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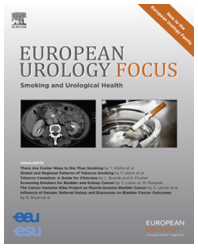

Review – Stone Disease

Medical Expulsive Therapy in Urolithiasis: A Review of the Quality of the Current Evidence

Andreas Skolarikos [a], *Khurshid R. Ghani* [b], *Christian Seitz* [c], *Brandon Van Asseldonk* [d], *Matthew F. Bultitude* [e,*]

[a] *National and Kapodistrian University of Athens, Sismanoglio Hospital, Athens, Greece;* [b] *Department of Urology, University of Michigan, Ann Arbor, MI, USA;* [c] *Department of Urology, Medical University of Vienna, Vienna, Austria;* [d] *University of Toronto, Toronto, Canada;* [e] *Guy's and St. Thomas' NHS Foundation Trust, London, UK*

Article info

Article history:
Accepted May 2, 2017

Associate Editor: James Catto

Keywords:
Kidney stone
Medical expulsive therapy
Ureteric stone
Urolithiasis

Abstract

Context: Medical expulsive therapy (MET) is widely used to promote spontaneous passage of urinary stones. However, there is conflicting evidence on the actual role of MET.
Objective: To evaluate the conformance of published randomized controlled trials (RCTs) on MET with the Consolidated Standards for Reporting Trials (CONSORT) criteria, and to clarify the current role of MET in management of urinary stones on the basis of our findings.
Evidence acquisition: We carried out an electronic search of the Cochrane Library, PubMed, and Embase databases for RCTs on MET. For each RCT included, we created a checklist table documenting the minimum essential items that should be included in reports of RCTs according to the CONSORT 2010 statement.
Evidence synthesis: Clinical heterogeneity between pooled studies in terms of the MET given, inclusion criteria, sample size, pre- and post-treatment imaging, and differential follow-up was profound. The overall methodological rigor of the pooled studies was low, as indicated by the moderate to poor conformance of the studies with the CONSORT criteria. The aforementioned reasons may explain the discrepancies found between the supporting results of several meta-analyses and those of well-designed placebo-controlled double-blind studies revealing no benefit from MET. Recent well-designed RCTs have shown no benefit from α-blockers versus placebo. However, on the basis of sensitivity analyses in a recently published meta-analysis, α-blockers may still promote spontaneous expulsion of large stones.
Conclusions: Conflicting data on MET may be explained by clinical heterogeneity and methodological flaws. Urologists must decide whether to follow single, large, well-conducted RCTs or pooled data from meta-analyses. The latter still support selective use of MET for larger urinary stones.
Patient summary: In this review we tested the accuracy of the studies published on various medications given to promote spontaneous passage of stones from the ureter. Although the majority of the studies were not designed properly, there is still some evidence to support medical expulsive therapy.

* Corresponding author. Urology Centre, Southwark Wing, Guy's and St. Thomas NHS Foundation Trust, Great Maze Pond, London SE1 9RT, UK. Tel. +44 20 71889099.
E-mail address: matthew.bultitude@gstt.nhs.uk (M.F. Bultitude).

http://dx.doi.org/10.1016/j.euf.2017.05.002

1. Introduction

The prevalence of urinary stone disease is high among the general population, with a significant risk of recurrence. Acute presentation and treatment of urolithiasis may significantly affect the health-related quality of life of patients [1]. Medical expulsive therapy (MET) is aimed at promoting spontaneous passage of ureteral stones and reducing the stone expulsion time after lithotripsy. Pharmaceutical agents such as calcium channel blockers, corticosteroids, nonsteroidal anti-inflammatory drugs, terpene compound products, plant extracts, and α-blockers have been investigated as methods to enhance spontaneous stone passage [2]. The most widely studied agents are α-blockers. The rationale for using α-blockers is to decrease both the frequency and amplitude of ureteral peristalsis above the stone and reduce ureteral spasm at the stone location [3]. These changes are accompanied by an increase in the intraureteral

Table 1 – CONSORT 2010 checklist for information to include when reporting a randomized trial.

Section/topic	Item	
	No.	Description
Title and abstract	1a	Identification as a randomized trial in the title
	1b	Structured summary of trial design, methods, results, and conclusions
Introduction		
Background and objectives	2a	Scientific background and explanation of rationale
	2b	Specific objectives or hypotheses
Methods		
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons
Participants	4a	Eligibility criteria for participants
	4b	Settings and locations where the data were collected
Interventions	5	Interventions for each group with sufficient details to allow replication, including how and when they were actually administered
Outcomes	6a	Completely defined prespecified primary and secondary outcome measures, including how and when they were assessed
	6b	Any changes to trial outcomes after the trial commenced, with reasons
Sample size	7a	How sample size was determined
	7b	When applicable, explanation of any interim analyses and stopping guidelines
Randomization		
Sequence generation	8a	Method used to generate the random allocation sequence
	8b	Type of randomization; details of any restriction (such as blocking and block size)
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions
Blinding	11a	If done, who was blinded after assignment to interventions (eg, participants, care providers, those assessing outcomes) and how
	11b	If relevant, description of the similarity of interventions
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses
Results		
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome
	13b	For each group, losses and exclusions after randomization, together with reasons
Recruitment	14a	Dates defining the periods of recruitment and follow-up
	14b	Why the trial ended or was stopped
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group
Numbers analyzed	16	For each group, the number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group and the estimated effect size and its precision (such as 95% confidence interval)
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended
Ancillary procedures	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing prespecified from exploratory analyses
Harms	19	All important harms or unintended effects in each group
Discussion		
Limitations	20	Trial limitations; addressing sources of potential bias; imprecision; and, if relevant, multiplicity of analyses
Generalizability	21	Generalizability (external validity, applicability) of the trial findings
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence
Other information		
Registration	23	Registration number and name of trial registry
Protocol	24	Where the full trial protocol can be accessed, if available
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders

CONSORT = Consolidated Standards for Reporting Trials.