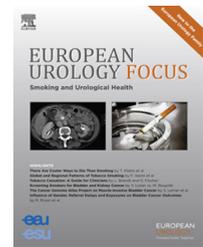


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Point of Focus Debate: For

Role of Medical Expulsive Therapy for Ureteral Stones: Pro MET

Thomas Knoll^{a,*}, Christian Türk^b

^aDepartment of Urology, Sindelfingen-Böblingen Medical Centre, University of Tübingen, Sindelfingen, Germany; ^bUrologische Praxis und Steinzentrum, Vienna, Austria

Observation is an accepted option for ureteral stones in patients with controlled symptoms. In 2007, the collaborative European Association of Urology (EAU)/American Urological Association Urolithiasis Working Groups published a systematic review that demonstrated a beneficial effect of α -blockers on the spontaneous stone passage rate of distal ureteral stones [1]. The term *medical expulsive therapy* (MET) was born, and the use of α -blockers was recommended as an adjunct for uncomplicated distal ureteral stones <10 mm [2]. A huge number of randomised trials and several systematic reviews have been published since, mostly showing a significant benefit for MET using α -blockers, and—although off-label—the use of tamsulosin became accepted [3–5].

However, three placebo-controlled and double-blinded studies recently raised doubts about the effectiveness of α -blockers. In 2015, Pickard et al [6] published results for a large, multicentre randomised controlled trial (RCT) comparing tamsulosin, nifedipine, and placebo for ureteral stones <10 mm. The primary endpoint was the need for intervention. No differences could be observed [6]. Furyk et al [7] conducted another randomised trial comparing tamsulosin and placebo. Only the subgroup with stones of 5–10 mm showed an increased passage rate with tamsulosin [7]. Another multicentre RCT comparing the α_1 -antagonist silodosin to placebo showed a significant benefit for stones in the distal ureter only [8].

These discrepancies between a few large, high-quality, multicentre, double-blinded, placebo-controlled studies and a large number of small, single-centre RCTs of heterogeneous quality and several meta-analyses based

on the data therein are alarming. However, the question arises as to whether these three studies are indeed contradictory. As always, it is advisable to analyse the studies in detail. All three studies show a perfect methodology of randomisation and blinding. The primary outcome in the study by Furyk et al [7] was the stone passage rate evaluated by computed tomography (CT) after 28 d. By contrast, Pickard et al [6] defined the primary endpoint as the difference in necessary interventions. However, they did not assess the stone-free rate objectively via CT to avoid costs and radiation. There can be no doubt that clinical assessment of stone passage is an imprecise surrogate parameter for MET efficacy. Furthermore, the study was underpowered for stones >5 mm (75% of all stones were \leq 5 mm). Sur et al [8] evaluated patients weekly and the primary endpoint was defined as stone passage, as determined via CT, kidney/ureter/bladder X-ray, or ultrasound imaging.

The results have been extensively discussed by various expert panels. Most groups concluded that the three placebo-controlled, double-blinded RCTs could not exclude a benefit of MET using α -blockers, as the study endpoints were either insufficiently controlled or the results supported the use of MET, at least in patients with stones >5 mm in the distal ureter. Smaller stones might have such a high spontaneous passage rate that any effect of MET cannot be shown. MET for proximal stones could be effective in some patients, as all stones have to pass the distal ureter; however, the data available do not allow a clear conclusion as yet. This conclusion is underlined by the most recent review by Hollingsworth et al [9], who

* Corresponding author. Department of Urology, Sindelfingen-Böblingen Medical Centre, University of Tübingen, Arthur-Gruber-Strasse 70, 71065 Sindelfingen, Germany.
E-mail address: t.knoll@klinikverbund-suedwest.de (T. Knoll).

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concluded that MET is efficacious in patients with ureteric stones who are amenable to conservative management. The greatest benefit might be among those with larger stones. Therefore, the EAU Guideline Panel kept the recommendation to offer α -blockers for patients with distal ureteral stones of 5–10 mm [2].

Conflicts of interest: The authors have nothing to disclose.

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