Anticholinergic drugs in patients with bladder outlet obstruction and lower urinary tract symptoms: a systematic review
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CRD summary
The authors concluded that there was insufficient evidence to support the use of α-blockers plus anticholinergic agents in patients with voiding symptoms and urodynamically proven detrusor overactivity. Further research is required. The authors' conclusions appear to reflect the limited evidence and are likely to be reliable.

Authors' objectives
To evaluate the effects of anticholinergic drugs, either alone or combined with an α-blocker, in patients with lower urinary tract symptoms (LUTS) due to, or associated with, benign prostatic hyperplasia (BPH), benign prostatic enlargement (BPE) or bladder outlet obstruction (BOO).

Searching
MEDLINE, EMBASE and Web of Science were searched in February 2006; the search terms were reported. In addition, the Cochrane Database of Systematic Reviews, reference lists of selected studies and abstracts of the annual meetings of three specified associations (2000 to 2005) were screened.

Study selection
Although inclusion criteria were not explicitly specified, it was clear that studies that evaluated anticholinergic drugs, alone or in combination with an α-blocker, in patients with LUTS due to BPH, BPE or BOO were eligible for inclusion. Studies in patients with neurogenic voiding dysfunction or overactive bladder syndrome without BPH, BPE or BOO were excluded, as were those of paediatric patients.

Comparative studies in the review compared anticholinergic agents (propiverine or tolterodine) in combination with an α-blocker (tamsulosin or doxazosin) with the α-blocker alone, or compared the anticholinergic with placebo, in patients with detrusor overactivity and BOO. The duration of comparative studies ranged from 1 to 3 months. Case series evaluated anticholinergic agents (propiverine or tolterodine), either alone or combined with an α-blocker (doxazosin, terazosin or unspecified). The duration of case series ranged from 1 to 7.8 months. The included studies assessed a variety of outcomes including urodynamic measures, quality of life, frequency and adverse effects (details were reported).

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection. [A: Three authors selected the studies.]

Assessment of study quality
Validity was assessed and scored using the Jadad scale, which considers the reporting and handling of randomisation, blinding and withdrawals. In addition, major weaknesses were discussed and the level of evidence provided by each study was graded (from 1a to level 4) using the hierarchy of evidence described by Phillips and Sackett.

The authors did not state how the validity assessment was performed. [A: Two reviewers independently assessed validity and resolved any disagreements by discussion.]

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. [A: One author extracted the data, which a second author checked.]

Methods of synthesis
For each study, major findings were presented in the tables and text. The results of the quality assessment were also
tabulated. The authors also graded the level of recommendation for each study from A to C, as described by the Oxford Centre for Evidence-based Medicine.

Results of the review
Four randomised controlled trials (RCTs; n=617) and 5 prospective case series (n=273) were included. Only one of the RCTs was placebo-controlled.

The highest quality RCT (Jadad score 3, double-blind, placebo-controlled; n=222 with BOO) only reported urodynamic measures. It reported that tolterodine was associated with a statistically significant increase in the volume to first detrusor contraction, maximum cystometric capacity and voiding efficacy and a significant decrease in the Bladder Contractility Index. The authors stated that the other 3 RCTs that evaluated combinations of α-blockers plus anticholinergic agent had ‘significant methodological or clinical drawbacks’. Methodological flaws included small sample sizes, short duration, and lack of reporting of randomisation procedure and blinding. These RCTs reported that combination treatment was associated with significant improvements in urinary frequency (2 studies), quality of life (1 study), reductions in maximum detrusor pressure during micturition and filling (1 study), patient satisfaction (1 study) and average micturition volume (1 study).

Methodological flaws in the case series included small sample sizes and short duration.

Authors' conclusions
Although the results were encouraging, there was insufficient evidence to support the use of α-blockers plus anticholinergic agents in patients with voiding symptoms and urodynamically proven detrusor overactivity. Further research is required.

CRD commentary
The review question was stated but inclusion criteria were not explicitly defined for the study design or outcomes; inclusion criteria for the participants appeared broad. The lack of defined criteria for outcomes has the potential to lead to selective reporting of the results. Several relevant sources were searched and attempts were made to locate unpublished studies. It was not clear whether any language limitations had been applied. The methods used to select studies, assess validity and extract the data were not described in the publication, but additional information provided by the review authors indicated that appropriate methods were used to reduce reviewer error and bias. Validity was assessed using specified criteria, and the results of this assessment reported and taken into account when considering the evidence. In view of the differences between the studies, a narrative synthesis that focused on methodological flaws was appropriate. However, it was not always clear if the reported results represented differences from baseline or differences between treatments. The authors' conclusions appear to reflect the limited evidence and are likely to be reliable.

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

Research: The authors stated the need for well-designed, large, double-blind placebo-controlled RCTs to evaluate the long-term efficacy and safety of anticholinergics agents, either alone or in combination with α-blockers, in patients with LUTS associated with BPH, BPE or BOO.

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