

DISCONTINUATION OF ALPHA-BLOCKER THERAPY IN MALE LOWER URINARY TRACT SYMPTOMS: A SYSTEMATIC REVIEW

Hypothesis / aims of study

Alpha-blockers are the cornerstone for the medical treatment of male LUTS [1]. Despite the positive recommendation in all relevant guidelines, the efficacy of these drugs has been debated [2]. The Dutch general practitioners guideline *Male LUTS* recommends the discontinuation of α -blockers after a successful period of treatment for 3 to 6 months [3]. No evidence is provided to support that recommendation. The 2015 EAU guideline *Treatment of Non-neurogenic Male LUTS* recommends that the discontinuation of the α 1-blocker after six months might be considered in men with moderate LUTS, who are treated with combination therapy [1]. This recommendation is based on one randomised controlled trial and one open label study. In this study, we systematically reviewed the literature for studies evaluating the effect of discontinuation of α -blockers in uncomplicated male LUTS. We were particularly interested in the effect of discontinuation on symptom severity and urinary flow rates.

Study design, materials and methods

A systematic review of the literature was conducted according to PRISMA guidelines. The review protocol was registered at the PROSPERO database (number blinded to allow anonymous review of abstract).

On January 15th 2016, The PUBMED, EMBASE and COCHRANE databases were searched without limitations on study design or time limits. The following search terms were used:

Adrenergic alpha blockers [MeSH] AND (LUTS OR BPH OR lower urinary tract symptoms OR benign prostate hypertrophy OR benign prostate enlargement) AND (discontin* OR interrup* OR cessa* OR stop* OR withdra* OR intermit*). We included all studies in which the discontinuation of α -blocker treatment in men with LUTS was assessed with at least one of the following outcomes: symptom score (International Prostate Symptom Score [IPSS], or other), quality of life outcomes, uroflowmetric assessment, post voided residual urine volume (PVR).

Two reviewers independently selected the studies and extracted all data; in case of disagreement consensus was found. Risk of bias was assessed using the Cochrane Collaborations tool for assessing risk of bias.

Results

We included 16 studies out of 876 potential publications. Nine studies (with 1,440 patients) reported on α -blocker monotherapy discontinuation (2 double-blind RCTs, 3 open label RCTs and 4 cohort studies). Seven other studies (with 1,148 participants) reported on discontinuation of an α -blocker following combination of α -blocker and 5- α -reductase inhibitors therapy (1 blinded RCT, 4 open label RCTs and 2 cohort studies). All studies were performed in secondary or tertiary care centres. The 10 RCTs are further discussed. The quality of the 10 RCTs was generally poor, with high risk of selection bias, performance bias and detection bias (Figure 1).

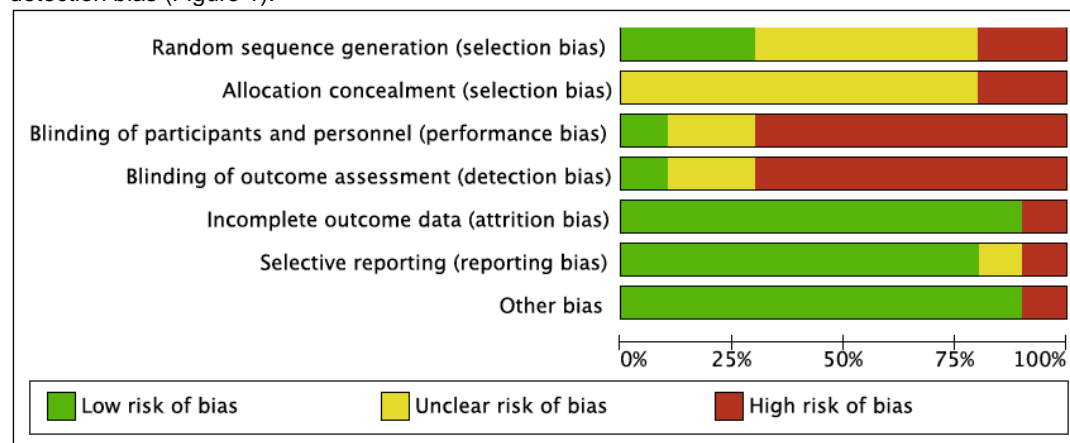


Figure 1. Quality assessment of the 10 randomised controlled trials according to Cochrane Tool

Pooling of data was possible for IPSS outcomes and urinary flow rates (Q_{max}) at 3 and 6 months after discontinuation. At 3 months, men who continued α -blocker treatment had lower IPSS scores than those who discontinued (3 studies, 157 participants): mean difference (CI95%) -3.65 (-5.04, -2.25). At 6 months (4 studies, 226 participants) this difference was -3.25 (-5.74, -0.76).

At 3 months (3 studies, 157 participants), Qmax did not differ between discontinuation and continuation groups 1.20 ml/sec (-1.10, 3.50). At 6 months, in men who were on combination therapy, discontinuation of α -blocker therapy did not result in a change in Qmax, when compared to men who continued therapy (See Figure 2).

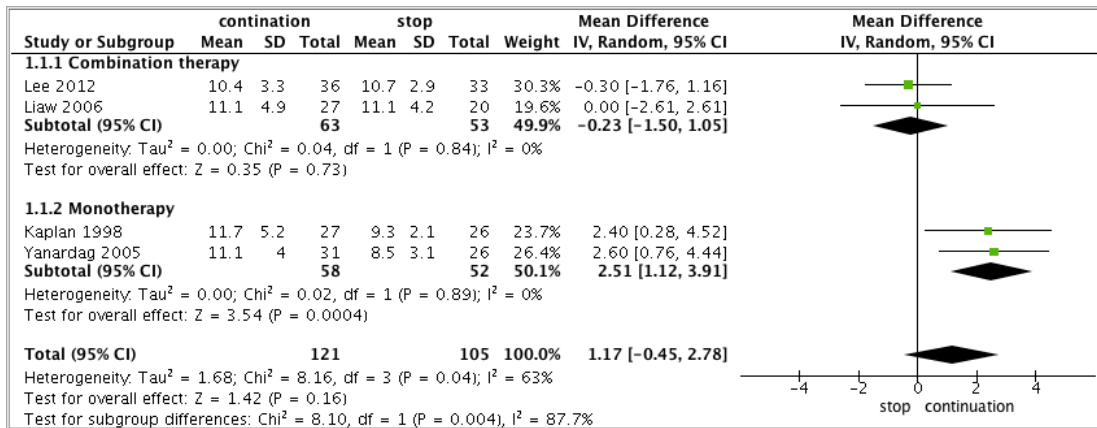


Figure 2. Mean difference in urinary flow rate 6 months after discontinuation of α -blocker therapy

Interpretation of results

Only a small number of studies were found on the effect of (dis)continuation of α -blocker use, and only short-term outcomes are reported. The methodological quality of these studies was generally poor, especially with respect to selection, randomisation and blinding.

Mean difference in symptom scores was 3.65 and 3.25 at 3 and 6 months, respectively. This difference is around the effect that patients may note as 'slight change'.

Differences in Qmax were noted in men who discontinued α -blocker monotherapy, but not in those on combination therapy.

Concluding message

Discontinuation of α -blocker therapy results in a slight symptom deterioration, when compared to continuation of treatment. This supports both the Dutch GP guideline *Male LUTS* [3], as well as the EAU guideline *Treatment of Non-neurogenic Male LUTS* [1]. We believe, however, that strong conclusions cannot be drawn, because only a few studies of generally poor methodological quality were available, reporting on short-term outcomes only.

(Level of Evidence 1a).

References

1. Gratzke C, et al. EAU guidelines on the assessment of non-neurogenic male lower urinary tract symptoms including benign prostatic obstruction. *Eur Urol*. 2015;67:1099-109.
2. Blanker MH, et al. Measuring symptomatic relief in men with lower urinary tract symptoms. *BMJ*. 2014;349:g6664.
3. Blanker MH, et al. Summary of the NHG practice guideline 'Lower urinary tract symptoms in men'. *Ned Tijdschr Geneesk*. 2013;157(18):A6178.

Disclosures

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