Management of urinary retention in patients with benign prostatic obstruction: A systematic review and meta-analysis

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Abstract

Background: Practice patterns for the management of urinary retention (UR) secondary to benign prostatic obstruction (BPO) (UR/BPO) vary widely and remain unstandardized. **Objective:** To review the evidence for managing patients with UR/BPO with pharmacological and non-pharmacological treatments included in the European Association of Urology Guidelines on Non-neurogenic Male lower urinary tract symptoms. **Evidence acquisition:** Search was conducted using CENTRAL, MEDLINE, Embase, ClinicalTrials.gov, and WHO ICTRP; searched up to 22 April 2018. This systematic review included randomized control trials (RCTs) and prospective comparative studies. Methods as detailed in the Cochrane Handbook were followed. Certainty of evidence (CoE) was assessed using GRADE approach. **Evidence synthesis:** Literature search identified 2,074 citations. Twenty-one studies were included (qualitative synthesis). The evidence for managing patients with UR/BPO with pharmacological or non-pharmacological treatments is limited. CoE for most outcomes was low/very low. Only α1-blockers (alfuzosin, tamsulosin) have been evaluated in over one RCT. Pooled results indicated that α1-blockers provided significantly higher successful trial without catheter (TWOC) rates compared to placebo [alfuzosin:322/540 (60%) vs 156/400 (39%) (OR 2.28, 95%CI 1.55 to 3.36;participants=940;studies=7;I^2=41%;low CoE); tamsulosin:75/158 (47%) vs 40/139 (29%) (OR 2.40, 95%CI 1.29 to 4.45;participants=297; studies=3;I^2=30%;low CoE)] with rare adverse events. Similar rates were achieved with tamsulosin or alfuzosin [51/87 (59%) vs 45/84 (54%) (OR 1.28, 95%CI 0.68 to 2.41; participants=171;studies=2;I^2=0%;very low CoE)]. Non-pharmacological treatments have been evaluated in RCTs/prospective comparative studies only sporadically.

Conclusions: There is some evidence that usage of α1-blockers (alfuzosin and tamsulosin) may improve resolution of UR/BPO. As most non-pharmacological treatments have not been

evaluated in patients with UR/BPO, the evidence is inconclusive about benefits and harms. **Patient summary:** There is some evidence that alfuzosin and tamsulosin may increase successful trial without catheter rates but little or no evidence on various non-pharmacological treatment options for managing patients with urinary retention secondary to benign prostatic obstruction.

1. Introduction

Urinary retention (UR) is the inability of a patient to completely or partially empty the bladder by voluntary micturition. UR can be acute or chronic. Acute UR (AUR) is defined as a painful, palpable or percussible bladder, when the patient is unable to pass any urine [1, 2]. Chronic UR (CUR) is defined as a non-painful bladder, which remains palpable or percussible after the patient has passed urine [1, 2]. The term implies a significant post void residual urine volume (PVR); a minimum figure of 300mL has been mentioned [1, 2]. Nevertheless, the exact definitions of AUR and CUR remain controversial [3]. The exact incidence of UR in the general population remains unclear with various estimates suggested from 2.2 to 6.8 events/1,000 patient-years [4, 5]. Benign prostatic obstruction (BPO) is considered the most prevalent cause of UR in men [5].

Several α1-adrenoceptor antagonists (α1-blockers) have been tested in patients with AUR to increase successful trial without catheter (TWOC) rates; including alfuzosin [6-8], tamsulosin [6, 9] and silodosin [10], most of which demonstrate a higher success compared to placebo. The alfuzosin in AUR (ALFAUR) study, the largest clinical trial to date, evaluated the role of alfuzosin 10mg OD administrated 2-3 days before TWOC and showed that alfuzosin almost doubled the successful TWOC rate [11]. Since most patients having a successful TWOC have no AUR relapse in the short-term, administration of an α1-blocker before catheter withdrawal is considered a valuable treatment [12]. It has been reported that >80% of patients who did not receive any treatment after an AUR episode were submitted to surgery within 5 years [13]. As a result, pharmacological intervention should be considered not only an aid to increase the successful TWOC chance, but also a mean to reduce AUR recurrence risk, which could lead to further interventions in the long-term. Data from five studies, which evaluated the long-term use of α1-blockers showed that patients receiving α1-blockers had significantly lower risk of

recurrent AUR [14]. The use of 5α reductase inhibitors (5ARIs) as a combination therapy with α1-blockers in AUR treatment is still controversial [15, 16]. Urgent prostatic surgery is another therapeutic option for AUR, however with a higher risk of intra-operative and/or postoperative complications, and mortality compared to elective surgery [17]. Therefore, elective surgery is the treatment of choice for most men who fail TWOC. Increased perioperative morbidity is also associated with presence of indwelling urinary catheter in cases operated after TWOC failure [18].

Management of UR secondary to BPO (UR/BPO) varies widely. Relevant systematic reviews (SRs) are scarce [19-21]. The European Association of Urology (EAU) Non-neurogenic Male lower urinary tract symptoms (LUTS) Guidelines Panel acknowledges the current lack of high certainty evidence (CoE), the growing scientific base, and cites the need to understand more about management options. This SR is a product of this panel and compared the effectiveness of various treatment options currently available for patients with UR/BPO. The objective was to address these questions:

- What are the benefits of treatments for UR (AUR or CUR) in adults with BPO?
- What are the harms of treatments for UR (AUR or CUR) in adults with BPO?

2. Evidence acquisition

Randomized controlled trials (RCTs); quasi-RCTs (QRCTs) and prospective comparative studies were included. Any other studies were excluded, such as: non-comparative studies, retrospective studies, and case series. Studies were included only if:

- UR (AUR or CUR)/BPO was addressed as a study outcome
- A sub-analysis (or post-hoc analysis) on participants presenting with UR (AUR or CUR)/BPO was reported
- Pharmacological treatment had been evaluated in an RCT or QRCT setting

- Non-pharmacological treatment had been evaluated in an RCT, QRCT or prospective comparative setting
- At least one of the primary or secondary outcomes of this SR was reported.

Adult men (≥18 years) with UR (AUR or CUR defined as persistently elevated PVR ≥300mL)/BPO were included. Individuals with UR attributed to drug side effects, pharmacological/non-pharmacological procedures; suspected or confirmed urethral/bladder pathology (such as malignancy, urethral stricture, bladder neck contracture, bladder stones, neurogenic bladder, and infection/inflammation) or prostate cancer were excluded.

The following comparisons of intervention vs comparator were investigated:

Intervention:

Any pharmacological or non-pharmacological treatment included in the EAU Guidelines on Non-neurogenic Male LUTS (2018), as defined below:

- Pharmacological treatment (monotherapy or combination therapy): α1-blockers, 5ARIs, phosphodiesterase 5 inhibitors (PDE5Is), plant extracts (phytotherapy)
- Non-pharmacological treatment: any kind of instrumental intervention (surgical treatment; such as transurethral resection of the prostate (TURP)), including suprapubic catheterization (SPC) or urethral catheterization irrespective of duration prior to TWOC
- Any combination of the above pharmacological and non-pharmacological treatments

Comparator:

- No treatment
- Placebo or sham treatment
- Any pharmacological or non-pharmacological treatment, as defined above (any comparison within intervention was accepted such as comparison of different pharmacological treatments, and/or comparison of different types of catheterization)

We performed a broad search of the Core Outcome Measures in Effectiveness Trials (COMET) database (http://www.comet-initiative.org/) for a core outcome set (COS) using the term "Urology" in the disease category. No directly applicable COS existed for the disease or treatments dealt in this SR. Therefore, the EAU guideline panel reached consensus on what they regarded as most important outcomes for this condition. No patient advocates or other stakeholders were involved in the consensus process.

The primary benefit outcomes were:

- Successful TWOC rate as defined by trials in each single study
- UR (AUR or CUR) recurrence rate following a successful TWOC

The primary harm outcomes were:

- Harms of treatment for UR (AUR or CUR) including any adverse effects reported (such as death, pharmacological/non-pharmacological treatment complications). Surgical complications occurring up to 1 month postoperatively, which were specifically graded according to the modified Clavien classification system [22, 23].

The secondary outcomes included:

- Maximum flow rate (Q_{max}), International Prostate Symptom Score (IPSS) questionnaire results (including Quality of Life (QoL) score) and PVR; absolute values and changes from baseline at each follow up time point
- Specific measures for evaluating non-pharmacological treatment (operation duration, bladder irrigation duration, postoperative catheterization and hospitalization duration)

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was used to assess CoE for each comparison [24]. CoE of outcomes considered critical/important from patients' perspective in decision-making was rated on study design, limitations in study design/execution (risk of bias (RoB)), inconsistency of results, indirectness

of evidence, imprecision and publication bias. Final decision on the selection of the outcomes to be rated was based on a consensus among the SR authors. We used the GRADEpro Guideline Development Tool (GDT) to assess the CoE of the critical and important outcomes. Summary of findings (SoF) tables are available as supplementary material (SM), and following outcomes were chosen, listed according to priority:

- Successful TWOC rate (at 1 month after the intervention)
- Modified Clavien classification system grade ≥3 (at 1 month after the intervention)
- UR (AUR or CUR) necessitating additional pharmacological or non-pharmacological intervention rate following successful TWOC (at 12 months after the intervention)
- IPSS score (at 12 months after the intervention)
- QoL score (at 12 months after the intervention)

The literature was systematically searched in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement [25, 26]. We followed the methodology as detailed in the Cochrane Handbook for Systematic Reviews of Interventions [27]. Search strategies are available (SM 1).

The following electronic databases were searched up to April 22, 2018:

- The Cochrane library databases (Cochrane Central Register of Controlled Trials <March 2018>, Cochrane Database of Systematic Reviews <2005 to April 18, 2018>)
- Medline (Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) <1946 to April 2018>);
- Embase (OvidSP <1974 to April 2018>)

Hand searches of the following trial registers/websites were also performed:

- ClinicalTrials.gov (https://clinicaltrials.gov/)

- World Health Organization International Clinical Trials Registry Platform (WHO ICTRP; http://www.who.int/ictrp/en/)
- For new(er) pharmacological compounds manufacturers' websites, Food and Drug Administration (FDA) and European Medicines Agency (EMA) websites were searched (no restriction on date of publication)

Other potentially eligible studies were searched for using reference lists of included studies, other SRs/health technology assessment reports. Search was supplemented by manually searching the reference list of the EAU Guidelines on Non-neurogenic Male LUTS.

Two review authors (MK, IK) independently scanned the title, abstract content, or both, of every record retrieved to determine which studies should be assessed further, extracted all data and assessed RoB of each included study. Any disagreements were resolved through consensus or by consultation with a third author (CM). RoB in RCTs was assessed using the Cochrane "RoB" assessment tool [27, 28]. "RoB" domains were judged as either low, high, or unclear risk [27]. RoB in non-randomized comparative studies was assessed using all the domains of Cochrane RoB tools [29]. In addition, a list of the six most important potential confounders for harm and benefit outcomes were developed *a priori* with clinical content experts (EAU Non-neurogenic Male LUTS Guidelines Panel): 1) age, 2) severity of LUTS (IPSS score), 3) prostate volume, 4) active and previous medical treatment for BPO, 5) prior history of UR and 6) history of prostatic infection. When at least two included trials were available for comparison of a given binary/dichotomous/categorical benefit or harm outcome, data were expressed as odds ratio (OR) with 95% confidence interval (CI) and p value where available. For continuous outcomes measured on the same scale, the intervention effect was estimated using mean difference (MD; (95%CI)). Meta-analysis was performed where there was more than one RCT reporting the same outcome. In the event of substantial clinical/methodological heterogeneity, trial results

were not reported as pooled effect estimate. Heterogeneity was identified by visually inspecting forest plots and by using a standard Chi² test with a significance level of α=0.1. In view of the low power of this test, I² statistic was also considered, which quantifies inconsistency across trials to assess heterogeneity impact on the meta-analysis [30]. Heterogeneity was dealt as suggested in the Cochrane Handbook for Systematic Reviews of Interventions [27].

The protocol of the present SR was published on PROSPERO (SM 2).

3. Evidence synthesis

A total of 21 studies (18 RCTs [6-11, 31-42] and three prospective comparative studies [43-45]) were included. Figure 1 illustrates literature flow. Table 1 presents baseline characteristics of included studies. RoB assessment is illustrated in Fig. 2.

3.1 Pharmacological treatments

Among the pharmacological treatments included in the EAU Guidelines on Non-neurogenic Male LUTS, only α1-blockers (alfuzosin, tamsulosin, silodosin, doxazosin) and the PDE5I sildenafil have been evaluated for treating patients with UR/BPO in RCTs. No RCT addressing results on any other pharmacological treatment (monotherapy or combination therapy) included in the EAU Guidelines on Non-neurogenic Male LUTS such as 5ARIs (finasteride, dutasteride) was detected.

Alfuzosin was compared to placebo in seven RCTs [6-8, 11, 31, 34, 38]. Pooled results indicated that alfuzosin provided significantly higher successful TWOC rates compared to placebo; 322/540 (60%) vs 156/400 (39%) (OR 2.28, 95%CI 1.55 to 3.36; participants=940;studies=7;I^2=41%;low CoE; Fig. 3). Adverse events were generally rare, most commonly including dizziness, headache and orthostatic hypotension, without difference between arms. Tamsulosin was compared to placebo in three RCTs [6, 9, 34]. In two of them, patients were randomized to three arms (tamsulosin vs. alfuzosin vs. placebo) [6, 34]. Pooled

results indicated that tamsulosin provided significantly higher successful TWOC rates compared to placebo; 75/158 (47%) vs 40/139 (29%) (OR 2.40, 95%CI 1.29 to 4.45;participants=297;studies=3;I^2=30%;low CoE; Fig. 4) but similar rates compared to alfuzosin; 51/87 (59%) vs 45/84 (54%) (OR 1.28, 95%CI 0.68 to 2.41; participants=171;studies=2;I^2=0%;very low CoE). Tamsulosin was also compared to tamsulosin/alfuzosin combination in one RCT [33] and tamsulosin/sildenafil combination in another RCT [37]. No difference between monotherapy vs tamsulosin/alfuzosin combination was detected regarding successful TWOC rates; 11/35 (31%) vs 14/35 (40%) (OR 0.69, 95%CI 0.26 to 1.84;participants=70;studies=1;very low CoE). Most common adverse events in the combination arm included dizziness, headache and retrograde ejaculation, which were not significantly higher than those in the monotherapy arm [33]. Tamsulosin/sildenafil combination was also similar to monotherapy regarding successful TWOC rates; 41/50 (82%) vs 37/51 (73%) (OR 1.46, 95%CI 0.66 to 3.25;participants=101;studies=1;very low CoE) [37]. Three-day vs 7-day tamsulosin treatment for AUR was compared in one RCT [32]. No significant difference in successful TWOC rates; 18/30 (60%) vs 21/30 (70%) (OR 0.64, 95%CI 0.22 to 1.87;participants=60;studies=1;very low CoE). Silodosin was compared to placebo in one RCT, showing a significantly higher successful TWOC rate at 3 days: 23/30 (77%) vs 11/30 (37%) (OR 5.68, 95%CI 1.84 to 17.5;participants=60;studies=1;very low CoE) [10]. Silodosin was also compared to tamsulosin in one RCT showing no significant differences in successful TWOC rates: 48/80 (60%) vs 54/80 (68%) (OR 1.44, 95%CI 0.76 to 2.71;participants=160;studies=1;very low CoE) or complication rates between arms [35]. Doxazosin was compared to no medication in one RCT showing no difference in successful TWOC rates: 13/22 (59%) vs 13/24 (54%) (OR 1.22, 95%CI 0.38 to 3.93;participants=46;studies=1;very low CoE) [36].

3.2 Non-pharmacological treatments

Very few non-pharmacological treatment options included in the EAU Guidelines on the management of Non-neurogenic Male LUTS have been evaluated for managing patients with UR/BPO in RCTs/prospective comparative studies. None of them has been evaluated in more than one trial. An international multicentre RCT evaluated bipolar TURP (B-TURP) vs monopolar TURP (M-TURP) in 279 patients with BPO [40, 46-48]. A sub-analysis [46, 47] and post hoc analysis (SM 3) on patients presenting with UR (B-TURP: n=50; M-TURP: n=63) revealed no difference between arms either for successful TWOC rates: 47/50 (94%) vs 57/63 (90%) (OR 1.65, 95%CI 0.39 to 6.95;participants=113;studies=1;low CoE) or for any of the outcomes of interest of this SR. In a RCT comparing transurethral microwave thermotherapy (TUMT) to TURP or open prostatectomy in patients with UR, no difference was detected in successful TWOC rates between arms: 48/61 (79%) vs 52/59 (88%) (OR 0.58, 95%CI 0.22 to 1.52;participants=120;studies=1;very low CoE) [41]. More complications were seen in TURP/enucleation arm. The efficacy of bladder training before catheter removal was evaluated in one RCT on patients with a first episode of AUR secondary to BPO randomized to pharmacological treatment (combination of tamsulosin 0.2mg/finasteride 5mg OD) with free catheter drainage for 7 days (n=405) or pharmacological treatment combined with bladder training (n=440) prior to TWOC [42]. Similar successful TWOC rates: 190/405 (47%) vs 187/440 (43%) (OR 0.84, 95%CI 0.64 to 1.10;participants=840;studies=1;moderate CoE) and adverse event rates were observed in both arms. Transurethral catheterization vs SPC in patients with AUR was assessed in a prospective comparative study [44]. Thirty patients received transurethral catheterization and 56 patients received SPC (12F Cystofix). Patients were followed up for 3 years. TWOC failure was observed in seven out of 11 patients (64%) in the transurethral group vs seven out of 22 patients (32%) in the SPC group. Complication rates

were notably higher in the transurethral group (urinary tract infections (UTIs): 12 out of 30 patients; 40% vs 10 out of 56 patients;18% and urethral strictures: five out of 30 patients; 17% vs none out of 56 patients;0.0%). Dislodgement was the only complication repeatedly associated with SPC;13 patients (23%;11 of these patients needed catheter replacement) vs one patient (3.4%), potentially necessitating a more secure form of catheter fixation such as a Foley catheter placement through a suprapubic introducer. Finally, our search criteria revealed an old study from 1993, comparing prostatic spiral (Uromed) to prostatic stent (Urolume) regarding effectiveness and complications [43]. Detailed results are available as SM 3-4. SoF tables summarizing CoE assessment based on the GRADE approach are available as SM 5.

4. Discussion

The evidence for managing patients with UR/BPO with pharmacological or non-pharmacological treatments is limited. CoE for most outcomes was low or very low. All selective α1-blockers (alfuzosin, tamsulosin and silodosin) appear to be superior to placebo in terms of successful TWOC rates after a short period of catheterization [6, 7, 9-11, 31, 34, 38]. In contrast, no benefit has been revealed with the use of the non-selective α1-blocker doxazosin and adding sildenafil to tamsulosin does not offer additional benefit compared to tamsulosin monotherapy but these studies are under powered, CoE is very low and therefore no definite conclusions can be drawn for these comparisons [36, 37]. Pooled results indicate that alfuzosin and tamsulosin monotherapy provide significantly higher successful TWOC rates compared to placebo with rare adverse events. Similar successful TWOC rates are achieved with alfuzosin or tamsulosin. Non-pharmacological treatments have been evaluated in RCTs/prospective comparative studies only sporadically.

B-TURP and TUMT have both been tested against M-TURP and found to have comparable efficacy/safety for the management of patients with UR according to the authors of these studies

[40, 41, 46-48] but this conclusion should be interpreted with caution. SPC appears to safeguard against some of the potential complications of urethral catheterization such as UTI and urethral stenosis, allowing assessment of spontaneous voiding and avoiding re-catheterization after a failed attempt [44]. Although it has been suggested that SPCs might be associated with lower rates of UTI and urethral stricture formation, less patient discomfort, and easier management; a Cochrane SR failed to demonstrate lower risk of symptomatic UTIs with use of SPC [49]. Three-day rather than 7-day period of catheterization after a first episode of AUR in addition to α1-blocker treatment should be preferred since longer catheterization times increase the complication rates without increasing significantly TWOC success [32]. A short period of intermittent self-catheterization might be beneficial to maximize recovery of bladder function before TURP and should be preferred over indwelling catheterization in case of delayed surgery as it is associated with less infectious complications [32, 36].

A SR on the management of AUR including pharmacological and non-pharmacological treatment options, recommended use of α1-blockers before TWOC, discouraging emergency operative management [21]. SPC over indwelling catheter use was debatable and catheterization duration was controversial but <3 days appeared to be a safe option in avoiding catheterization-related complications [21]. Although TURP remained the gold standard, there was emergence of newer operative management utilizing laser techniques [21]. Nevertheless, conclusions were limited due to low CoE [21].

In another SR, the effectiveness and comparative effectiveness of pharmacological and non-pharmacological treatments for CUR were evaluated [19]. A total of 11 studies (RCTs and prospective cohort studies) enrolling patients with CUR were included. Results were analyzed by etiology: obstructive, non-obstructive, and mixed populations/unknown causes. Only three studies addressed obstructive causes of CUR. Low quality evidence suggested that TURP and

TUMT achieved similar improvements in successful TWOC rates at 6 months post-treatment. Evidence was insufficient to draw conclusions regarding other outcomes. Evidence for other treatment comparisons for CUR from obstructive causes was insufficient to conclude that one treatment was more effective than the comparison. Evidence on harms was inconsistently reported across all interventions, and no differences were detected across treatment groups; however, studies were not adequately powered to detect differences in harms across groups. Further studies of patients with CUR are needed.

A Cochrane SR assessed α1-blocker effectiveness on successful resumption of micturition following removal of urethral catheter after an episode of AUR in men [20]. Nine RCTs were included. There was moderate CoE to suggest that successful TWOC rates favored α1-blockers over placebo. The incidence of recurrent AUR was lower in groups treated with α1-blockers. CoE was moderate favoring alfuzosin, tamsulosin and silodosin, but not doxazosin. Of the trials mentioning adverse effects, there was not enough information to detect statistically significant differences between groups and CoE was low. Overall, adverse effect rates were low for both placebo and α1-blockers [20].

4.1 Strengths and limitations of this SR

The major strengths are:

- Performed a comprehensive literature search
- Adopted a robust/transparent methodological approach based on Cochrane Handbook
- Assessed CoE with the GRADE approach

The principal limitations are:

- Although every effort was made following strict/specific trial exclusion criteria to exclusively include trials summarizing results from individuals with UR/BPO, the slight possibility of including few patients with neurological/bowel conditions-/detrusor

underactivity-associated UR or even few patients without (urodynamically proven) BPO cannot be completely ruled out since access on raw individual patient data was not possible

- Significant heterogeneity among identified studies
- Included studies had a relatively small number of participants, short follow up and methodological flaws with inadequate reporting. Although authors were contacted for information whenever needed, the majority did not reply as usual in real life. Therefore, following the guidelines of the Cochrane Handbook, many RoB domains were judged as unclear i.e. insufficient information to permit judgment.

4.2 Recommendations for the future research:

- Several contemporary non-pharmacological treatment options included in the EAU Guidelines on the Management of Non-neurogenic Male LUTS were not assessed in this SR based on the inclusion criteria. For example, no comparative studies evaluating holmium, greenlight or thulium laser were detected. This represents a significant gap in the literature. Such a lack of evidence needs to be addressed by future studies since the subpopulation of UR patients is unique, harvesting specific perioperative risk factors.
- Further studies on CUR are needed as well as on 5ARIs after successful TWOC would be logical-as these, and not α1-blockers, have been shown to reduce AUR rates.
- Previous UR is a well-established risk factor for ongoing AUR episodes. Older data indicated that only 16% of patients presenting with UR had remained catheter-free for a period of 5 years [13]. According to the EAU Guidelines on the Management of Non-neurogenic Male LUTS, surgical treatment is usually required when patients have experienced among others recurrent/refractory UR or overflow incontinence (absolute operation indication, need for surgery) [50]. Nevertheless, future studies which will help

to reliably identify which patients could respond to prolonged medical treatment and which should be scheduled for prompt or elective surgery are deemed necessary.

- The optimum treatment management for frail patients with significant comorbidities in the long-term remains poorly documented, at least from the respect of studies directly comparing different treatment modalities (e.g. surgery vs long-term catheterization). Future research should focus on this area.
- The observed heterogeneity of TWOC success definitions among studies has not only important impact on the assessment of treatment outcomes but also renders adoption of a universally-accepted definition of TWOC success necessary in future studies.
- CoS should be developed for UR/BPO, by following the COMET initiative.
- Future studies should be adequately powered/follow the principle/recommendation of Consolidated Standards of Reporting Trials (CONSORT) statement.

5. Conclusions

The evidence for managing patients with UR/BPO with pharmacological or non-pharmacological treatments is limited. CoE is generally low. There is some evidence that usage of α1-blockers (alfuzosin and tamsulosin) may improve resolution of UR/BPO. As most non-pharmacological treatments have not been evaluated in patients with UR/BPO, the evidence is inconclusive about their benefits and harms.

Legends

Figure 1. PRISMA Flow diagram. Citations in conference abstract form and those written in non-English language were excluded.

Figure 2. Risk of Bias assessment of included studies (Red: High risk of bias; Yellow: Unclear risk of bias; Green: Low risk of bias). A) RCTs. B) non-RCTs prospective comparative studies)

Figure 3. Alfuzosin vs placebo; Successful TWOC rate at TWOC

Figure 4. Tamsulosin vs placebo; Successful TWOC rate at TWOC

Supplementary Material 1. Appendix 1: Literature search strategy

Supplementary Material 2. PROSPERO protocol (Protocol number: CRD42017077152) that includes detailed information about how the SR process was handled; including data extraction, data analysis, data synthesis, and sub-group analysis.

Supplementary Material 3. M-TURP vs B-TURP in catheterized patients (Tables 2-4)

Supplementary Material 4. Forests plots showing all pooled estimates of effects calculated in this SR (at least two RCTs included)

Supplementary Material 5. Summary of findings tables (all comparisons)

Abbreviations

5ARI: 5α reductase inhibitor

ALFAUR: Alfuzosin in Acute Urinary Retention

AUR: Acute Urinary Retention

B-TURP: Bipolar Transurethral Resection of the Prostate

BPO: Benign Prostatic Obstruction

CI: Confindence Interval

CoE: Certainty of Evidence

COMET: Core Outcome Measures in Effectiveness Trials

CONSORT: Consolidated Standards of Reporting Trials

COS: Core Outcome Set

CUR: Chronic Urinary Retention

EAU: European Association of Urology

EMA: European Medicines Agency

FDA: Food and Drug Administration

GDT: GRADEpro Guideline Development Tool

GRADE: Grading of Recommendations Assessment, Development, and Evaluation

IPSS: International Prostate Symptom Score

LUTS: Lower Urinary Tract Symptoms

M-TURP: Monopolar Transurethral Resection of the Prostate

MD: Mean Difference

OD: Once Daily

OR: Odds Ratio

PDE5I: Phosphodiesterase 5 Inhibitor

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses

PVR: Post void Residual Urine Volume

Q_{max}: Maximum Flow Rate

QoL: Quality of Life

QRCT: Quasi-Randomized Control Trial

RCT: Randomized Control Trial

RoB: Risk of Bias

SM: Supplementary Material

SoF: Summary of Findings

SPC: Suprapubic Catheterization

SR: Systematic Review

TUMT: Transurethral Microwave Thermotherapy

TURP: Transurethral Resection of the Prostate

TWOC: Trial Without Catheter

UR: Urinary Retention

UR/BPO: Urinary Retention secondary to Benign Prostatic Obstruction

UTI: Urinary Tract Infection

WHO ICTRP: World Health Organization International Clinical Trials Registry Platform

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