THIS IS WHY
with Dr. Busti

TRIAL NAME

Title

SUSPEND Trial: Medical Expulsive Therapy for Ureteric Stones — Did Tamsulosin or Nifedipine Prevent Intervention?

Reference

Pickard R, Starr K, MacLennan G, et al. Medical expulsive therapy in adults with ureteric colic: a multicentre, randomised, placebo-controlled trial. Lancet. 2015;386(9991):341-349. doi:10.1016/S0140-6736(15)60933-3. PMID: 25998582.

Related full HTA report: Pickard R, et al. Use of drug therapy in the management of symptomatic ureteric stones in hospitalised adults: a multicentre, placebo-controlled, randomised controlled trial and cost-effectiveness analysis of a calcium channel blocker and an alpha-blocker: the SUSPEND trial. Health Technol Assess. 2015;19(63):vii-viii, 1-171. PMID: 26244520.

Background / Rationale

Before SUSPEND, smaller trials and meta-analyses suggested that medical expulsive therapy — especially alpha-blockers such as tamsulosin and calcium channel blockers such as nifedipine — might improve spontaneous ureteral stone passage and reduce need for procedures. However, the quality and generalizability of the evidence were uncertain, and a large pragmatic randomized trial was needed to test whether these drugs actually improved clinically meaningful outcomes in routine practice.

PICOTS

P (Population): Adults 18–65 years old with ureteric colic, a single ureteric stone ≤10 mm identified by CT, and a clinical plan for expectant management rather than immediate intervention. Patients with urgent indications for active treatment — such as severe infection, uncontrolled pain, or impaired renal function — were excluded.
I (Intervention): Tamsulosin 400 micrograms orally once daily for up to 4 weeks.
C (Comparator): Placebo; the trial also included nifedipine 30 mg orally once daily as a second active comparator.
O (Outcome): Primary outcome was “spontaneous stone passage” operationalized as no further intervention required to facilitate stone passage within 4 weeks. Secondary outcomes included pain, analgesic use, time to stone passage, health-related quality of

life, safety, and cost-effectiveness.
T (Timing): Treatment for up to 4 weeks; primary outcome assessed at 4 weeks, with additional follow-up in the HTA report at 12 weeks.
S (Setting): Pragmatic, multicenter UK National Health Service trial conducted across 24 UK hospitals.

Objective / Purpose

To determine whether tamsulosin or nifedipine improved spontaneous passage of ureteric stones, reduced need for further intervention, improved patient-centered outcomes, and was cost-effective compared with placebo in adults managed conservatively for ureteric colic.

Study Design & Methods

Design: Multicenter, randomized, double-blind, placebo-controlled, pragmatic clinical trial. Randomization was 1:1:1 to tamsulosin, nifedipine, or placebo, using minimization by center, stone size, and stone location. Participants, clinicians, and trial personnel were masked.
Participants: Adults 18–65 years old with symptomatic ureteric colic and a single CT-confirmed ureteric stone ≤10 mm, for whom expectant management was appropriate.
Intervention: Tamsulosin 400 micrograms daily, nifedipine 30 mg daily, or placebo for up to 4 weeks.
Sample size: 1,167 randomized; 1,136 included in the primary analysis. Seventeen were excluded as ineligible and 14 were lost to follow-up.
Baseline characteristics: Mean age was approximately 43 years. Women made up about 19% of the study population. Mean stone size was approximately 4.5–4.6 mm; about 75% of stones were ≤5 mm, about 25% were >5 mm, and about 64–65% were lower ureteric stones.

Outcomes (Endpoints)

Primary:
No further intervention required to facilitate stone passage within 4 weeks after randomization.

Secondary:
Pain, analgesic use, time to stone passage, health-related quality of life, adverse events, further healthcare use, and cost-effectiveness.

Results / Key Findings

- **Primary outcome:** No further intervention was required in 307/378 patients receiving tamsulosin, 304/379 receiving nifedipine, and 303/379 receiving placebo — approximately 81%, 80%, and 80%, respectively.
- **Tamsulosin vs placebo:** Adjusted risk difference was 1.3 percentage points, 95% CI −5.7 to 8.3; p=0.73.
- **Nifedipine vs placebo:** Adjusted risk difference was 0.5 percentage points, 95% CI −5.6 to 6.5; p=0.88.
- **Any active MET vs placebo:** Adjusted risk difference was 0.9 percentage points, 95% CI −5.1 to 6.8; no statistically significant benefit.
- **Secondary outcomes:** No clear differences were found in pain, days of analgesic use, time to stone passage, or quality of life. Time-to-passage data were limited because a clear date of stone passage was available for only 237 participants, about 21% of the analyzed population.
- **Cost-effectiveness:** Neither tamsulosin nor nifedipine was likely to be cost-effective compared with placebo in the NHS analysis.
- **Adverse effects:** Serious adverse events occurred in 3 patients assigned to nifedipine and 1 assigned to placebo. Premature discontinuation because of intolerable side effects was reported in approximately 6% of placebo patients, 10% of tamsulosin patients, and 17% of nifedipine patients. Non-serious adverse events were not systematically collected.

Number Needed to Treat (NNT)

Event rates:
Tamsulosin: 307/378 = 81.2% with no further intervention.
Placebo: 303/379 = 79.9% with no further intervention.
Absolute Risk Difference (ARD): Tamsulosin vs placebo adjusted ARD: +1.3 percentage points; 95% CI −5.7 to +8.3.
Formula: NNT = 1 ÷ absolute risk difference.
Interpretation: A nominal point-estimate NNT using the adjusted risk difference would be approximately 77, but this should not be interpreted as a reliable treatment effect because the confidence interval crosses no benefit and includes possible harm. The trial did not demonstrate a statistically significant or clinically persuasive benefit for tamsulosin or nifedipine in the overall SUSPEND population.
Note: The primary endpoint was not radiographic confirmation of stone passage. It was absence of further intervention within 4 weeks. Therefore, the NNT would apply only to "avoiding further intervention," not confirmed stone expulsion.

Conclusions

In adults 18–65 years old with CT-confirmed ureteric stones ≤10 mm managed expectantly, neither tamsulosin 400 micrograms nor nifedipine 30 mg reduced the need for further intervention over 4 weeks compared with placebo. The trial challenged routine, broad use of medical expulsive therapy for all ureteric stones, especially given the high spontaneous passage/no-intervention rate and predominance of small stones.

Location of the Trial

United Kingdom; 24 UK NHS hospitals.

Funding

Funded by the UK National Institute for Health Research Health Technology Assessment Programme.

PMID

Lancet publication: 25998582.
HTA report: 26244520.

ClinicalTrials.gov ID Number

No ClinicalTrials.gov NCT number identified. The trial was registered as EudraCT 2010-019469-26 and ISRCTN69423238.

Study Limitations

- Primary endpoint was pragmatic but indirect: The trial defined stone passage as no further intervention, not CT-confirmed stone passage. This is clinically relevant but can miss persistent stones that did not trigger a procedure.
- No routine confirmatory imaging: Follow-up imaging was not required and was performed only if directed by local clinical care, limiting certainty about actual stone clearance.
- Very high placebo/no-intervention rate: Approximately 80% of placebo patients required no further intervention, leaving limited room for medication to show added benefit.
- Many stones were small: About 75% of stones were ≤5 mm, a group with high spontaneous passage rates and less biologic room for benefit from MET.

- Potential dilution of benefit in larger distal stones: Later evidence suggests alpha-blockers may be more useful for distal stones >5 mm; SUSPEND's overall result may dilute that subgroup effect.
- Outcome depended on clinical decision-making: "No further intervention" can be influenced by local urology thresholds, patient preferences, imaging patterns, and health-system access.
- Time-to-passage data were incomplete: A date of stone passage was available for only about 21% of participants.
- Non-serious adverse events were not systematically collected: This limits assessment of common tolerability issues such as dizziness, orthostasis, or other bothersome side effects.
- Generalizability limits: Adults older than 65 were excluded, and women were underrepresented at about 19% of the study population.
- Excluded complicated presentations: Findings should not be applied to infected obstruction, uncontrolled pain, impaired renal function, or patients requiring urgent urologic intervention.

Current Guidelines or Position Statements

- **American Urological Association:** Current AUA surgical management guidance supports offering alpha-blocker MET for adults and children with ≤10 mm distal ureteral stones, generally for about 30 days, and allows MET as an option for selected middle or proximal stones. This is more favorable toward MET than a broad reading of SUSPEND alone.
- **European Association of Urology:** EAU acknowledges contradictory evidence, including well-designed placebo-controlled trials showing limited or no benefit overall, but concludes the greatest benefit is in distal ureteral stones >5 mm. EAU recommends offering alpha-blockers as one option for distal ureteral stones >5 mm, noting that this is off-label.
- **NICE guideline NG118:** NICE recommends considering alpha-blockers for adults, children, and young people with distal ureteric stones <10 mm. NICE specifically notes that UK practice changed after SUSPEND, but after reviewing the totality of evidence, including newer data, the committee concluded alpha-blockers can help some patients with small distal stones and pain.
- **Emergency medicine interpretation:** Formal emergency medicine practice is often more cautious because ED populations include many small stones that pass spontaneously. ACEP Now commentary after SUSPEND and later negative trials emphasized skepticism about routine MET for all ureterolithiasis, although this

should be viewed as expert commentary rather than a formal ACEP clinical policy.

- **Primary care / internal medicine interpretation:** AAFP commentary highlights that tamsulosin appears most useful for 5–10 mm distal ureteral stones, with little expected benefit for stones <5 mm because spontaneous passage is already high.

Expert Commentary from Reputable Medical Sources or Experts

- SUSPEND is best interpreted as a trial against routine, broad, all-comers MET for ureteric stones ≤10 mm, not as definitive proof that alpha-blockers never help any patient.
- The pragmatic design was a major strength because the outcome — avoiding intervention — matters to patients and health systems. But it was also a limitation because it did not directly confirm stone passage radiographically.
- Later evidence clarified the likely effect modifier: stone size and location. Alpha-blockers appear least useful for stones ≤5 mm and most plausible for distal stones >5 mm, especially 5–10 mm.
- The 2016 Furyk trial found no overall benefit for distal stones ≤10 mm, but in the prespecified 5–10 mm subgroup, tamsulosin improved CT-confirmed passage: 83.3% vs 61.0%, risk difference 22.4%, NNT about 4.5.
- The 2018 STONE trial found no significant benefit of tamsulosin for symptomatic ureteral stones <9 mm in a US ED population; however, mean stone size was only 3.8 mm, again raising the issue that many enrolled stones were too small to benefit meaningfully.
- A large Chinese multicenter trial found improved CT-confirmed expulsion with tamsulosin for distal stones, driven by stones >5 mm, with no effect for stones ≤5 mm.
- A 2018 Cochrane review concluded alpha-blockers probably increase stone clearance overall, but subgroup analyses suggest substantially greater benefit for stones >5 mm than for stones ≤5 mm; alpha-blockers may slightly increase major adverse events.

Clinical Practice Implications and/or Application

- Do not interpret SUSPEND as “tamsulosin never works.” Interpret it as: routine MET for every uncomplicated ureteric stone, especially small stones, is not supported.
- For a patient with a small stone ≤5 mm, especially if distal, spontaneous passage is already common; the incremental benefit of tamsulosin is likely small.

- For a patient with an uncomplicated distal ureteral stone >5 mm and ≤10 mm, alpha-blocker MET remains reasonable as an option, consistent with EAU, NICE, and AUA-style guidance.
- Nifedipine is not commonly favored in modern practice for MET; contemporary guidelines and evidence discussions focus primarily on alpha-blockers.
- MET should not delay urgent intervention when red flags are present: fever or infected obstruction, sepsis, acute kidney injury, solitary kidney with obstruction, bilateral obstruction, uncontrolled pain, persistent vomiting/dehydration, or inability to follow up.
- The practical bedside question is: What is the stone size, where is it located, and is the patient safe for observation?
- Shared decision-making matters. Discuss that tamsulosin is often off-label for this use, benefit is most plausible for larger distal stones, and adverse effects such as dizziness or orthostasis may occur.
- Follow-up is essential. A patient who does not pass the stone, has persistent symptoms, develops infection, or has renal function concerns needs reassessment and often urologic involvement.