Drug therapy of urinary urge incontinence: a systematic review

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Authors' objectives
To evaluate the efficacy of drug therapies for urinary urge incontinence.

Searching
MEDLINE (since 1966), EMBASE (since 1989) and the Cochrane Controlled Trials Register were searched to October 2000 for reports published in the English language. The keywords were given.

Study selection
Study designs of evaluations included in the review
Double-blind randomised controlled trials (RCTs) were eligible for inclusion. The included studies were of parallel-group and crossover designs.

Specific interventions included in the review
Studies that compared drug therapy (apart from hormone treatment) with placebo were eligible for inclusion. Studies of terodiline were excluded. The included studies used anticholinergic agents, an agent with anticholinergic and calcium antagonist properties (propiverine), and non anticholinergic agents. The anticholinergic agents were oxybutinin chloride, emepronium bromide, tolterodine, fentonium bromide, trosplum chloride, penthianate and scopolamine. The non anticholinergic agents were prazosin, baclofen, bromocryptine, doxepin, capsaicin, thiphenamil hydrochloride, a combination of emepronium bromide and flavoxate hydrochloride, flavoxate hydrochloride alone and flurbiprofen. The duration of treatment ranged from a single 30-minute treatment to 12 weeks.

Participants included in the review
Studies of patients with urge incontinence, as confirmed by urodynamic assessment, were eligible for inclusion. The included studies were of women or a combination of women and men. The groups of participants included were elderly institutionalised people, postmenopausal women, people with neurological disease or injuries, and men with prostate enlargement.

Outcomes assessed in the review
Studies were eligible for inclusion if they assessed at least one of the following outcomes: subjective improvement reported by the patients, any urodynamic evaluation, and adverse effects. The primary outcomes in the review were patients' report of subjective improvement, bladder stability and adverse events. The secondary outcomes were intended to be the results of urodynamic evaluation, including the number of voluntary and involuntary micturitions, maximum bladder capacity, bladder volume at first sensation or first bladder contraction, maximum detrusor pressure, maximum urine flow and residual urine. The included studies reported these secondary outcomes so inconsistently that it was not possible to tabulate relevant data.

How were decisions on the relevance of primary studies made?
Two or three researchers independently selected the studies and reached consensus.

Assessment of study quality
Validity was assessed by considering the method of randomisation, the number excluded after randomisation, and whether patient compliance was assessed. Two or three researchers independently assessed validity and reached consensus.

Data extraction
Two or three researchers independently extracted the data and reached consensus. Data were extracted on the number...
of patients in the treatment and control group, the study population, patient inclusion and exclusion criteria, treatment regimen, validity criteria, patient outcomes and study exclusions. The odds ratios and 95% confidence intervals were calculated for treatment effects in each study. Studies comparing more than one active agent were counted as separate trials.

Methods of synthesis
How were the studies combined?
The original intent had been to undertake a meta-analysis, but this was not possible due to clinical and statistical heterogeneity (different inclusion and exclusion criteria, different types of drugs and different results) among the studies. Therefore, a narrative synthesis of the studies was undertaken.

How were differences between studies investigated?
The studies were grouped according to the properties of the drug investigated (anticholinergic agents and other) and a narrative synthesis was undertaken.

Results of the review
Thirty-six RCTs (approximately 2,000 patients) were included.

Twelve RCTs reported the method of randomisation and 12 RCTs assessed patient compliance.

Eighteen different drugs were evaluated; 15 drugs were only evaluated in one or two RCTs. Anticholinergic agents (24 RCTs).

Thirteen out of 16 RCTs found that anticholinergic agents increased the rates of subjective improvement; in 5 RCTs the increase was statistically significant. Three out of 4 RCTs found that anticholinergic agents improved bladder stability, but in none of the RCTs was the increase statistically significant. Compared with placebo, anticholinergic agents were found to increase any side-effect in 12 out of 15 RCTs, to increase dry mouth in 20 out of 21 RCTs, and to increase withdrawals due to side-effects in 9 out of 19 RCTs. The most common adverse events other than dry mouth were blurred vision, constipation, dizziness and headache.

Other agents (12 RCTs).

Eight RCTs of other agents reported subjective improvement and 3 RCTs reported bladder stability. Doxepin (tricyclic antidepressant), capsaicin (neurotoxin) and flurbiprofen (prostaglandin synthase inhibitor) significantly increased subjective and/or objective improvement in comparison with placebo. Bromocryptine, prazosin and baclofen also increased subjective and/or objective improvement, compared with placebo, but the increase was not statistically significant. There was no difference between flavoxate and placebo. There were insufficient data to assess propiverine and thiphenamil. The most common adverse events with non anticholinergic agents were nausea and dizziness, dry mouth and blurred vision.

Authors' conclusions
The evidence supported the use of anticholinergic agents as the first choice of drug therapy for urge incontinence.

CRD commentary
The review question was clear in terms of the study design, intervention, participants and outcomes. Several relevant sources were searched and the search terms were stated. Limiting eligible studies to those published in English may have resulted in the omission of other relevant studies. The lack of an attempt to locate unpublished material raises the possibility of publication bias. At least two reviewers selected the studies, assessed validity and extracted the data; this reduces the potential for bias and errors. Validity was assessed using defined criteria and relevant data were extracted and tabulated.

A narrative synthesis of the data was appropriate given the heterogeneity among the studies. Some discussion of the
evidence for specific agents would have been helpful. Only 5 of the 16 RCTs of anticholinergic agents found that active treatment significantly improved outcomes; this does not seem an adequate basis on which to recommend treatment. In addition, reasons for the non significance of the other results were not discussed. The text of the review gave no indication of the size of the treatment effect or rates for adverse events, though such information was accessible in the tables. The authors’ conclusions do not convey the weakness of the evidence base.

Implications of the review for practice and research
Practice: The authors stated that the first choice of drug treatment for urge incontinence is an anticholinergic agent such as oxybutinin or tolterodine. The second choice would be non anticholinergic drugs.

Research: The authors stated that there is a need for basic science research to improve the understanding of the pathophysiology of bladder contractility.

Bibliographic details

PubMedID
12423868

Other publications of related interest
These additional published commentaries may also be of interest. Pannill FC. Review: drugs do not improve symptoms in urinary urge incontinence and may have side effects. Evid Based Med 2003;8:182. Pannill FC. Review: drugs do not improve symptoms in urinary urge incontinence and may have side effects. ACP J Club 2003;139:76.

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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.