Intravesical oxybutynin for children with poorly compliant neurogenic bladder: a systematic review

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CRD summary
The review concluded that, whilst intravesical oxybutynin was a potential alternative therapy for children with neurogenic bladder refractory to oral oxybutynin, or those who experience severe side effects with oral oxybutynin, there was insufficient evidence to recommend this treatment. The authors' conclusions are suitably cautious and reflect the limited evidence base.

Authors' objectives
To determine the effectiveness and tolerability of intravesical oxybutynin in children with poorly compliant neurogenic bladder.

Searching
The authors searched MEDLINE, EMBASE, LILACS, the Cochrane Library, CINAHL, ProQuest Nursing and Allied Health Source, and SciELO for English language studies up to July 2007; search terms were reported. Two clinical trials registries (ClinicalTrials.gov and controlled-trials.com) were also searched. Specialised journals and references of relevant articles were handsearched. Corresponding authors and industry representatives were contacted for additional studies.

Study selection
Studies of oxybutynin instilled into the bladder (with or without oral oxybutynin) in children (less than 18 years) with poorly compliant neurogenic bladder, that was refractory to oral oxybutynin or who had experienced severe side effects, were eligible for inclusion in the review. Eligible study designs were randomised controlled trials (RCTs), non-randomised controlled trials, quasi-experimental studies and non-comparative case series. Case controlled studies or studies of intravesical treatment using a drug other than oxybutynin were excluded.

The primary outcome was bladder compliance. Secondary outcomes included maximum bladder capacity, detrusor pressure at maximum bladder capacity, detrusor leak point pressure, neurogenic detrusor overactivity, urinary tract infection, episodes of urinary incontinence and side effects.

In most studies, patients received 10mg oxybutynin daily (range 10 to 20mg/day or 0.1 to 0.2kg/day) instilled into the bladder with a urethral catheter. In most studies, patients used crushed pills diluted in sterile water; one study used a pharmacy prepared oxybutynin solution. Most of the included patients had a clinical diagnosis of myelomeningocele; their mean age ranged from 4.2 years to 9.5 years (range 0.3 to 18), where reported. The duration of studies ranged from three to 36 months.

Two reviewers independently selected studies for inclusion in the review.

Assessment of study quality
Non-comparative studies were evaluated using an instrument developed for the study; specific criteria were not reported. A calibration exercise was conducted beforehand.

Two reviewers independently assessed the quality of the included studies; any disagreements were resolved through discussion with a third reviewer.

Data extraction
Two reviewers independently extracted data in order to calculate weighted mean differences (WMD) with 95% confidence intervals (CIs). Tolerability and side effects were evaluated as functions of compliance with treatment.
Authors were contacted in order to obtain missing information. Any disagreements were resolved through discussion with a third reviewer.

**Methods of synthesis**
Where possible, studies were pooled using a random effects model and summary estimates reported as WMDs with 95% CIs. Visual examination of the forest plot and the $I^2$ statistic were used to assess statistical heterogeneity. Publication bias was assessed based on visual inspection of funnel plots.

**Results of the review**
Eight studies were included in the review (n=263 patients, taken from table 1; range 10 to 67); these were two prospective studies (including one controlled study) and six retrospective case series.

An improvement in mean change in bladder compliance was found with intravesical oxybutynin compared with baseline (7.4mL/cm H$_2$O to 13.8 ml/cm H$_2$O; three studies); maximum bladder capacity (WMD 78mL, 95% CI 55.7 to 103.7; $I^2$=62%) and pressure at maximum bladder capacity (WMD -16cmH$_2$O, 95% CI -22.8 to -10.0; $I^2$=69%; eight studies) were found to improve compared to baseline measurements. The percentage of patients considered continent and improved ranged from 36 to 83% (seven studies). An improvement in urinary tract infection episodes was reported in two studies. Both studies reporting on detrusor leak point pressure found a significant improvement. Detrusor neurogenic overactivity improved in 33 to 77% of patients across the reviewed studies.

The most commonly reported drug side effects were dry mouth, facial flushing, constipation, blurred vision, and orthostatic hypotension or dizziness. Discontinuation of treatment due to side effects was reported in 28 patients (9%), and an additional 38 patients (13%) were reported to have withdrawn due to ‘other causes’.

The funnel plot of pressure at maximum bladder capacity did not suggest evidence of publication bias.

**Authors’ conclusions**
Adjunctive intravesical oxybutynin therapy increased mean maximum bladder capacity and decreased bladder pressure in children with neurogenic bladder. It is a potential alternative treatment for children with neurogenic bladder refractory to oral oxybutynin or those who experience severe side effects. However, the level of evidence of the studies was low and there was insufficient evidence to recommend this treatment for children with neurogenic bladder.

**CRD commentary**
The review question and inclusion criteria were clearly defined. Searches included attempts to locate unpublished studies but were restricted to English language studies, raising the possibility of language bias. Steps were taken to minimise the likelihood of error or bias in the selection of studies, data extraction and assessment of study quality.

Validity of the studies was assessed, but the criteria used were not reported. Characteristics of the individual studies were presented. Where studies were pooled, heterogeneity was assessed but not investigated. Only three studies, with a low level of evidence, reported data on the primary outcome of interest.

The authors’ conclusions are suitably cautious and reflect the limited evidence base.

**Implications of the review for practice and research**
**Practice:** The authors stated that there is insufficient evidence to recommend this treatment for children with neurogenic bladder.

**Research:** The authors suggested that further research using robust study designs, such as RCTs, is needed to assess the efficacy of intravesical oxybutynin in children.

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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.