Tolterodine versus oxybutynin in the treatment of urge urinary incontinence: a meta-analysis

Harvey M A, Baker K, Wells G A

Authors' objectives
To compare tolterodine with oxybutynin in the treatment of urge incontinence.

Searching
The following sources were searched: MEDLINE from 1966 to March 2000; EMBASE from 1988 to March 2000; HealthSTAR from 1974 to January 2000; CINAHL from 1982 to December 1999; Current Contents from 1998 to March 2000; the Cochrane Controlled Trials Register (Issue 4, 1999); and Dissertation Abstracts from 1990 to 1996. The search terms included 'tolterodine', 'oxybutynin', 'Detro', 'Detrusitol', 'PNU 200577' and 'PNU 200583'. Specialist journals, meeting abstracts and the bibliographies of the retrieved articles were searched manually. In addition, the relevant pharmaceutical company was contacted for unpublished data.

Study selection
Study designs of evaluations included in the review
Double-blind, randomised or quasi-randomised trials were eligible for inclusion.

Specific interventions included in the review
Comparisons of tolterodine (1 to 2 mg) twice daily with oxybutynin (2.5 to 5 mg) three times daily were included. Studies were excluded if the cotreatments were used 14 days before trial initiation or during the trial.

Participants included in the review
The participants had to be adults (greater than 18 years) complaining of urge urinary incontinence or an association of frequency (more than 8 times per day) and urgency, or they had to have received a diagnosis of detrusor instability.

Outcomes assessed in the review
The primary outcomes were changes in the number of incontinent episodes per 24-hour period, quantity of pad use per 24-hour period, number of micturitions per 24-hour period, and the mean voided volume per micturition. The secondary outcomes were adverse events, urologic measurements and quality of life.

How were decisions on the relevance of primary studies made?
Two reviewers independently applied a priori inclusion criteria. Any disagreements were resolved through discussion and, if necessary, through a mediator.

Assessment of study quality
Validity was assessed using the scale of Jadad et al. (see Other Publications of Related Interest), and the studies were graded according to adequacy of allocation concealment. The authors do not state how the papers were assessed for validity, or how many of the reviewers performed the validity assessment.

Data extraction
The data were extracted by one reviewer and independently checked by another. Aside from the outcomes of interest (noted in a previous field), it was unclear what data were extracted from the included studies.

Methods of synthesis
How were the studies combined?
A weighted treatment effect (fixed-effect model) was calculated across the trials. The results were expressed as the weighted mean difference (WMD) and 95% confidence interval (CI) for continuous outcomes, and as the relative risk (RR) and 95% CI for dichotomous outcomes.

How were differences between studies investigated?
Sources of heterogeneity, when present, were investigated by conducting sensitivity analyses according to publication type and quality score. Subgroup analyses were pre-planned for age and gender.

Results of the review
Four randomised controlled trials were included, but the number of participants involved in these four trials was not reported in the review.

Quality: the quality scores ranged from 3 to 5 out of a maximum of 5. All the studies were graded 'B' (unclear) for adequacy of concealment.

Number of incontinent episodes per 24-hour period: oxybutynin was superior to tolterodine in decreasing the number of episodes (WMD 0.41, 95% CI: 0.04, 0.77).

Quantity of pad use per 24-hour period: only one study reported 24-hour pad use, with the tolterodine group using 1.1 pads less (p<0.0003).

Number of micturitions per 24-hour period: there was no significant difference between the treatments (WMD 0.00; 95% CI: -0.38, 0.38).

Mean voided volume per micturition: oxybutynin was superior to tolterodine; the change in volume voided was -8.24 mL (95% CI: -14.11, -2.38).

Adverse events: fewer patients taking tolterodine had dry mouth (RR 0.54, 95% CI: 0.48, 0.61) and withdrew from the study because of side-effects (RR 0.63, 95% CI: 0.46, 0.88).

Urologic measurements: none of the included studies reported on urodynamic variables.

Quality of life: no data were reported.

Authors' conclusions
Oxybutynin and tolterodine share a similar efficacy profile (although oxybutynin is statistically superior), but tolterodine is better tolerated and leads to fewer withdrawals as a result of adverse events.

CRD commentary
This was a well-conducted review. The study question was stated clearly and was well supported by the inclusion criteria. The search was adequate and attempts were made to identify unpublished material. The validity of the included studies was assessed with a validated methodological instrument. Much of the review process was reported clearly, although the data extracted were not tabulated. Information about the included studies was somewhat limited, and it would have been more useful to have presented the study details in clearly formulated tables.

Nevertheless, this is a well-conducted review and the conclusions follow from the results presented.

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

Research: The authors state that a comparative trial between long-acting oxybutynin and tolterodine would be interesting.
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Other publications of related interest

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.