Cost-effectiveness of botulinum toxin type A in the treatment of post-stroke spasticity


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
The study compared three strategies for the treatment of post-stroke patients with flexed wrist or clenched fist spasticity.

Strategy one was oral therapy alone with benzhexol, baclofen or tizanidine.

Strategy two was injection with botulinum toxin Type A (BTX-A).

Strategy three was oral therapy, followed by BTX-A as the second-line treatment option should oral therapy be unsuccessful.

Patients were assumed to receive physiotherapy.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
As this was a modelling study, the target population comprised all patients in the UK population with wrist or clenched fist spasticity as a result of a stroke, and who were thus eligible for treatment. No further inclusion or exclusion criteria were reported.

Setting
As this was a modelling study, a setting was not explicitly stated at the outset. The economic study was carried out in the UK.

Dates to which data relate
Demographic data and data on the incidence rates of disease were derived from sources published between 1995 and 2001. Dates for the treatment effectiveness data and the resources used were not reported. The cost data were derived from sources published between 2002 and 2004. The price year was not explicitly reported.

Source of effectiveness data
The effectiveness data were based on expert opinion derived using a Delphi panel. Demographic and epidemiological data on the incidence of disease were derived from published sources.

Modelling
A decision tree model was constructed to compare the three treatment strategies in terms of their costs and effectiveness. The time horizon of the model was one year. The effectiveness of the treatment was assessed 3 months after its initiation. It was assumed that patients successfully treated at 3 months carried on with the treatment for the remainder of the year or until their death. In the oral therapy alone scenario, patients who were unsuccessfully treated at 3 months were assumed to discontinue treatment, while in the combination treatment scenario, such patients were assumed to receive BTX-A.

Outcomes assessed in the review
The following input parameters were used in the model:

- the proportion of patients treated with each of the three treatment options (oral therapy alone, BTX-A alone and oral therapy followed by BTX-A),
- the mean success rate of each of the three treatment options,
- the incidence of stroke by age,
- the acute mortality rate due to stroke,
- the percentage of post-stroke patients with disability,
- the percentage of patients with clenched fist spasticity,
- the percentage of patients eligible for treatment, and
- hospitalisation due to spasticity.

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
The authors did not use any criteria to ensure the validity of the primary studies.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
The authors included 2 primary studies as sources of effectiveness data. They also derived effectiveness data from the Clinical Practice Guideline published by the Public Health Service Agency for Health Care Policy and Research, USA.

Methods of combining primary studies
The results of individual primary studies were not combined.

Investigation of differences between primary studies
Differences between the primary studies were not investigated.
Results of the review
Acute mortality due to stroke was 20%.

Methods used to derive estimates of effectiveness
Most of the estimates of effectiveness were based on expert opinion.

Estimates of effectiveness and key assumptions
Several outcomes were based on expert opinion. Specifically, the effectiveness (mean success rate) of each treatment option, the percentage of patients with fist spasticity, the percentage of patients eligible for treatment, and the proportion of patients treated with each of the three options. A Delphi panel of 33 UK clinicians was surveyed to ascertain these estimates. The survey achieved a 45% response rate, which included 14 clinicians and 1 physiotherapist. No explanation for the response rate was reported.

Measure of benefits used in the economic analysis
The authors used successfully treated months (STM) as the measure of benefit in the economic analysis. It was derived directly from the model.

Direct costs
The health care costs included in the analysis were for oral therapy, vial of BTX-A, professionals' time (including neurologist, orthopaedic surgeon, rehabilitation physician, nurse, physiotherapist, general practitioner), biofeedback session, surgery, hospitalisation due to spasticity, stress management session, electrical simulation and orthotics. Apart from the oral therapy drug costs, all further costs were reported separately from the quantities. The costs were derived from published sources, while the costs of drugs were derived from the British National Formulary and the company Allergan Ltd. Resource use data were based on expert opinion, as derived from the Delphi Panel. Discounting was not relevant as the costs were incurred during a short time (less than 2 years). The price year was not reported.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
UK pounds sterling (€).

Sensitivity analysis
A one-way sensitivity analysis was conducted to assess the robustness of the results to variability in the data. The efficacy of BTX-A and oral therapy was varied using the upper and lower limit of the 95% confidence intervals of the estimates reported by the Delphi panel.

Estimated benefits used in the economic analysis
The percentage of STM was estimated to be 35% (128 days) per year in the oral therapy alone group, 73% (266 days) per year in the BTX-A first-line therapy group, and 68% (248 days) per year in the BTX-A second-line therapy group.
Cost results
The total intervention costs incurred by the National Health Service equalled 13,595,175 in the oral therapy alone group, 16,027,186 in the BTX-A first-line group, and 21,068,469 in the BTX-A second-line group.

Synthesis of costs and benefits
The cost per STM was 942 for BTX-A as first-line therapy, 1,387 for BTX-A as second-line therapy, and 1,697 for oral therapy alone.

The sensitivity analysis demonstrated the robustness of the results.

Authors' conclusions
The analysis demonstrated that botulinum toxin Type A (BTX-A) constitutes a cost-effective option for the treatment of post-stroke spasticity.

CRD COMMENTARY - Selection of comparators
The authors compared the use of BTX-A versus oral therapy for the treatment of post-stroke patients with flexed wrist or clenched fist spasticity. The selection of the comparators was not explicitly justified and, as further available alternative treatment options are available, the results presented could represent only a partial analysis.

Validity of estimate of measure of effectiveness
The estimates of effectiveness were based on expert opinion. A Delphi panel of 14 clinicians and one physiotherapist was assembled to derive the estimates of effectiveness. Although the authors invited 33 UK clinicians to participate in the Delphi panel, only 45% responded. No explanation for the response rate was reported. In addition, the authors did not report how the members of the Delphi panel were selected. Although this is a valid method for deriving estimates of effectiveness, a systematic review of the literature would have provided more robust estimates. It was unclear whether a systematic review was a viable option for this study.

Validity of estimate of measure of benefit
The authors used STMs as the measure of benefit in the economic analysis. These were derived directly from the decision model.

Validity of estimate of costs
Although the perspective adopted in the economic analysis was not reported, it was clearly not societal as the indirect costs were not included. The authors reported that the cost of treating adverse effects of oral therapy were not included in the analysis (i.e. the costs of treating gastrointestinal upset, liver toxicity and dry mouth). However, it is most likely that their inclusion would have strengthened the authors' conclusions. With the exception of drug costs used in oral treatment, the costs and the quantities were reported separately, thus enhancing the reproducibility of the study in other settings. The quantities of resources used were based on expert opinion, but no sensitivity analysis on the quantities was performed. This may limit the interpretation of the study findings. The costs were derived from published sources and were treated deterministically, and no sensitivity analysis was performed to assess the robustness of the cost estimates used. The price year was not explicitly reported, which may limit any future reflation exercises.

Other issues
The authors did not compare their study findings with those from published studies, so it is not known how far their results agree with other published results. The issue of the generalisability of the results to other settings was not directly addressed. The authors do not appear to have presented their results selectively. The study enrolled post-stroke patients with flexed wrist or clenched fist spasticity, but the authors generalised their conclusion across all forms of post-stroke spasticity. The authors acknowledge, as a limitation to their study, that the effectiveness data were only derived
from a Delphi panel and thus might be subject to bias and uncertainty.

**Implications of the study**
The authors did not make any explicit recommendations for changes in policy or practice. However, whilst acknowledging the limitations to their study, they called for further research to validate the resources used in terms of physiotherapy and nursing time, to confirm the number of patients eligible for BTX-A treatment, and to identify with precision the most important cost-drivers.

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