Phosphodiesterase 5 inhibitors for lower urinary tract symptoms secondary to benign prostatic hyperplasia: a systematic review

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CRD summary
The review concluded that phosphodiesterase-5 inhibitors used in the clinical setting could significantly improve lower urinary tract symptoms, erectile function, and quality of life in men with benign prostatic hyperplasia, but that further research is needed. The review had some methodological problems and data limitations, which limit the reliability of the authors’ conclusions and recommendations.

Authors’ objectives
To determine the effectiveness of phosphodiesterase-5 inhibitors for lower urinary tract infections in men with benign prostatic hyperplasia.

Searching
MEDLINE and the Cochrane Library were searched, with no year limitations, for articles in any language. Search terms were reported.

Study selection
Randomised controlled trials (RCTs) that compared phosphodiesterase-5 inhibitors versus placebo in men with benign prostatic hyperplasia suffering from lower urinary tract symptoms were eligible for inclusion. Trials that compared phosphodiesterase-5 inhibitors versus alpha blockers or that used a combination of both were excluded.

The primary outcome was the change from baseline in the International Prostate Symptom Score (I-PSS). Secondary outcomes were quality of life, maximum urinary flow rate, and the International Index of Erectile Function Erectile Function domain.

The included trials studied the phosphodiesterase-5 inhibitors sildenafil (50 to 100mg), tadalafil (2.5 to 20mg) and vardenafil (10mg) versus placebo in patients aged 45 years and over. Most trials only included men who had benign prostatic hyperplasia lower urinary tract symptoms for at least six months. The I-PSS score was at least 12 (where reported).

Two reviewers performed study selection, and disagreements were resolved by consultation with a third reviewer.

Assessment of study quality
Trial quality was assessed using the Jadad scale, which appraised randomisation, blinding, and withdrawals/drop-outs to give a maximum score of 5 points. Trials that scored less than 3 were deemed poor quality. The Consort statement was also used.

The authors did not state how many reviewers performed quality assessment.

Data extraction
Data were extracted on primary and secondary outcomes.

The authors did not state how many reviewers extracted data.

Methods of synthesis
A narrative synthesis was presented. Statistical heterogeneity was assessed using $I^2$ and Cochran's Q test.

Results of the review
Four RCTs were included in the review (n=1,928 patients). The trial sample size ranged from 222 to 1,056 patients. The quality of the included data was variable: one trial scored 5 out of 5 points, one scored 4 points and two scored 3 points on the Jadad scale. Individual trials were analysed on an intention-to-treat basis. Trial duration ranged from eight...
to 12 weeks.

All trials found statistically significantly improved International Prostate Symptom Scores (I-PSS) compared with placebo (I-PSS range –2.8 to –6.32 with phosphodiesterase-5 inhibitor; I-PSS range –1.2 to –3.6 with placebo).

All trials also found a statistically significant improvement in quality of life measures and erectile function with phosphodiesterase 5 inhibitors compared with placebo.

All trials showed no difference in maximum urinary flow rate.

There was significant substantial heterogeneity when attempting to pool trials ($I^2=96\%$).

**Authors' conclusions**

Phosphodiesterase 5 inhibitors used in the clinical setting could significantly improve lower urinary tract symptoms, erectile function, and quality of life in men with benign prostatic hyperplasia, but further research is needed.

**CRD commentary**

Inclusion criteria for the review were broadly defined. Two relevant data sources were searched with no language restrictions. Publication bias was not assessed and could not be ruled out. Attempts were made to reduce reviewer error and bias during study selection, but it was not clear if the same methodology was employed for data extraction or quality assessment.

Quality assessment indicated that the included trials were of a moderately good to high quality, although specific quality issues were not fully discussed. However, many of the trials had relatively small sample sizes, and only four trials were found. Trials were narratively synthesised due to the high level of statistical heterogeneity detected when attempting to pool them, which appeared reasonable. However, grouping of trials by outcome and/or drug would have aided interpretation.

The review had some methodological problems and data limitations, which limit the reliability of the authors’ conclusions and recommendations.

**Implications of the review for practice and research**

**Practice:** The authors stated that phosphodiesterase-5 inhibitors could be an acceptable alternative or adjunctive treatment for patients presenting with lower urinary tract symptoms secondary to benign prostatic hyperplasia and erectile dysfunction.

**Research:** The authors stated that further research is needed to understand the physiological and pharmacological actions of phosphodiesterase-5 inhibitors in prostate, urethra, and bladder tissues. Trials should adopt similar inclusion criteria, methodology and outcome measures, and should also have a larger number of patients and longer follow-up period. Trials comparing the effectiveness and costs of the treatment with a daily phosphodiesterase-5 inhibitor versus treatment with a daily alpha blocker associated with an on-demand phosphodiesterase-5 inhibitor would likely be the best design.

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