Cost-effectiveness of botulinum toxin type A injection in patients with spasticity following stroke: a German perspective

Wallesch C W, Maes E, Lecomte P, Bartels C

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
Treatment of stroke induced spasticity using either physiotherapy alone or in combination with one of two drugs, oral baclofen or botulinum toxin A injection.

Type of intervention
Treatment; rehabilitation.

Economic study type
Cost-effectiveness analysis.

Study population
The study looked at hypothetical adult patients with spasticity of an arm and/or leg that had suffered a stroke during the previous 6 weeks. The full range of spasticity severity measured on the Ashworth scale from mild, moderate to severe was considered.

Setting
Hospital, nursing home and rehabilitation centre. The economic analysis was conducted in Magdeburg, Germany.

Dates to which data relate
Effectiveness and resource data were determined by an expert panel. The expert panel used estimates of effectiveness published between 1989 and 1996. The dates for data collected were not provided and no price base year was stated.

Source of effectiveness data
Effectiveness data were derived from a review of the literature and an expert panel.

Modelling
A 1-year decision analysis model was used to synthesise data from the expert panel on the effectiveness and resource use of the different interventions. An expert panel determined treatment paths in the model.

Outcomes assessed in the review
The review assessed additional effectiveness of BTX-A or baclofen compared with physiotherapy alone in the treatment of spasticity in patients who had recently suffered a stroke.

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

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

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

Number of primary studies included
Five studies were included in the review. One of these studies was a double blind crossover trial comparing baclofen with placebo treatment. The other four studies all examined BTX-A. One of these was stated to be a randomised placebo controlled trial; it is unclear what protocol was used in the other three studies.

Methods of combining primary studies
Primary studies were not combined, information from studies was provided to experts as part of the Delphi panel process.

Investigation of differences between primary studies
Not stated.

Results of the review
Results were not reported in the analysis although it was stated that these studies concluded that there was evidence of additional effectiveness of both drug interventions in combination with physiotherapy compared with physiotherapy alone, in the treatment of spasticity.

Methods used to derive estimates of effectiveness
A Delphi Panel approach was used to identify estimates of effectiveness. 35 neurologists, each with at least 5 years experience in the field, were invited to participate. Thirteen of those invited 13 (35%) returned questionnaires. Twelve of these experts were previously aware of BTX-A, and all were involved in the treatment of spasticity and stroke rehabilitation. After initial questionnaires and feedback to the panel, the group members were asked to estimate the change in the level of spasticity for mild, moderate and severe patients' one year after stroke, for each of the three possible interventions. Three expert opinions from neurologists based on published literature were also used in this process. At the time of writing the original paper, preliminary results from the second phase of the Delphi process had been received from 9 of the expert panel.

Estimates of effectiveness and key assumptions
The probability of improvement was reported to improve when using drug therapy compared with physiotherapy alone. The greatest probability of improvement would occur in patients treated in the BTX-A group. In the paper, these results are presented as a graph rather than in numeric form. The probability of improvement for patients with moderate, severe and very severe spasticity treated with BTX-A ranged from more than 50% to nearly 70%. Similarly for patients treated with baclofen, the probability of improvement ranged from just under 30% to approximately 35%, and for patients receiving physiotherapy alone this estimate of improvement ranged between 15% and 20%. Adverse effects were also considered by the panel and the incidence of major adverse events was estimated to be 3.2% for patients
treated with oral baclofen compared with 0.9% of those treated with BTX-A.

**Measure of benefits used in the economic analysis**
Units of improvement in spasticity gained on the Ashworth scale were used as the measure of benefits.

**Direct costs**
The expert panel estimated all resource and cost data. Resource data were estimated separately from costs. Costs were weighted by the panel to take account of the relative contribution of spasticity to overall costs of stroke treatment. This data included length of stay in both hospital and rehabilitation centres as well the number of treatments required by patients with different levels of severity, and the median yearly dosages of drug therapy required. Additional hospital stay required to deal with adverse events was also estimated. Costs were not discounted, which was appropriate given that the duration of the study was only one year. Base price years do not appear to have been stated. Costs appear to have been estimated from the joint perspectives of the hospital, nursing home and rehabilitation centre.

**Indirect Costs**
No indirect costs were included.

**Currency**
German Marks (DM).

**Sensitivity analysis**
No sensitivity analysis was conducted.

**Estimated benefits used in the economic analysis**
For all degrees of spasticity, the incremental gain over one year in units of improvement using physiotherapy plus BTX-A compared with physiotherapy alone was 0.486, whilst similarly comparing oral baclofen plus physiotherapy with physiotherapy alone this was 0.127. For all degrees of spasticity the average number of units of improvement gained on the Ashworth scale was 0.052 for physiotherapy alone, 0.179 for physiotherapy plus oral baclofen and 0.538 for physiotherapy plus BTX-A. Adverse events were included in the analysis.

**Cost results**
The average annual expected costs per patient (for all levels of spasticity) were DM 25,596 for physiotherapy alone, DM 24,378 for physiotherapy plus baclofen and DM 27,097 for physiotherapy plus BTX-A. The incremental reduction in costs of using baclofen therapy compared with physiotherapy alone was DM 1,218, similarly the incremental costs of BTX-A therapy compared with physiotherapy alone were DM 1,501. Adverse events were included in the cost analysis.

**Synthesis of costs and benefits**
The incremental cost per unit of improvement gained per patient, when using BTX-A compared with physiotherapy alone, was estimated to be DM 3,088. No synthesis was required to compare baclofen with physiotherapy alone as baclofen was a dominant intervention. No analysis was conducted to compare baclofen with BTX-A.

**Authors' conclusions**
The use of BTX-A therapy in addition to physiotherapy alone appears to be a highly cost effective intervention. However clinical and economic studies are required to confirm the results of this study, and also to take account of quality of life issues and costs to all groups in society.
CRD COMMENTARY - Selection of comparators
A justification was provided for the two comparators used, namely that both physiotherapy alone or with oral baclofen are widely used treatments for post stroke spasticity in Germany.

Validity of estimate of measure of benefit
Effectiveness data were determined by an expert panel of 13 specialists in the treatment of spasticity. The Delphi method was used and, in this preliminary report, data from 9 of the 13 panellists were available. The authors adopted this approach due to a lack of empirical data, although 5 studies identified non-systematically from the literature were used as part of the Delphi process. Participants were invited to modify their responses on both the effectiveness and resource requirements of treatments in light of information provided by three expert neurologists (whom had access to the five studies identified in the literature). Estimates identified were not investigated by sensitivity analysis. The estimate of benefits was obtained directly from the Delphi panel. This choice of estimate was justified.

Validity of estimate of costs
It would appear that all costs relevant to the perspective adopted were included in the analysis. Quantities were reported separately from costs and only aggregate rather than disaggregated costs were presented. Costs were estimated from the perspective of service providers, and it may be useful were future analyses to consider costs to others in society such as informal caregivers; a fact recognised by the authors. No sensitivity analysis was conducted of costs or resources used, which were determined by the expert panel. This may limit the interpretability of study findings. Since all costs were incurred over one year, discounting was unnecessary. The price dates do not appear to have been reported.

Other issues
The authors did not make comparisons with other studies; this was to be expected given the lack of empirical data. They did, however, note that the conclusions of the Delphi panel over the relative effectiveness of the three interventions were in line with those studies they had identified in the literature. The authors did not consider the issue of generalisability to settings outside Germany and results appear to have been presented selectively. Although data were collected on effectiveness of treatments for different levels of spasticity severity, only final results for aggregate levels of spasticity were presented. The authors acknowledged that their study did not address issues of quality of life. They were unsure whether members of the expert panel were able to differentiate appropriately between spasticity and spastic hemiparesis. It would have been useful to compare the incremental cost-effectiveness of using BTX-A therapy rather than oral baclofenac, as this strategy had been shown to be dominant over the alternative of physiotherapy alone.

Implications of the study
The authors noted that future studies, both clinical and economic, are required to examine all three interventions. Any studies should include an analysis of quality of life, as well as costs and burden of spasticity, including costs to relatives and other informal caregivers. Such studies should also examine the interactions between physiotherapy and the different drug treatments.

Source of funding
None stated.

Bibliographic details

PubMedID
11541177