Neurotoxin treatments for urinary incontinence in subjects with spinal cord injury or multiple sclerosis: a systematic review of effectiveness and adverse effects

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CRD summary
The review concluded that BTX-A may be a treatment option for urinary incontinence in patients with MS or SCI; adverse events limited the applicability of Capsaicin. The ideal patient, dose and interval of use, and the long-term effectiveness were uncertain. Although the authors' conclusions reflected the evidence presented, methodological limitations made the reliability of the conclusions unclear.

Authors' objectives
To evaluate the efficacy and safety of neurotoxin treatments for urinary incontinence in adults with spinal cord injury (SCI) or multiple sclerosis (MS).

Searching
MEDLINE (1966 to 2007), The Cochrane Library and The Cochrane Urinary Incontinence Review Group special registry were searched; search terms were reported. Reference lists of relevant studies and reviews were checked for additional studies. Only studies published in the English language were eligible.

Study selection
Randomised controlled trials (RCTs) in adults with urinary incontinence secondary to SCI or MS were eligible for inclusion. Non randomised trials of BTX-A were also eligible. This abstract would concentrate on the analysis of RCTs due to the classification of a systematic review as a non-randomised study. Patients in the included trials had either SCI (43 per cent) or MS (52per cent) and rarely other spinal disorders (5 per cent). The interventions were Botulinum toxin-A (BTX-A) injected into the detrusor muscle of the urinary bladder, or intravesical instillation of Capsaicin or Resiniferatoxin (RTX). Outcomes of interest included changes in the number of episodes of urinary incontinence and adverse events. The mean or median age of trial participants ranged from 35.3 to 47 years. The duration of the condition at the time of intervention ranged from one to 17.5 years. The average daily urinary incontinence episodes at the baseline ranged from two to 5.5. Study duration ranged from four weeks to 18 months, with five studies of at least 90 days duration.

The authors stated neither how many reviewers screened studies for relevance nor how any discrepancies were resolved.

Assessment of study quality
Validity was assessed based on the quality of concealment of treatment allocation, blinding of interventions, intention to treat analysis and loss of follow up. The authors stated neither how many reviewers performed the assessment nor how any discrepancies were resolved.

Data extraction
Mean differences for continuous data and relative risks (RR) for dichotomous data were calculated, along with their 95% confidence intervals (CI). The authors stated neither how the data were extracted for the review nor how many reviewers performed the data extraction.

Methods of synthesis
The pooled RR or weighted mean difference (WMD) and their 95% CI were calculated using a fixed-effect model, when heterogeneity was not observed. Heterogeneity was assessed using the $X^2$ and $I^2$ tests.

Results of the review
Ten trials (n=288; range 12 to 59) were included; one had cross over design. Seven were reported to be double blinded. Two reported adequate allocation concealment. Eight reported using an intention to treat analysis.
BTX-A significantly reduced the number of daily episodes of incontinence at 24 weeks when compared to placebo (-1.1 episodes for BTX-A and -0.1 episodes for placebo; p=0.019; one RCT, n=59). When compared to RTX, BTX-A significantly reduced the number of incontinent episodes (WMD -1.30; 95% CI: -2.09, -0.51; one RCT; n=25). There was no significant difference in the incidence of adverse events between groups in either trial.

Three out of four trials (n=77) showed that Capsaicin significantly reduced the episodes of incontinence per day at 30 days compared to placebo; two trials were pooled (WMD -3.8; 95% CI: -4.7, -2.9, n=32). One trial showed Capsaicin to reduce the number of incontinence pads per day compared to placebo (four versus 10; p=0.02). Capsaicin therapy was associated with increased risk of pelvic pain (RR 2.07, 95% CI: 1.04, 4.14; three RCTs) and facial flush (RR 2.53, 95% CI: 1.01, 6.31; three RCTs).

When Capsaicin was compared to RTX (two RCTs; n=63). One trial reported a decrease in daily urinary incontinence episodes for both agents, with no significant difference between drugs (number of episodes ranged from 0 to 7 for RTX and 0 to 22 for Capsaicin at 90 days). The other trial reported a reduction in urinary leakages with RTX only (5/10 receiving RTX and 9/10 receiving Capsaicin were using pads at 60 days). The incidence of pelvic pain was significantly greater in the Capsaicin group compared to RTX (RR 3.86; 95% CI: 1.50, 9.92, two RCTs).

When RTX was compared to placebo, there was no significant difference in daily incontinence episodes (two RCTs; n=63). Pelvic pain (39.3 per cent) and autonomic dysreflexia (14.2 per cent) were reported with RTX; no adverse events were reported with placebo.

Authors’ conclusions
BTX-A may be an effective treatment option for the treatment of urinary incontinence in patients with MS or SCI. Capsaicin was superior to placebo, but adverse events limited its applicability. The ideal patient, dose and interval of use, and effectiveness of the agents in the long term were uncertain.

CRD commentary
This review addressed a well-defined question in terms of study designs, participants, interventions and outcomes. The authors searched several relevant sources for published studies. The inclusion of only studies reported in English languages might have resulted in the omission of other relevant studies. It appears that the authors did not make specific searches for unpublished research, which introduced the possibility of publication bias. Some details of the primary studies were provided. It was not clear if the processes for study selection, data extraction and quality assessment were carried out with adequate attempts to minimise errors and bias. Full details of quality assessments of individual trials were not provided. All the included studies were small. Even when studies pooled, the number of participants was small. The results of the tests for statistical heterogeneity were not reported. Although the authors’ conclusions reflected the evidence presented, some of the methodological limitations made the reliability of the conclusions unclear.

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

Research: The authors stated that randomised trials with adequate sample size and long-term follow up were necessary to evaluate BTX-A and other neurotoxin therapies in urinary incontinence secondary to spinal cord injuries and multiple sclerosis.

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