Treatment of daytime urinary incontinence in children: a systematic review of randomized controlled trials

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CRD summary
This review assessed interventions for children with daytime urinary incontinence. The review was well conducted, but few relevant studies were found. The authors concluded that there was no evidence in support of any intervention tested and that further research is required. The authors' conclusions are likely to be reliable.

Authors' objectives
To assess the benefits and harms of interventions for children with daytime urinary incontinence.

Searching
MEDLINE (from 1966 to June 2001), EMBASE (from 1988 to June 2001) and the Cochrane Controlled Trials Register (Issue 1, 2001) were searched for studies published in any language; the search terms were stated. Abstracts from conference proceedings were also searched, as were the reference lists in identified studies and the World Health Organization report on the management of childhood bladder dysfunction. Experts in the field were contacted for details of unpublished trials.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion. Parallel group and crossover RCTs were included. The maximum duration of follow-up was 9 months.

Specific interventions included in the review
Studies of any treatment, either alone or in combination with other treatments, were eligible for inclusion. The included studies compared the following treatments: imipramine (25 mg daily) versus placebo; terodiline (12.5 mg twice daily) versus placebo; contingent versus non contingent alarms; biofeedback versus oxybutynin (0.03 mg/kg per day) versus placebo; and biofeedback plus standard treatment (treatment of constipation and prophylaxis with antibiotics) versus standard treatment alone. The duration of the treatment ranged from 8 weeks to 6 months.

Participants included in the review
Studies of children (aged younger than 18 years) with a primary diagnosis of daytime urinary incontinence, with or without nocturnal enuresis, were eligible for inclusion. The participants could have any primary functional bladder problem causing daytime urinary incontinence. Studies of children with an identified organic or structural cause of urinary incontinence or untreated urinary tract infection were excluded. The included studies involved boys and girls aged 5 to 15 years with the urge syndrome, voiding dysfunction or 'daytime wetting'; some studies did not provide the diagnostic category of the participants. The participants were recruited from out-patient clinics, enuresis clinics, health care centres and paediatric renal centres.

Outcomes assessed in the review
The review analysed all outcomes reported in the identified studies. The primary review outcome was the proportion of children with a decrease in the frequency and/or severity of daytime wetting. Other outcomes assessed in the review included functional bladder capacity and adverse effects.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies.
Assessment of study quality
Validity was assessed on the basis of allocation concealment, blinding, completeness of follow-up and intention-to-treat analysis. Two reviewers independently assessed validity and resolved any disagreements through discussion with a third reviewer.

Data extraction
Two reviewers independently extracted the data and resolved any disagreements through discussion with a third reviewer. The extracted data included criteria used to diagnose daytime urinary incontinence, characteristics of the participants and interventions, study design and results.

For crossover RCTs, only data from the pre-crossover period were extracted. For each study, the difference in means and 95% confidence intervals (CIs) from baseline to post-treatment were calculated for continuous outcomes, while the relative risks (RR) and 95% CIs were calculated for dichotomous outcomes. The risk difference (RD) and 95% CI were calculated for adverse effects. Authors of studies with missing or incomplete data were contacted for additional information.

Methods of synthesis
How were the studies combined?
A narrative synthesis of the studies was undertaken. Each study was described in the text, while additional descriptive information was presented in tabular format. The pooled RR and 95% CIs were calculated using data from RCTs of terodiline.

How were differences between studies investigated?
The heterogeneity of the results was assessed by examining plots and using the Q statistic.

Results of the review
Five RCTs (381 children) were included.

The authors pointed out that terodiline has been withdrawn from the market, owing to adverse effects, and that imipramine is no longer used for incontinence because of safety concerns.

The quality of the studies varied. In two RCTs, allocation was adequately concealed. Three RCTs reported analysis on an intention-to-treat basis. Four RCTs reported drop-out rates ranging from 0 to 11%. None of the studies stated that the outcome assessment was blinded. Other methodological problems included inadequately powered studies with small sample sizes and poor definition of the underlying diagnosis.

Imipramine (1 RCT, 27 children): there was no significant difference between imipramine and placebo in maximum functional bladder capacity (no values reported in the RCT, P>0.05).

Terodiline (2 RCTs, 103 children): the meta-analysis showed that terodiline for 4 weeks significantly reduced the proportion of children with daytime wetting, compared with placebo, but there was no improvement in the frequency of wetting. The RR was 0.55 (95% CI: 0.34, 0.88). No significant heterogeneity was detected (P=0.9).

Contingent versus non contingent alarms (1 RCT, 50 children): there was no significant difference between alarms in the proportion of children with persistent wetting. The RR was 0.67 (95% CI: 0.29, 1.56).

Biofeedback (2 RCTs, 201 children): neither RCT found any significant difference between biofeedback and placebo in the proportion of children with no improvement in daytime wetting. The RRs were 0.92 (95% CI: 0.59, 1.43) and 1.10 (95% CI: 0.67, 1.79), respectively. One of the RCTs found no significant difference between biofeedback and oxybutynin in the proportion of children with no improvement in daytime wetting (RR 1.05, 95% CI: 0.65, 1.70).

Oxybutynin (1 RCT): the RCT found no significant difference between oxybutynin and placebo in the proportion of children with no improvement in daytime wetting. The RR was 0.74 (95% CI: 0.26, 2.16). For oxybutynin versus
biofeedback, see above paragraph.

Adverse effects: the RCTs of terodiline and oxybutynin reported adverse effects. Compared with placebo, one RCT found that terodiline significantly increased adverse effects (stomach pain, insomnia, bad temper and dizziness) (RD 0.23, 95% CI: 0.04, 0.41) while the other found it non statistically significantly increased adverse effects (RD 0.08, 95% CI: -0.22, 0.05). The RCT of oxybutynin found non statistically significantly increased adverse effects compared with placebo (RD 0.04, 95% CI: -0.08, 0.16)

**Authors' conclusions**
There was no evidence supporting the use of any intervention in children with daytime urinary incontinence.

**CRD commentary**
This was a well-conducted and clearly presented review. The review question was clear in terms of the study design, intervention, participants and outcomes. Several relevant sources were searched, the search terms were stated, no language restrictions were applied, and attempts were made to locate unpublished material. Two reviewers selected the studies, assessed validity and extracted the data, thus reducing the potential for bias and errors. Validity was assessed using established criteria and methodological limitations in the included studies were discussed in the text of the review. The authors also discussed some of the limitations of the evidence in the text. Given the small number of studies, a narrative synthesis was appropriate. The evidence presented appears to support the authors' conclusions.

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

Research: The authors stated that further adequately powered trials are required to assess the effectiveness of interventions currently in use for children with daytime urinary incontinence. They stated that RCTs are required to compare standard therapy, no intervention or placebo with oxybutynin, newer anticholinergics and bladder management; and that studies should strictly define the group targeted, use standardised methods for measuring outcomes, and report the results separately for children with urgency alone and those with dysfunctional voiding.

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