Botulinum toxin type A in the management of equinus in children with cerebral palsy: an evidence-based economic evaluation

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Two treatments for the conservative (non-surgical) management of equinus due to calf spasticity, in children with cerebral palsy, were examined. The treatments were intramuscular injection of botulinum toxin type A (BTX-A) and serial casting (SC). The dose of BTX-A was individualised for each patient. However, the recommended dose was 12 U of BTX-A per kg of body weight, with a maximum of 300 U per child on one occasion and 50 U per injection site. The SC was generally a series of two to three casts over 4 to 6 weeks.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of children with cerebral palsy.

Setting
The setting was secondary care. The economic study was carried out in Australia.

Dates to which data relate
The effectiveness and resource use data were derived from studies published between 1998 and 1999. A unique price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies.

Outcomes assessed in the review
The outcomes estimated from the literature were:

the duration of treatment and time to surgery;

efficacy;

safety (i.e. frequency of adverse events); and

the parents’ or patient's preference (parent satisfaction questionnaire, or treatment choice following study completion).
Study designs and other criteria for inclusion in the review
A systematic review of the literature was undertaken to identify relevant studies. Data on the efficacy of the study interventions were derived from two randomised clinical trials (RCTs), each of which included 20 children. A long-term, prospective, naturalistic study (130 patients) was used to provide data on treatment patterns and patient demographics. Details of the three studies were satisfactorily reported.

Sources searched to identify primary studies
MEDLINE, EMBASE and the Cochrane Database were searched for clinical trial evidence.

Criteria used to ensure the validity of primary studies
PBAC guidelines were used to assess the validity of the primary studies. Clinical trials were used as the main source of evidence. The quality of the primary study was established on the basis of explicit criteria such as randomisation and blinding. The choice of the primary study was also based on the patients’ characteristics. A patient population comparable with that likely to receive treatment through the Australian Pharmaceutical Benefit Schedule was preferred.

Methods used to judge relevance and validity, and for extracting data
The authors discussed the relevance and validity of the primary studies.

Number of primary studies included
Three primary studies were included in the review.

Methods of combining primary studies
The primary estimates were combined using a narrative approach.

Investigation of differences between primary studies
Difference in the patients’ characteristics, treatment duration and dosages were reported, and reasons for these differences were justified.

Results of the review
The mean duration of BTX-A treatment was 3.7 years (95% confidence interval, CI: 3.3 - 4.0).

The median duration of BTX-A treatment was 4.1 years (95% CI: 3.2 - 5.0).

The mean time to surgery in the BTX-A cohort was 1,292 days (3.5 years) with a maximum observed time to surgery of 1,675 days (4.6 years).

The 95% CI for the mean time to surgery, using Kaplan-Meier analysis, was 1,193 to 1,392 days (3.3 to 3.8 years). The SC regimen continued until a neutral position of the ankle was achieved.

Both treatments were equally effective since a similar improvement in gait was observed. However, gait improvements lasted longer in the BTX-A group.

The safety profile was slightly better for BTX-A patients.

Strong preferences for BTX-A over SC were observed in both trials.

Measure of benefits used in the economic analysis
The health outcomes were left disaggregated and no summary benefit measure was used in the economic analysis. The authors stated that a cost-consequences analysis was carried out.

**Direct costs**
Discounting was relevant when a treatment duration of 3.7 years was considered. An annual rate of 5% was applied. The unit costs were presented separately from the quantities of resources used. The health services included in the economic evaluation were BTX-A administration, and casting application and removal. BTX-A administration covered vials, paediatric physician and nurse consultations, anaesthetic and consumables. Casting covered the physiotherapist, physiotherapy and consumables. The costs associated with the treatment of adverse events, and those related to physiotherapy and orthotics, were not considered because such costs were assumed to have been similar between the groups. The costs were estimated in patients with hemiplegia and in patients with diplegia.

The cost/resource boundary of the study was that of the Australian health care system. Resource use was estimated from published data. Two alternative time horizons were used in the analysis, depending on the assumptions on the treatment duration (10 months and 3.7 years). The costs were estimated from typical PBAC sources such as the Pharmaceutical Benefits Scheme, Medicare Benefits Scheme and hospital financial data. A unique price year was not reported, but the unit costs were obtained from sources published in 1998, 1999 and 2000.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not considered.

**Currency**
Australian dollars (Aus$).

**Sensitivity analysis**
Univariate sensitivity analyses were carried out to examine the robustness of the estimated costs to variations in BTX-A dose, number of casts, treatment interval, and using SC in concomitance with BTX-A. The ranges of values were generally derived from the literature.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
In patients with hemiplegia, the average cost per patient was Aus$595 with BTX-A and Aus$435 with SC (difference Aus$160) when assuming a time horizon of 10 months.

In patients with diplegia, the average cost per patient was Aus$1,045 with BTX-A and Aus$870 with SC (difference Aus$175) when assuming a time horizon of 10 months.

With a time horizon of 3.7 years, the additional cost for BTX-A over SC was Aus$864 (Aus$793 when discounted) for patients with hemiplegia, and Aus$945 (Aus$867 when discounted) for patients with diplegia.

Changes in the BTX-A dose did not change the base-case results substantially. The incremental cost of BTX-A over SC ranged from $97 to $340 in patients with hemiplegia, and from $310 to $485 for diplegia. When BTX-A and SC were provided concomitantly, the additional costs of BTX-A and SC over SC alone were $251 and $270 for children with
hemiplegia and diplegia, respectively.

**Synthesis of costs and benefits**
A synthesis of the costs and benefits was not relevant since a cost-consequences analysis was performed.

**Authors’ conclusions**
Botulinum toxin type A (BTX-A) was an effective, safe and acceptable conservative treatment for the management of equinus in children with cerebral palsy. It was associated with a modest increase in costs compared with serial casting (SC).

**CRD COMMENTARY - Selection of comparators**
The selection of the comparators was clear. The authors stated that BTX-A and SC were the only available conservative treatments for calf spasticity and equinus gait. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness evidence came from a systematic review of the literature. The methods and conduct of the review were clearly reported and followed the recommendations of the PBAC. RCTs were selected as the main source of evidence, in order to ensure the validity of the clinical data. A naturalistic study was also used to determine treatment patterns. A narrative method was used to combine the primary estimates, although a final measure of outcome was not developed. The robustness of the study results to variations in clinical estimates was investigated in the sensitivity analysis. The authors noted that a weakness of the study was the lack of reliable information on relative compliance with therapy.

**Validity of estimate of measure of benefit**
No summary benefit measure was used in the analysis because a cost-minimisation analysis was conducted. Please refer to the comments above in the ‘Validity of estimate of measure of effectiveness’ field.

**Validity of estimate of costs**
The authors acknowledged that the adoption of a societal perspective would have been appropriate. However, a more restricted perspective, namely that of the health care system, was used since the indirect costs were not available. It was noted that the inclusion of the indirect costs would have clearly reduced the extra costs associated with BTX-A. The unit costs and the quantities of resources used were presented separately, which enhances the possibility of replicating the results of the analysis. The source of the costs was reported. The costs were treated deterministically, but alternative estimates for resource use were considered in the sensitivity analysis. However, the price year was not reported, which makes reflation exercises in other settings difficult. Discounting was performed, as recommended in Australian guidelines.

**Other issues**
The authors did not make extensive comparisons of their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. Sensitivity analyses were performed. These enhanced, in part, the external validity of the analysis. The study referred to equinus due to calf spasticity in children with cerebral palsy, and this was reflected in the authors’ conclusions.

**Implications of the study**
The current results supported the use of BTX-A for the conservative management of equinus in children with cerebral palsy. The authors noted that in December 1999, the PBAC recommended BTX-A be funded by the Australian...
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**Other publications of related interest**


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