy for stones 4 to 8 mm in diameter, but >8 mm stones were cleared faster with lithotripsy compared with tamsulosin (1 study).¹⁰ The alfuzosin meta-analysis included more than 700 patients from 7 trials and found an 85% improvement in clearance rate with alfuzosin 10 mg daily compared with control.¹¹ The silodosin meta-analysis included more than 1000 patients from 7 trials and found a 69% improvement with silodosin 8 mg daily in clearance rate compared with control.¹² The alpha-blocker meta-analysis included almost 6000 patients from 55 trials and found a 49% improvement in clearance rate with alpha-blockers over control. The results were not stratified by drug or dose.¹³

Five RCTs, 1 case-control study, and 2 meta-analyses (tamsulosin, alpha-blockers) examined alpha-blockers as adjunctive therapy post-lithotripsy for renal or ureteral stones.¹⁴⁻²¹ For the RCTs, stone sizes were 4 to 20 mm in diameter. Tamsulosin 0.4 mg daily was studied in 4 of the 5 RCTs. Its clearance rate at 4 weeks was 73% to 86% versus 55% to 69%, at 8 weeks was 95% versus 57%, and at 12 weeks was 78% to 91% versus 46% to 74% compared with control. The results were significant for all but one of the 12-week trials.^{15-18,21} Three RCTs found tamsulosin to be beneficial in reducing renal colic.^{14,16,21} One tamsulosin RCT stratified for stone size and found it to be more effective for larger stones (11-20 mm) compared with smaller stones (≤ 10 mm).¹⁷ The clearance rate for alfuzosin 10 mg

daily compared with control in one RCT was 76.7% versus 46.7% for renal stones 11 to 15 mm. There was no difference for stones 5 to 10 mm.¹⁸ The tamsulosin meta-analysis included more than 1300 patients from 15 trials and found a 24% improvement in clearance rate with tamsulosin 0.4 mg daily compared with control for upper urinary tract stones. The results were not stratified by stone size. It also found more benefit with 0.4 mg compared with 0.2 mg daily.¹⁴ The alpha-blocker meta-analysis included almost 2900 patients from 26 studies and found significant improvement in stone-free rate (odds ratio 2.77) with both alpha-blockers and nifedipine compared with control for upper urinary tract stones. Results were not affected by stone size or location.²⁰ In a case-control study, Taiwanese patients that used alpha-blockers post-lithotripsy were monitored for up to 180 days, and it was found that the longer the patients received alpha-blockers the less likely they were to have a recurrence. The recurrence rate for the first (days 1-45) and fourth (days 135-180) quartiles were 45.64 and 18.52, respectively, per 1000-person years.¹⁹

Reports of adverse events in the studies were rare, and no serious adverse events were associated with alpha-blocker use. Reported adverse effects included dizziness, hypotension, headache, and ejaculatory dysfunction. There was no difference in adverse effects based on alpha-blocker uroselectivity.⁸⁻²¹ Dilation of the vasculature by alpha-blockers results in a moderate lowering of blood pressure, averaging -8 mm Hg systolic and -5 mm Hg diastolic, according to a Cochrane review.²² This decrease in blood pressure is responsible for dizziness (3% to 19%) and headache (0% to 21%), which are the most common adverse events associated with alpha-blockers. Orthostatic hypotension has also been reported in patients initiating alpha-blocker therapy (0% to 19%) but occurs less frequently with chronic use (0% to 4%).²³

Overall, studies of alpha-blockers as MET for kidney stones were small with variable study design and quality. Because of the different study designs (randomized but open label or blinded), drug/dose/duration, primary endpoint, adverse effect reporting, and follow-up periods for the studies included in the meta-analyses, heterogeneity was present and expected and can lead to potential bias for the results. Despite that, studies found benefit with alpha-blockers as MET. A large clinical trial comparing the selective alpha-blockers (alfuzosin, silodosin, and tamsulosin) in terms of stone clearance and time to stone clearance based on stone size and location and safety is needed.

Conclusion

Current studies support the use of alpha-blockers as MET without lithotripsy for facilitating passage and time to passage of symptomatic ureteral stones <10 mm in diameter.

Table 2. Summary of Studies.

Reference	Study Design	Inclusion Criteria	Exclusion Criteria	Patients	Treatment (# Trials for Meta-Analyses)	Efficacy	Safety
<i>Treatment without lithotripsy</i>							
Ohgaki et al (2010) ⁸	RCT in Japan	Ureter stone <10 mm	>1 stone, UTI, renal colic >24 hours, hypotension, history of taking calcium channel blocker or alpha-blocker	132	Conservative treatment + either tamsulosin 0.2 mg, nifedipil 50 mg, or urapidil 30 mg daily	Clearance rate hazard ratio at 1 month for control vs tamsulosin: 1.415 (0.697-2.871, $P = .336$)	No major adverse effects
Zhou et al (2011) ⁹	RCT in China	Distal ureter stone 4-9 mm	>1 stone, severe incarcerated stone, history of stone surgery, renal colic >24 hours	131	Tamsulosin 0.4 mg, nifedipil 10 mg, or placebo daily	Clearance rate at 2 weeks for tamsulosin vs nifedipil vs placebo: 82.2% vs 72.1% vs 30.2% ($P < .05$ drug vs placebo)	Tamsulosin vs nifedipil: dizziness 16% vs 9%, headache 13% vs 5%
Lu et al (2012) ¹⁰	Meta-analysis	Published RCT or quasi-RCT of tamsulosin for ureter stones	Studies using SWL or uroscopy with tamsulosin	2763 (29 trials)	Tamsulosin 0.2 (5) or 0.4 mg (25) daily or control daily (standard therapy, calcium channel blocker, other alpha-blocker)	Clearance rate risk ratio for tamsulosin vs control: 1.33 (1.23-1.44); one study compared tamsulosin 0.4 and 0.2 mg and found no difference in clearance rate (17/25 [68%] vs 10/25 [40%], $P > .05$); tamsulosin decreased stone passing by 3.4 days vs control ($P < .00001$)	10 trials reported adverse events with tamsulosin; overall well-tolerated; side effects included dizziness, headache, hypotension, retrograde ejaculation
Liu et al (2015) ¹¹	Meta-analysis	Published RCTs of alfuzosin for ureteral stones (only 1 US trial)	Studies using SWL	705 (7 trials)	Alfuzosin 10 mg or control daily (tamsulosin 0.4 mg, placebo, or dologesic)	Clearance rate odds ratio for alfuzosin vs control: 1.85 (1.35-2.55, $P < .001$), results not affected by stone location; alfuzosin decreased stone passing by 4.2 days vs control ($P < .00001$); no difference in results vs tamsulosin	Retrograde ejaculation: alfuzosin 2 patients, tamsulosin 10 patients
Ding et al (2016) ¹²	Meta-analysis	Published RCTs of silodosin for ureteral stones ≤10 mm (only 1 US trial)	Not listed	1035 (7 trials)	Silodosin 8 mg or control daily (water, placebo, nifedipil 50 mg, tamsulosin 0.4 mg [3])	Clearance rate odds ratio for silodosin vs control: 1.69 (1.19-2.40, $P = .003$), most benefit for >5 mm and distal stones, odds ratio 2.82 (1.79-4.44, $P < .00001$) for silodosin vs tamsulosin; silodosin decreased expulsion time by 4.5 days ($P < .00001$) vs control, by 4.25 days vs tamsulosin ($P = .11$)	No difference between silodosin and tamsulosin for retrograde ejaculation, dizziness, orthostatic hypotension, or headache
Hollingsworth et al (2016) ¹³	Meta-analysis	Published RCTs of alpha-blockers for ureteral stones (only 4 US trials)	Studies using SWL	5990 (55 trials)	Tamsulosin (40), silodosin (6), alfuzosin (6), doxazosin (4), terazosin (4), nifedipil (3) or control (41)/placebo (14) (doses not given)	Clearance rate risk ratio for alpha-blocker vs control/placebo: 1.49 (1.39-1.61), benefit seen with all stone locations, most benefit seen with stones >5 mm; decreased stone passing by 3.79 days vs control/placebo; decreased risk of surgical intervention and hospitalization vs control/placebo	Adverse effects uncommon and similar between groups; some abnormal ejaculation

(continued)

Table 2. (continued)

Reference	Study Design	Inclusion Criteria	Exclusion Criteria	Patients	Treatment (# Trials for Meta-Analyses)	Efficacy	Safety
<i>Treatment post-lithotripsy</i>							
Zheng et al (2010) ¹⁴	Meta-analysis	Published RCTs of SWL for upper urinary tract stones	Not reported	1326 (15 trials)	SWL alone or with tamsulosin 0.4 mg (11) or 0.2 mg (4) daily	Clearance rate risk ratio for tamsulosin vs SWL alone: 1.24 (1.12-1.37; $P < .0001$), no difference in stone location, results not stratified for stone size, subgroup analysis found more benefit with 0.4 mg vs 0.2 mg (RR 1.29 vs 1.13); decreased renal colic, expulsion time, and analgesic use vs SWL alone	10 trials reported adverse effects with tamsulosin; low incidence of dizziness, hypotension, and ejaculatory dysfunction
John and Razdan (2010) ¹⁵	RCT in the United States	Renal or ureteral stone 10-20 mm	Not reported	78	Uroscopic laser lithotripsy once, ureteric stent, analgesic alone or with tamsulosin 0.4 mg daily	Stone free at 4 weeks for tamsulosin vs control: 86.5% vs 69.4% ($P < .01$), results not stratified for stone size or location Renal colic episodes: 5.4% tamsulosin vs 22.2% control ($P < .01$)	No adverse effects reported with tamsulosin
Georgiev et al (2011) ¹⁶	RCT in Bulgaria	5-20 mm stone anywhere in ureter or upper-mid calyx	Orthostatic hypotension	248	SWL once and either standard therapy or tamsulosin 0.4 mg daily	Clearance rate for tamsulosin vs standard therapy: 4 weeks: 73.4% vs 55.9% ($P < .001$), 12 weeks: 91.3% vs 74.6% ($P < .05$); results not stratified for stone size or location Renal colic episodes at 12 weeks: tamsulosin 21.7% vs 68.4% standard therapy ($P < .001$) Rehospitalization at 12 weeks: tamsulosin 6.9% vs standard therapy 24.6% ($P < .05$)	No difference in treatment groups; dizziness and variations in blood pressure occurred
Pirzada et al (2011) ¹⁷	RCT in Pakistan	5-15 mm stone in renal pelvis or mid-upper calyx	>1 stone, serum creatinine >2 mg/dL, UTI, taking calcium channel blocker	60	SWL and either standard therapy or alfuzosin 5 mg twice daily	Clearance rate at 4 weeks for alfuzosin or standard therapy: 76.7% vs 46.7% ($P = .01$); 56.7% vs 23.3% for stones 11-15 mm; no difference for stones 5-10 mm; benefit in mid-upper calyx stones with alfuzosin ($P < .05$)	Alfuzosin adverse effects reported as mild, completely reversible, and did not lead to discontinuation
Qadri et al (2014) ¹⁸	RCT in Pakistan	Radiopaque renal stone 5-20 mm	>1 stone, past unsuccessful SWL	120	SWL every 2 weeks until stone passage or 8 weeks and tamsulosin 0.4 mg or placebo daily	Clearance rate for tamsulosin vs placebo: 95.8% vs 57.1% ($P < .003$) for 11-15 mm stones, 80% vs 20% ($P < .05$) for 16-20 mm stones; no difference for ≤ 10 mm stones ($P = .13$)	Not reported

(continued)

Table 2. (continued)

Reference	Study Design	Inclusion Criteria	Exclusion Criteria	Patients	Treatment (# Trials for Meta-Analyses)	Efficacy	Safety
Liu et al (2015) ¹⁹	Case-control study in Taiwan	First time stone removal therapy from 2000 to 2010	Previous stone removal procedure	1259	Post-lithotripsy alpha-blocker (alfuzosin, doxazosin, tamsulosin, terazosin) for up to 180 days, monitored for recurrence (doses not given)	Need for surgical intervention: tamsulosin 1.7% vs placebo 16.7% ($P < .004$) Alpha-blockers were associated with less kidney stone recurrence when comparing 4th (135-180 days) to 1st quartile (1-45 days) use (8% vs 14%); hazard ratio 0.46 (95% confidence interval = 0.24-0.89), results not stratified for stone size	Not reported
Skolarikos et al (2015) ²⁰	Meta-analysis	Published RCTs of MET after SWL for upper urinary stones	Short (<14 days), nonrandomized, or noncomparator studies; bladder stones	2884 (26 trials) 2113 received alpha-blockers	Post-lithotripsy MET [alfuzosin 10 mg (1), doxazosin 4 mg (4), tamsulosin 0.2-0.4 mg (16), terazosin 2 mg (1), urapidil 30 mg (1), nifedipine 20-30 mg (2), choreito 7.5 g (2), uriston 2 g (1), rowatinex 300 mg (2)] or control daily	Stone-free odds ratio for alpha-blockers vs control: 2.77 (1.92-4.01), no difference based on stone size or location; stone free 78%, nifedipine 64.1%; alpha-blockers reduced time to stone expulsion by 2.6 days vs control	Not reported
Ahmed et al (2016) ²¹	RCT in Egypt and Saudi Arabia	<20 mm renal stone	Stone in lower calyx, UTI, renal impairment, taking calcium channel blocker or alpha-blocker	271	SWL alone or with tamsulosin 0.4 mg daily	Stone free at 12 weeks for tamsulosin vs control: 78% vs 69% ($P = .108$); results not stratified for stone size or location Renal colic episodes: 8.1% vs 19.8% ($P = .008$)	Not reported

Abbreviations: MET, medical expulsive therapy; RCT, randomized controlled trial; SWL, shockwave lithotripsy; UTI, urinary tract infection.

Studies also support their use post-lithotripsy for increasing clearance rate, shortening time to passage, and reducing renal colic, with most benefit for stones >10 mm in diameter located in the renal pelvis, mid-upper calyx, or mid-upper ureter. Guidelines also support alpha-blockers for MET. Additionally, long-term alpha-blocker use may be a viable method to prevent stone recurrence. Tamsulosin 0.4 mg daily is the alpha-blocker and dose with the most data to support its use in stone treatment. Providers prescribing tamsulosin 0.2 mg daily for MET should be encouraged to increase the dose to 0.4 mg daily. Alpha-blockers are usually well tolerated. While alpha-blockers may be used to prevent recurrence, patients continuing MET therapy for longer than 3 months should be reevaluated for stone progression and other causes of renal colic.

Authors' Note

William H. Zufall graduated with his PharmD from Ferris State University in August 2017. Currently he is not associated with any institution.

Declaration of Conflicting Interests

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References

1. Scales CD Jr, Smith AC, Hanley JM, Saigal CS; Urologic Diseases in America Project. Prevalence of kidney stones in the United States. *Eur Urol*. 2012;62:160-165. doi:10.1016/j.eururo.2012.03.052.
2. Sakhaee K, Maalouf NM, Sinnott B. Clinical review. Kidney stones 2012: pathogenesis, diagnosis, and management. *J Clin Endocrinol Metab*. 2012;97:1847-1860. doi:10.1210/jc.2011-3492.
3. Fwu CW, Eggers PW, Kimmel PL, Kusek JW, Kirkali Z. Emergency department visits, use of imaging, and drugs for urolithiasis have increased in the United States. *Kidney Int*. 2013;83:479-486. doi:10.1038/ki.2012.419.
4. Curhan GC. Nephrolithiasis. In: Kasper DL, Fauci AS, Hauser SL, Longo DL, Jameson JL, Loscalzo J, eds. *Harrison's Principles of Internal Medicine*. 19th ed. New York, NY: McGraw-Hill; 2015.
5. Pearle MS, Goldfarb DS, Assimos DG, et al; American Urological Association. Medical management of kidney stones: AUA guideline. *J Urol*. 2014;192:316-324. doi:10.1016/j.juro.2014.05.006.
6. Türk C, Petřík K, Sarica K, et al. EAU guidelines on diagnosis and conservative management of urolithiasis. *Eur Urol*. 2016;69:468-474. doi:10.1016/j.eururo.2015.07.040.
7. Assimos D, Krambeck A, Miller NL, et al. Surgical management of stones: American Urological Association/Endourological Society guideline, Part II. *J Urol*. 2016;196:1161-1169. doi:10.1016/j.juro.2016.05.091.
8. Ohgaki K, Horiuchi K, Hikima N, Kondo Y. Facilitation of expulsion of ureteral stones by addition of α 1-blockers to conservative therapy. *Scand J Urol Nephrol*. 2010;44:420-424. doi:10.3109/00365599.2010.497769.
9. Zhou SG, Lu JL, Hui JH. Comparing efficacy of α 1D-receptor antagonist naftopidil and α 1A/D-receptor antagonist tamsulosin in management of distal ureteral stones. *World J Urol*. 2011;29:767-771. doi:10.1007/s00345-011-0739-3.
10. Lu Z, Dong Z, Ding H, Wang H, Ma B, Wang Z. Tamsulosin for ureteral stones: a systematic review and meta-analysis of a randomized controlled trial. *Urol Int*. 2012;89:107-115.
11. Liu C, Zeng G, Kang R, et al. Efficacy and safety of alfuzosin as medical expulsion therapy for ureteral stones: a systematic review and meta-analysis. *PLoS One*. 2015;10:e0134589. doi:10.1371/journal.pone.0134589.
12. Ding H, Ning Z, Dai Y, Shang P, Yang L. The role of silodosin as a new medical expulsive therapy for ureteral stones: a meta-analysis. *Ren Fail*. 2016;38:1311-1319. doi:10.1080/0886022X.2016.1215221.
13. Hollingsworth JM, Canales BK, Rogers MA, et al. Alpha blockers for treatment of ureteric stones: systematic review and meta-analysis. *BMJ*. 2016;355:i6112. doi:10.1136/bmj.i6112.
14. Zheng S, Liu LR, Yan HC, Wei Q. Tamsulosin as adjunctive treatment after shockwave lithotripsy in patients with upper urinary tract stones: a systematic review and meta-analysis. *Scand J Urol Nephrol*. 2010;44:425-432. doi:10.3109/00365599.2010.523014.
15. John TT, Razdan S. Adjunctive tamsulosin improves stone free rate after ureteroscopic lithotripsy of large renal and ureteric calculi: a prospective randomized study. *Urology*. 2010;75:1040-1042. doi:10.016/j.urology.2009.07.1257.
16. Georgiev MI, Ormanov DI, Vassilev VD, et al. Efficacy of tamsulosin oral controlled absorption system after extracorporeal shockwave lithotripsy to treat urolithiasis. *Urology*. 2011;78:1023-1026. doi:10.1016/j.urology.2011.01.073.
17. Pirzada AJ, Anwar A, Javed A, Memon I, Mohammad A. Role of alpha-1 blocker in expulsion of stone fragments after extracorporeal shockwave lithotripsy for renal stones. *J Ayub Med Coll Abbottabad*. 2011;23:125-129.
18. Qadri SS, El Khalid S, Mamud S. Effects and outcome of tamsulosin more than just stone clearance after extracorporeal shockwave lithotripsy for renal calculi. *J Pak Med Assoc*. 2014;64:644-648.
19. Liu CC, Hsieh HM, Wu CF, et al. Long-term prescription of α -blockers decrease the risk of recurrent urolithiasis needed for surgical intervention—a nationwide population-based study. *PLoS One*. 2015;10:e0122494. doi:10.1371/journal.pone.0122494.
20. Skolarikos A, Grivas N, Kallidonis P, et al. The efficacy of medical expulsive therapy (MET) in improving stone-free rate and stone exclusion time, after extracorporeal shock

- wave lithotripsy (SWL) for upper urinary stones: a systematic review and meta-analysis. *Urology*. 2015;86:1057-1064. doi:10.1016/j.urology.2015.09.004.
21. Ahmed AF, Shalaby E, El-feky M, et al. Role of tamsulosin therapy after extracorporeal shockwave lithotripsy for renal stones: randomized controlled trial. *Urol Int*. 2016;97:266-272. doi:10.1159/000445840.
 22. Heran BS, Galm BP, Wright JM. Blood pressure lowering efficacy of alpha-blockers for primary hypertension. *Cochrane Database Syst Rev*. 2012;(8):CD004643. doi:10.1002/14651858.CD004643.pub3.
 23. Wolters Kluwer Clinical Drug Information. Facts & Comparisons® eAnswers. <http://www.wolterskluwercli.com/facts-comparisons-online/>. Accessed November 17, 2017.
 24. Truven Health Analytics. Micromedex® solutions. Web applications access. <http://www.micromedexsolutions.com/>. Accessed November 17, 2017.