Silodosin is effective for treatment of LUTS in men with BPH: a systematic review

CRD summary
The review concluded that silodosin was effective for lower urinary tract symptoms in men with benign prostatic hyperplasia (non-malignant prostate enlargement), but that the incidence of retrograde ejaculate was higher than with placebo or tamsulosin. The authors appropriately acknowledged that the small volume of short-term evidence of unknown quality may weaken the reliability of their findings, which seems appropriate.

Authors' objectives
To evaluate the efficacy and safety of silodosin for lower urinary tract symptoms in men with benign prostatic hyperplasia.

Searching
PubMed, EMBASE (from inception up to December 2011) and The Cochrane Library (2011, Issue 12) were searched. Search terms were reported. Reference lists of retrieved articles were examined. The search was not restricted by publication year or language.

Study selection
Randomised controlled trials (RCTs) that compared silodosin versus placebo or other medical treatments for lower urinary tract symptoms in men with benign prostatic hyperplasia were eligible for inclusion. Randomised crossover trials were excluded. Outcome measures of interest were the International Prostate Symptom Score (IPSS), overall quality of life (QoL) score, peak urine maximum flow rate (Qmax) and quality of life specifically related to urinary symptoms and adverse effects.

All the included trials used 8mg of silodosin; comparators were placebo or tamsulosin (0.2mg). Trials were conducted in Europe, USA and Asia. All trials were of 12 weeks' duration. The mean age of participants ranged from 64.6 to 67.5 years.

Two reviewers independently selected relevant studies; any disagreements were resolved by consultation with a third reviewer.

Assessment of study quality
Trial quality was assessed using the Cochrane Risk of bias tool.

Two reviewers independently assessed study quality.

Data extraction
Data were extracted to calculate risk ratios for dichotomous outcomes and mean difference for continuous outcomes, each with 95% confidence intervals.

Two reviewers independently extracted the data.

Methods of synthesis
Pooled risk ratios, mean differences and their corresponding 95% confidence intervals were calculated using a fixed-effect (where there was no evidence of heterogeneity) or a random-effects model. Heterogeneity was assessed using $\chi^2$ and $I^2$.

Results of the review
Four RCTs were included in the review (2,504 patients; 1,109 in the silodosin group, 736 in the placebo group and 659 in the tamsulosin group). Randomisation, allocation concealment, selective outcome reporting and other sources of bias were unclear for most of the included trials. All trials were double-blinded.
**Silodosin versus placebo:** The pooled results showed that silodosin was superior in International Prostate Symptom Score (IPSS; MD -2.78, 95% CI -3.42 to -2.14; I²%=0%; three RCTs), quality of life score (MD -0.42, 95% CI -0.71 to -0.13; I²%= 59%; two RCTs) and peak urine maximum flow rate (MD 1.17, 95% CI 0.78 to 1.57; I²%=0%; three RCTs) compared with placebo. The results also showed that patients in the silodosin group felt more satisfaction with the quality of life score for urinary symptoms. However, the incidence of ejaculation disorder was significantly higher in the silodosin group compared with the placebo group (RR 26.11, 95% CI 12.12 to 56.22; I²%=0%; three RCTs). No statistically significant difference in the incidences of headache, dizziness and diarrhoea was found.

**Silodosin versus tamsulosin:** Compared with tamsulosin, silodosin was superior in IPSS (MD -1.14, 95% CI -2.11 to -0.18; I²%=0%; two RCTs) and quality of life score (MD -0.26, 95% CI -0.47 to -0.05; I²%=0%; two RCTs) but inferior for peak urine maximum flow rate (MD -0.85, 95% CI -1.49 to -0.21; I²%=0%; two RCTs). There was no significant difference in the incidence of ejaculation disorder and dizziness between the two groups.

Subgroup analyses of IPSS were also reported.

**Authors’ conclusions**
The meta-analysis suggested that silodosin was an effective therapy for lower urinary tract symptoms in men with benign prostatic hyperplasia, but that the incidence of retrograde ejaculation was higher than with placebo or tamsulosin treatment.

**CRD commentary**
The review question and inclusion criteria were clear. No language or publication restrictions were applied, which reduced potential language and publication bias. Attempts were made to minimise reviewer errors and bias in the review process.

A relevant quality assessment tool was applied; it appeared that the reliability of most trials was unclear. Statistical heterogeneity was assessed and appropriate methods were used to pool the results.

The authors appropriately acknowledged the limitations of their review including the quality of the trials, short duration of follow-up and differing dosage schedules used in different countries.

The authors acknowledged that the small volume of short-term evidence of unknown quality may weaken the reliability of their findings; their conclusion that such limitations will weaken the reliability of the findings seems appropriate.

**Implications of the review for practice and research**
**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that higher-quality, long-term RCTs and studies comparing 8mg silodosin with 0.4mg tamsulosin were needed in the future.

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