

Kidney Stones? It's Time to Rethink Those Meds

Despite being recommended for ureteral stone expulsion, tamsulosin or nifedipine is no more effective than placebo.

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PRACTICE CHANGER

Do not prescribe tamsulosin or nifedipine for stone expulsion in patients with ureteral stones that are ≤ 10 mm.¹

STRENGTH OF RECOMMENDATION

A: Based on a high-quality randomized controlled trial (RCT).¹

Bob Z, age 48, presents to the emergency department (ED) with unspecified groin pain. CT of the kidney, ureter, and bladder (CT KUB) finds evidence of a single ureteral stone measuring 8 mm. He's prescribed medication for the pain and discharged. The day after his ED visit, he comes to your office to discuss further treatment options. Should you prescribe tamsulosin or nifedipine to help him pass the stone?

The most recent National Health and Nutrition Examination Survey found kidney stones affect 8.8% of the population.² Outpatient therapy is indicated for patients with ureteric colic secondary to stones ≤ 10 mm who do not have uncontrolled

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pain, impaired kidney function, or severe infection. Routine outpatient care includes oral hydration, antiemetics, and pain medications.

Medical expulsive therapy (MET) is also used to facilitate stone passage. MET is increasingly becoming part of routine care; use of MET in kidney stone patients in the United States has grown from 14% in 2009 to 64% in 2012.^{3,4}

The joint European Association of Urology/American Urological Association Nephrolithiasis Guideline Panel supports the use of MET.⁵ Meta-analyses of multiple RCTs suggest that an α -blocker (tamsulosin) or a calcium channel blocker (nifedipine) can reduce pain and lead to quicker stone passage and a higher rate of eventual stone passage when compared to placebo or observation.^{6,7} However, these reviews included small, heterogeneous studies with a high or unclear risk for bias.

STUDY SUMMARY

MET doesn't increase the rate of stone passage

The SUSPEND (Spontaneous Urinary Stone Passage Enabled by Drugs) trial¹ was a multicenter RCT designed to determine the effectiveness of tamsulosin or nifedipine as MET for patients ages 18 to 65 with a single ureteric stone measuring ≤ 10 mm on CT KUB, which has 98% diagnostic accu-

racy.⁸ (Stones > 10 mm typically require surgery or lithotripsy.)

In this RCT, 1,167 adults were randomized to take tamsulosin (0.4 mg/d), nifedipine (30 mg/d), or placebo for four weeks or until the stone spontaneously passed, whichever came first. The participants, clinicians, and research staff were blinded to treatment assignment. The primary outcome was the proportion of participants who spontaneously passed their stone, as indicated in patient self-reported questionnaires and case-report forms completed by researchers. Secondary outcomes were time to stone passage and pain as assessed by analgesic use and a visual analogue scale (VAS).

At four weeks, 1,136 (97%) of the randomized participants had data available for analysis. The proportion of participants who passed their stone did not differ between MET and placebo; 80% of the placebo group (303 of 379 participants) passed the stone, compared with 81% (307 of 378) of the tamsulosin group and 80% (304 of 379) of the nifedipine group. The odds ratio (OR) for MET vs placebo was 1.04 (95% confidence interval [CI], 0.77 to 1.43) and the OR for tamsulosin vs nifedipine was 1.07 (95% CI, 0.74 to 1.53). These findings did not change with further subgroup analysis, including by sex, stone size (≤ 5 mm vs > 5 mm), or stone location.

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There were no differences between groups in time to stone passage as measured by clinical report and confirmed by imaging. Time to passage of stone was available for 237 (21% of) participants. The mean days to stone passage was 15.9 (n = 84) for placebo, 16.5 (n = 79) for tamsulosin, and 16.2 (n = 74) for nifedipine, with a MET vs placebo difference of 0.5 days (95% CI, -2.9 to 3.9; $P = .78$). Sensitivity analysis accounting for bias from missing data did not change this outcome.

No differences in analgesic use or pain. Self-reported use of pain medication during the first four weeks was similar between groups: 59% (placebo patients), 56% (tamsulosin), and 56% (nifedipine). The mean days of pain medication use was 10.5 for placebo, 11.6 for tamsulosin, and 10.7 for nifedipine, with a MET vs placebo difference of 0.6 days (95% CI, -1.6 to 2.8; $P = .45$).

There was no difference between groups in the VAS pain score at four weeks. The MET vs placebo difference was 0.0 (95% CI, -0.4 to 0.4; $P = .96$) and the mean VAS pain score was 1.2 for placebo, 1.0 for tamsulosin, and 1.3 for nifedipine.

WHAT'S NEW

This large RCT contradicts results from previous meta-analyses

The SUSPEND study is the first large, multicenter RCT of MET with tamsulosin or nifedipine for kidney stones that used patient-oriented outcomes to find no benefit for stone expulsion, analgesic use, or reported pain compared to placebo. The discrepancy with prior meta-

analyses is not unusual. Up to one-third of meta-analyses that show positive outcomes of a therapy are subsequently altered by the inclusion of results from a single, large, well-designed, multicenter RCT.⁹

CAVEATS

This trial included fewer women than previous studies

The SUSPEND study included a smaller proportion of women than previously published case series due to a need for a diagnostic CT KUB, which excluded more women than men due to radiation concerns. However, the proportion of women was balanced across all groups in this trial, and there was no evidence that sex impacted the efficacy of treatment for the primary outcome.¹

CHALLENGES TO IMPLEMENTATION

We see no challenges to the implementation of this recommendation. **CR**

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