The effectiveness of intrathecal baclofen in the management of patients with severe 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 use of a continuous intrathecal baclofen infusion (CIBI) for the treatment of spasticity where standard multidisciplinary treatment has failed to control it, or for patients who have "unacceptable side-effects with oral drug therapy".

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised UK patients with spasticity, which had not been controlled by standard multidisciplinary treatment. The patients had to fulfil certain inclusion and exclusion criteria. The inclusion criteria were not stated. The exclusion criteria were contraindications to the insertion of an intrathecal catheter (for example, anticoagulant therapy), and no response from the patient to a test dose of up to 100 microg baclofen.

Setting
The setting was mixed inpatient and either outpatient or domiciliary. The economic study was conducted in the UK.

Dates to which data relate
The effectiveness evidence came from studies published between 1987 and 1998. The cost data came from studies published between 1995 and 1999. The price year was not stated.

Source of effectiveness data
The effectiveness data were derived from a review of published studies.

Outcomes assessed in the review
The outcomes assessed, which varied between studies, were:

- Ashworth score or a modified version for level of spasticity;
- Penn spasm score for frequency of spasms;
- non scored measures relating to function or quality of life, such as outcomes related to mobility, activities of daily living (ADL), the level of nursing, and pain; and
scores to measure function, for example, the Sickness Impact Profile and Functional Independence Measure. Complications were also listed.

**Study designs and other criteria for inclusion in the review**

Ninety-four studies were identified, of which 68 were excluded. The reasons for exclusion included: reports of complications only, the wrong outcomes measured, case reports, and a follow-up of less than 6 months. This left 26 original studies and a meta-analysis.

The meta-analysis was of 27 trials of CIBI, where the "average patient was 36 years old, seven years post-onset of CNS disorder, and had undergone follow-up evaluations for 18 months after implantation of pump". The design of the other studies was uncontrolled, except for one with a randomisation phase of 3 months. The number of patients ranged from 6 to 70, and the duration of follow-up ranged 6 to 79 months.

**Sources searched to identify primary studies**

MEDLINE, EMBASE, DARE and the Cochrane Library were searched. The reference lists of review articles were also examined.

**Criteria used to ensure the validity of primary studies**

Not reported.

**Methods used to judge relevance and validity, and for extracting data**

Not reported.

**Number of primary studies included**

Twenty-seven primary studies were included.

**Methods of combining primary studies**

The primary studies were combined in the narrative method. Also, the results of some studies were pooled by outcome measure, to give the number of patients whose condition improved or worsened out of the total number assessed.

**Investigation of differences between primary studies**

The validity of the results of the studies were compared in terms of:

- study design (randomised blinded versus observational);
- sample size;
- patient populations (spasticity of spinal or cerebral origin); and
- validity of outcome measurement (validated quality of life score versus non-validated quality of life description or measure of spasticity).

**Results of the review**

The meta-analysis showed that about 92% of the patients had a reduction in spasticity. For all patients, the improvement in the Ashworth or spasm score had significant results, (p<0.001). The p-value was only higher for cerebral palsy (0.34), but this was not significant.
Only the results from the pooling of studies are presented here.

Outcomes related to mobility:

50 of the 76 bedridden patients became able to sit in wheelchair;
31 of the 35 patients had an improved ability to sit comfortably;
13 of the 18 patients showed improved wheelchair mobility;
25 of the 26 patients had an improved ability to transfer;
4 of the 36 wheelchair-bound patients became ambulatory (with aids);
15 of the 47 ambulatory patients improved their capacity to ambulate, whilst 4 showed deterioration;
3 of the 29 patients became able to drive; and
45 of the 62 patients showed improvements in activities of daily living.

Outcomes related to nursing: there was improved ease of nursing care in 83 of the 90 patients.

Outcomes related to quality of life:

59 of the 66 patients with spasm-related pain had relief or complete resolution; and
27 of the 33 patients had improved urinary function.

Scoring systems (5 studies, each using a different measure):

the Functional Independence Measure showed there was an improvement in motor, but not cognitive domains; and
the Sickness Impact Profile improved from 29.7 to 21.7, \(p<0.005\).

Complications: these depended on the type of pump. The most frequent complications were catheter problems requiring surgery (37 cases out of 222 when using the Medtronic pump).

Measure of benefits used in the economic analysis

The effectiveness measures were not converted into a summary measure, thus giving a cost-consequences analysis. However, the minimum gain in the quality-adjusted life-years (QALYs) required for a given range of costs and threshold cost-effectiveness level, was calculated. The authors stated that the data on the number of QALYs gained due to CIBI were unavailable. They therefore assumed a change in utility on the Index of Health Related Quality of Life measure, thus producing a gain of between 0.149 and 0.226 QALYs.

Direct costs

The direct costs related to those of the health service. These were for CIBI, subsequent hospital stay, treatment of pressure sores, orthopaedic surgery, other therapies, orthoses and other aids or adaptations and care. The cost of CIBI was broken down into the constituent resource quantities and unit costs, giving a low and a high estimate. The other costs were reported as savings resulting from the introduction of CIBI. This assumed a level of effectiveness in reducing hospitalisation and the need for treatment. Estimates were derived from a review of the literature, which was conducted separately from that for effectiveness. However, no details of the methodology were provided. The costs were discounted at a rate of 6%. The price year was not given.

Statistical analysis of costs
The costs were not treated stochastically.

**Indirect Costs**
The indirect costs were not included. The authors stated that such data were unavailable.

**Currency**
UK pounds sterling (GBP).

**Sensitivity analysis**
Sensitivity analyses were conducted to examine the effect of varying the following on the minimum annual gain in QALYs:

- the cost-effectiveness ratio (range: 5,000 - 25,000 per QALY); and
- the initial treatment cost (range: 10,000 - 16,000).

Three scenarios were also examined to show the minimum gain required to produce a cost-effectiveness ratio of 20,000.

**Estimated benefits used in the economic analysis**
See the 'Results of the Review' section and the sensitivity analysis in the 'Cost Results' section.

**Cost results**
The initial treatment cost for CIBI was 11,772.13 per patient (mid point estimate). This ranged from 10,553.13 per patient (lower estimate) to 12,991.13 (upper estimate).

The cost of CIBI (including follow-up) was 15,400 per patient (mid point estimate), assuming treatment for 5 years at a discount rate of 6%.

The savings per year were:
- for a reduction in hospitalisation, 4,220 to 11,605 (20 to 55 days' reduction);
- for avoiding orthopaedic surgery, 1,500 to 5,000 (one tenotomy to hip dislocation); and
- for avoiding pressure sores, 8,500 to 13,000 (50% chance of avoidance at a cost of 17,000 to 26,000 per pressure sore).

**Synthesis of costs and benefits**
The sensitivity analysis showed that, in the base-case, discounting both the costs and benefits at 6% over 5 years, the number of QALYs gained to give a cost-effectiveness ratio of 20,000 would have to be 0.77 (0.17 in year 1).

Over 7 years, the figure would be 0.83 (0.14 in year 1).

For a discount rate of 0%, the total costs would be 17,600, thus requiring a benefit of 0.13 QALYs per year to give a cost-effectiveness ratio of 20,000.

Increasing the initial treatment cost to 16,000 would mean a gain of 0.21 QALYs in year 1, discounted over 5 years, to give the same cost-effectiveness ratio.
Authors’ conclusions
The patients who are most restricted in mobility would most likely achieve the greatest benefit from continuous intrathecal baclofen infusion (CIBI). For those who are ambulatory, some will improve and some will deteriorate. The amount of nursing care was reduced, and some patients might become more independent. Although complications occurred, major ones were rare. There were no data on the QALYs gained by CIBI. However, the use of a threshold analysis suggested that a gain of 0.16 QALYs would produce a cost-effectiveness ratio of 20,000. A net reduction in cost to the health service could result if the savings from reduced hospitalisation and avoided treatment are taken into account.

CRD COMMENTARY - Selection of comparators
The choice of the comparator was justified on the grounds that it represented standard practice. However, at present, this study would be very difficult to generalise to settings other than the National Health Service, as there seems to be a very particular mix of therapies, and the extent of the use of each was not given. Also, in the studies on effectiveness, the comparator was not given. This produced uncertainty as to whether CIBI was used in addition, or as an alternative, to standard therapy. Finally, for the costing, it appeared that the intervention was CIBI in addition to standard therapies, rather than instead of, since a cost for standard practice was not given or subtracted from that for CIBI to produce the incremental cost-effectiveness.

Validity of estimate of measure of effectiveness
The authors, in conducting a review of the literature, seem to have been hampered by much heterogeneity in the probability of bias between the studies. They seem to have conducted a thorough and well-described search of the literature. This was consistent with the purpose of the paper, which was to inform the purchasers of health care. The summary of the results was also clear, giving insight into the chances of bias due to small sample size, lack of randomisation and blinding. In addition, it highlighted the difficulty in pooling the results due to inconsistencies in the effectiveness measures. The main problem was the lack of information on the intervention and the comparator. The implication was that it was CIBI with or without other therapy versus some form of standard practice. The review and its reporting could have been improved by methods to reduce bias, such as the use of blinding and more than one independent reviewer.

Validity of estimate of measure of benefit
The authors essentially produced a cost-consequences analysis. They also estimated the gain in QALYs per annum per patient by assuming a change in utility. Given the limitations of this, they then conducted a sensitivity analysis to find the minimum gain required to achieve a particular level of cost-effectiveness. In fact, this is likely to be an underestimate, since, as the authors acknowledged, there is also likely to be an increase in longevity and an improvement in utility. Also, if, as they show, there is an overall net saving, at least for the most dependent patients, CIBI is dominant to standard practice (it produces a gain in benefit and reduction in expense).

Validity of estimate of costs
The costing was generally very clear with a breakdown of the resource quantities and the unit costs for CIBI. Unfortunately, the price year was not given, and we do not know whether the unit costs were adjusted if they came from an earlier period. The possible savings due to hospitalisation and treatment avoided, as the authors acknowledged, came from sources with a range of applicability, due to the studies being conducted on different populations and in different health care settings. The main problem was the lack of clarity in whether CIBI was combined with, or used instead of standard practice. Not subtracting a cost for standard practice would mean that either the cost input to cost-effectiveness was not incremental, or that it was combined. Nevertheless, the paper makes it clear that there is much uncertainty in estimating the cost-effectiveness of CIBI.

Other issues
The authors did not compare their results with those from other economic evaluations. They also did not discuss generalisability, although, given the local health service perspective, this would not have been a priority. The results
were comprehensively reported. In addition, the authors' conclusions were appropriate for the study population, particularly as they were tailored to various sub-populations.

**Implications of the study**
The authors provided a list of options for the purchasers given the uncertainty in the cost-effectiveness; in particular, because of the likely difference in benefit between more and less mobile patients. These options include providing CIBI for the least mobile only, or for the more mobile only as part of a trial. The study was generally well reported, except for the important issue of which technologies were being compared. The purchasers would want to know whether, if CIBI was funded, these results would be reproduced only by CIBI or with, for example, concomitant physiotherapy.

**Source of funding**
None stated.

**Bibliographic details**

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Subject indexing assigned by CRD

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Adult; Baclofen /administration & dosage /pharmacology /adverse effects; Drug Administration Schedule; Female; Humans; Injections, Spinal; Male; Middle Aged; Muscle Relaxants, Central /administration & dosage /pharmacology /adverse effects; Muscle Spasticity /drug therapy; Retrospective Studies; Severity of Illness Index; Treatment Outcome

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