Botulinum toxin type A injection for management of upper limb spasticity in children with cerebral palsy: a literature review

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CRD summary
The authors concluded that high quality evidence was too limited and data too conflicting for the efficacy of botulinum toxin type A for upper limb spasticity in children with cerebral palsy to be supported or refuted. This conclusion was supported by the evidence included in the review; but poor reporting of review methodology means that its reliability cannot be assessed.

Authors' objectives
To assess the outcome of botulinum toxin type A (BTX-A) for the management of upper limb spasticity in children with cerebral palsy (CP).

Searching
The databases MEDLINE and CINAHL were searched to June 2006. Search terms were reported. Only studies published in English as full reports were eligible for inclusion in the review.

Study selection
Studies of children, aged 0 to 19 years with CP were eligible for inclusion. Patients in included studies had spastic hemiplegia, spastic triplegia, spastic quadriplegia, and/or dystonia (where described). Eligible studies assessed the injection of BTX-A into upper limb muscles for the purpose of managing spasticity. Included studies used a variety of injection sites for each target area. The products used were Botox and Dysport. A wide range of doses and dilutions were employed. Interventions before the injections were general anaesthesia, topical anaesthesia and/or oral sedation, and no intervention. Techniques used for localising the injections varied and included electrical stimulation, palpation, and EMG-guidance. No inclusion criteria were stated for study design or outcomes. Included studies were randomised controlled trials (RCTs), prospective uncontrolled studies (case series), and case studies. The comparator treatments for the RCTs were not systematically reported. The included studies reported outcomes of reduction in spasticity at the elbow, the wrist, and in general, using the Ashworth scale, the modified Ashworth scale, and the Tardieu scale. Range of motion (ROM) was also reported using the following measures: active range of motion, passive range of motion, range of motion (Norkin and White Procedure), and web space. Functional gains were assessed using the Quality of Upper Extremity Skills Test (QUEST), the Pediatric Evaluation of Disability Inventory (PEDI), the Melbourne Assessment of unilateral upper limb function (Melbourne Assessment) and a range of specific tests. Adverse events were also reported.

The authors did not state how the papers were selected for the review or how many reviewers performed the selection.

Assessment of study quality
The level of evidence represented by the studies was assessed by two independent reviewers using the recommendations of the American Academy for Cerebral Palsy and Developmental Medicine (AACPDM), which also included an assessment of blinding. Within each level of evidence studies were rated as 'strong', 'moderate', or 'weak' based on the rigour with which the methodology was applied.

Data extraction
The authors did not state how the data were extracted for the review or how many reviewers performed the data extraction.

Methods of synthesis
The studies were combined in a narrative synthesis. Studies were grouped by the outcomes assessed and differences in assessment method and study design and quality were discussed.
**Results of the review**

Sixteen studies were included in the review (n=262), including four RCTs (n=105), of which one was double-blinded, eight case series (n=147) and four case studies (n=10). All the RCTs were rated as strong; all other studies, with the exception of one case series which was rated medium, were considered to be weak.

Spasticity/tone (four RCTs, six case series and two case studies):

There was conflicting evidence on the impact of BTX-A on spasticity/tone. Two RCTs showed significantly lower Ashworth scale scores in the intervention group, but two showed no difference between the groups. Four of the case series showed a significant reduction after treatment but two showed no differences.

ROM (three RCTs, six case series, one case study):

Two RCTs and two case series found significant improvements in ROM, while one RCT and four case series showed no significant benefit.

Functional gains of upper limb:

A wide range of functional outcomes were reported by studies with a high level of clinical heterogeneity. Three RCTs showed significant differences in favour of the BTX-A group in functional activities, while five case series reported improvements relative to baseline. One RCT showed no differences between the groups, while three case series showed no significant improvement following BTX-A treatment.

Adverse events:

The only adverse event reported was a weakening of grip strength in one RCT and one case series.

**Authors’ conclusions**

It was not possible to support or refute the usefulness of BTX-A for management of upper limb spasticity in children with CP due to the limited number of high quality studies and inconsistent results of the included studies.

**CRD commentary**

The review question was clear and the inclusion criteria were defined with respect to population and intervention, but not for outcomes or study design. The authors searched some relevant databases; however, the decision to restrict the review to published studies reported in English may have increased the possibility that some relevant studies were not included in the review. This may have introduced publication or language bias. The authors did not report using methods designed to minimise bias and error in the conduct of the review, with the exception of the validity assessment, and they did not report the detail of this assessment beyond the assignment of studies to levels of evidence. Given the heterogeneity of clinical characteristics and design of included studies, the decision to adopt a narrative synthesis appears appropriate. The failure to report statistical data for results means that it is difficult to fully assess the significance of study results. The authors' conclusions are an accurate reflection of the limited and conflicting evidence but, due to poor reporting of review methodology, their reliability cannot be established.

**Implications of the review for practice and research**

Practice: The authors stated that injections to the long finger flexor muscle or forearm muscles should be carefully planned to prevent grip strength weakness.

Research: The authors stated that further studies are required to determine the optimum dose, dilution volume, method of administration, and selection of target muscles for administration of BTX-A. Such research is also required to determine which patients are suitable for treatment, and the best means of assessing the outcomes of treatment.

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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.