Botulinum toxin B: a review of its therapeutic potential in the management of cervical dystonia

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Authors' objectives
To review the therapeutic potential of botulinum toxin B (BTX-B) in the management of cervical dystonia.

Searching
AdisBase, MEDLINE and EMBASE were searched from 1966. In addition, the reference lists of retrieved studies were searched and relevant pharmaceutical companies were contacted for unpublished evidence.

Study selection
Study designs of evaluations included in the review
The authors do not state any clear inclusion criteria relating to study design. However, all of the included studies were randomised, multicentre, double-blind placebo-controlled trials.

Specific interventions included in the review
Studies were included if the participants received BTX-B. The studies included in the review used doses of 2,500, 5,000 and 10,000 U BTX-B.

Participants included in the review
Studies which included patients with cervical dystonia were selected for the review. The participants were categorised as being either responsive or resistant to botulinum toxin A (BTX-A).

Outcomes assessed in the review
The primary efficacy measure in the included trials was the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS)-Total score (range: 0 to 87) at week 4 after injection. The TWSTRS scale incorporates three subscales: Severity (range: 0 to 35), Disability (range: 0 to 32) and Pain (range: 0 to 20).

The secondary efficacy measures were the TWSTRS-Total scores at weeks 8 and 12, and two visual analogue scale assessments (Patient Global Assessment of Change and Principal Investigator Global Assessment of Change) at week 4. The tertiary outcomes included the TWSTRS-Total score at week 16, the TWSTRS-Severity, -Disability and -Pain scores at week 4, and the Patient Analogue Pain Assessment at week 4.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
No formal assessment of quality was undertaken.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction. Data were extracted on: study details, treatment regimen, number of patients, and outcomes. The latter included the TWSTRS-Total score (at baseline and reduction from baseline), the Patient Global Assessment of Change score, the Principal Investigator Global Assessment of Change score, and the Patient Analogue Pain Assessment (at baseline and reduction from baseline).
Methods of synthesis
How were the studies combined?
A narrative synthesis was undertaken.

How were differences between studies investigated?
Heterogeneity between the studies was not formally assessed. Some characteristics of the included studies were presented in the text and tables of the review.

Results of the review
Three randomised controlled trials (RCTs; n=308) were included.

In two of the RCTs, the mean TWSTRS-Total score at week 4 after 10,000 U BTX-B was reduced by 11.7 (25%) or 11 (21%) compared with baseline. These changes were significantly greater than those obtained with placebo, i.e. 4.3 (10%) or 2 (4%), and were generally similar in patients who were responsive or resistant to BTX-A. Statistically-significant benefits compared with placebo were also evident for the TWSTRS-Severity, -Pain and -Disability subscales, patient-assessed pain, and patient- or physician-assessed global improvement ratings.

In the third RCT, the percentage of patients with BTX-A-resistant or -responsive cervical dystonia who had at least a 20% improvement in the TWSTRS-Total score between baseline and week 4 was significantly higher with 2,500 to 10,000 U BTX-B (58 to 77%) than with placebo (27%).

Overall, BTX-B was generally well tolerated. The most frequently reported treatment-related adverse events were dry mouth and dysphagia. Most of the adverse events in patients receiving BTX-B were mild or moderate; no serious adverse events or laboratory abnormalities were associated with the use of BTX-B and, where reported, no patients discontinued from any of the clinical trials as a result of adverse events.

Authors’ conclusions
BTX-B has shown clinical efficacy in patients with cervical dystonia at doses up to 10,000 U and is generally well tolerated. Its efficacy extends to patients who are resistant to BTX-A.

CRD commentary
The review was not conducted strictly according to systematic review methodology. However, it was based upon a reasonable search of the literature, which covered three electronic database searches, supplemented by scanning of reference lists and attempts to identify unpublished literature. Appropriate criteria were used to select studies on the basis of the interventions and participants. While the inclusion criteria pertaining to study design were not explicitly stated, only randomised, multicentre, double-blind placebo-controlled trials were included in the review. Although only studies of high methodological quality were included in the review, it would have been helpful if some formal assessment of the methodological quality of these individual RCTs had been undertaken. Details of the included trials beyond the drug/dose, number of participants and outcomes would also have been desirable. A narrative synthesis of the studies was undertaken, which appeared to be organised in a fairly sensible manner. The authors’ recommendations seem to follow from their results.

Implications of the review for practice and research
Practice: The authors state 'As injection with botulinum toxin is generally considered the treatment of choice for patients with cervical dystonia, botulinum toxin B should be considered a potential treatment option in this setting'.

Research: The authors state that there are no direct clinical comparisons of BTX-A and BTX-B in patients with cervical dystonia, but note that one manufacturer is planning such a comparison. The authors state 'such trials may assess in the optimal positioning of these different molecules'.
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