Management of Spasticity in Children with Cerebral Palsy, A National Randomised Controlled Study on Intrathecal Baclofen

Introduction:

Several approaches to the treatment of spasticity in children are available, aiming to improve ease of motion in the short term and reducing limb and spine deformity in the longer term. These approaches are based on a background regime of physiotherapy to improve joint ranges, muscle power and motor patterns. Single or combined oral medication, such as Baclofen, Tizanidine and Dantrolene can be considered, but the appropriate dose to reduce spasticity is often associated with unacceptable side effects.

Recently there has been an increase in the use of Botulinum toxin A injections to treat spasticity in individual muscles. This is usually given under mild sedation and produces significant improvement in muscle tone for approximately four months, after which the treatment needs to be repeated. There is extensive literature documenting the benefits in specific muscles of the lower limb in both ambulant and non-ambulant children with cerebral palsy. Injections to the upper limb can also be used for specific goals, including improved reach, ease of motion during dressing and other aspects of care as well as for the pure cosmetic appearance of the limb. The treatment is limited to approximately six large muscles in one session to avoid mild botulism as a side effect.

When a child has severe and global spasticity, which interferes with function, dorsal rhizotomy or intrathecal baclofen can be considered. Dorsal rhizotomy is carried out extensively in the USA and Europe and involves surgery to selectively cut afferent spinal roots, which inhibits the reflex arc in the spinal cord and so reduces muscle tone. This succeeds, but often with accompanying muscle weakness. Detrimental effects on bladder function and spinal integrity have been reported. A recent meta-analysis of three randomised controlled trials of dorsal rhizotomy concluded there was significant functional improvement, but that the improvement was limited and should be balanced against the time, effort and risks involved.

Continuous Intrathecal Baclofen [ITB] is the treatment of choice to reduce severe spasticity in a non-mobile child with severe quadriplegia [GMFM stage 5], especially when there is pain and spasms. Baclofen spreads throughout the CSF, reducing tone in all limbs, and sometimes improves dysphagia when oral-motor hypertonia is present. This approach can also be used in diplegics with severe hypertonia, GMFM stages 3-4, in order to reduce lower and upper limb spasticity. ITB is beneficial in dystonic cerebral palsy, an effect that is not reported with dorsal rhizotomy. ITB has the disadvantage compared to rhizotomy of being more expensive, and there is the relative inconvenience of regular 2-3 monthly refills of the pump reservoir. Conversely, ITB has the advantage of being a reversible, non-destructive technique.

While there have been excellent open studies describing the benefits of ITB in children, there are none with objective measures and we aim to address the need to show the effect of ITB in two randomised controlled trials.

Current results of the Nottingham ITB activity:

The programme began with the first tests in October 1998. Severe deformity was present in 52 Children. 17 could manage to walk short distances with a frame and some help, a further 7 could weight bear but not walk, while 28 were unable even to weight bear. All were wheelchair dependent for distances of more than a few tens of metres. One third have mainstream cognition, the remainder having various degrees of learning disability.

All patients in programme	
Awaiting test	5
Unsuccessful test	3
Successful test, parents declined implant	1
Successful test, awaiting implantation	11
Implanted	52
Total	**72**
Implanted patients	
Satisfied with treatment	48
Treatment stopped on request	3
Death (unrelated)	1
Total	**52**

Table I. Patients in the CIBI programme

Aetiology:

Of the 52 implanted patients, 48 (92%) had cerebral palsy in association with premature birth. 1 patient was dystonic, and the remaining 3 had suffered cerebral insults through drowning, trauma, and non-accidental injury (figure 1). Their ages ranged from 2.5 to 17 years. 34 (65%) were male, 18 female.

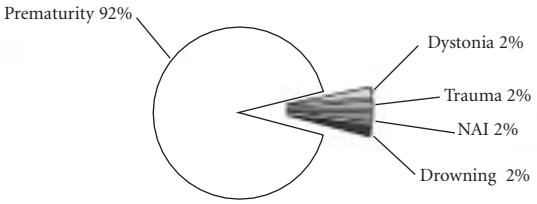

Figure 1. Aetiology of spasticity

Adverse events:

Adverse Event	Number of cases	Resolution
Pump infection	3	Pump removed
Catheter migration	4	Catheter revision
Catheter fracture	3	Catheter revision
Pressure sore	1	Pump replaced
Battery expiry	1	Treatment stopped
Baclofen side effects	1	Dose reduction

Table II. Adverse events

There were a variety of adverse events related to pump implantation and use (Table II). Most seriously, there were 3 infected pumps that had to be removed. In one case there was leakage of CSF from the lumbar wound, and there were 2 cases each of subcutaneous CSF collections in the lumbar and anterior abdominal regions. All of these settled with conservative management. The commonest problem was catheter migration (4 cases), or fracture (3 cases), all of which were treated uneventfully by catheter replacement. One of the patients with catheter migration later went on to have a repeat of the same complication. One pump has been replaced because of a low battery and another because of the development of a

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Richard Morton is Consultant Paediatrician at Derby Children's Hospital. He has particular research interests in feeding, gait and motor control in disabled children. Dr Morton runs a multidisciplinary clinic for hypertonia, and is keen to explore the relative advantages of oral anti-spasticity therapy, Botulinum, Intrathecal Baclofen, and dorsal rhizotomy in childen.

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pressure sore overlying it. One patient developed baclofen-related side effects (headaches and GI upset), which responded to dose reduction. One patient in the series died of unrelated causes 1.5 years following implantation.

In 3 of 52 implanted cases treatment was terminated on request. In one of these cases the pump battery expired and the parents decided to see how things went without treatment before committing their child to revision surgery. The parents refused further intervention in another case, after two catheter migrations. In the third case the baclofen appeared to work well but the consequent disruption of the dependent patient-carer relationship caused such psychological difficulties that both the patient and carer were dissatisfied and requested removal of the pump.

In all 49 other cases carers reported improvements in nursing care. All of these saw a reduction in spasticity and an improved range of motion in unfixed joints.

Optimum dosage was arrived at by iteration as described above and ranged from 50 – 900 ug/24h.

In addition to the reduction in spasticity and consequent effects on nursing care, additional benefits were noted. In most cases there were improvements in bulbar function (better speech and swallowing, less drooling) and upper limb function. In two cases pre-existing divergent squints disappeared. Many children appeared to become more socially interactive. Reduction in spasticity tended to cause the child to put on weight. This is to be expected, because a large fraction of the patient's energy intake is expended by their spasticity. Weight gain is to an extent desirable for a number of reasons, not least the improved soft tissue-cover for the bulky pump housing, but it is a mixed blessing as extra weight can make nursing more difficult.

Seizures have been observed to occur with increased frequency in epileptic patients on CIBI. This can be explained by the weight gain when CIBI is started when the anticonvulsants haven't been increased.

Description of the Randomised Controlled Trial for Ambulant and Non-Ambulant Children:

1) Patient Selection:

Non-ambulant and ambulant children between the ages 5 – 16 with severe spasticity, which is thought to interfere significantly with their function, mobility and quality of life, will be selected for participation in the trials. The non-ambulant children should be unable to walk 1 step, the ambulant children at least 1 step, with or without aids. They will have tried an oral anti-spasticity treatment beforehand. They may still be taking oral medication for spasticity but should not have received botulinum toxin or orthopaedic surgery in the previous six months. They should not have been previously planned to receive orthopaedic surgery over the course of the 18 months study. The worst affected muscle groups in the lower limbs should be Ashworth grade 3 or above.

A test dose of intrathecal baclofen is given (50 mcgs). Sufficient improvement to justify surgical insertion of a pump and admission to the study is considered if the two most severely affected lower limb muscle groups with spasticity improve on the Ashworth scale by at least one point. 40 children will be recruited for the non-ambulant trial and 60 to the ambulant trial.

2) Method

Both groups are assessed in the same way at 0, 9 and 18 months by the physician and by the physiotherapist (Table. III). In both trials the children will firstly be divided into age bands (5-10 or 11-16) and then randomly allocated to Group A or Group B. Group A are immediately implanted with a pump, Group B are implanted with a pump at 9 months. This allows for a 9 month comparison period between Group A and B.

Once the pump is implanted, baclofen dosage is increased according to clinical requirement at each refill (approximately every 2 months).

During this period there should be no additional intervention for spasticity (e.g. medications, botulium). The same aids and appliances should be maintained, although can be changed for growth if necessary.

Table III:

The assessments at 0, 9 and 18 months will consist of:

- Physician-led clinical examination; including weight, Ashworth Scale, assessment of range of movement.
- Hip x-ray
- Gilette Functional Assessment Questionnaire (9)
- Lifestyle Assessment Questionnaire (Marchie *et al* 1998)
- Care-givers Questionnaire (Schneider *et al*).
- Physiotherapist-led Paediatric Evaluation of Disability Inventory (Feldman *et al* 1990); Gross Motor Function Measure (GMFM); Tabulation of aids and appliances
- Orthopaedic Assessment – prediction of possible orthopaedic intervention

Conclusion:

The initiation of these studies was driven by the lack of formal controlled evidence on the effectiveness of ITB in Children with CP. Although the treatment is currently undertaken in Nottingham in the form of a clinical outcome study, hard objective evidence is necessary. The spectacular benefit seen in spastic quadriplegic patients answers the demand for improved quality of life and ease of care. The role of ITB in ambulant e.g. functional patient with severe spasticity remains unproven and is to be addressed by this trial. The pluridisciplinary team involved in this study aims to establish improved patient selection in both groups and to balance risk and morbidity to the benefit of ITB.

At the end of the study the results will be compared using repeated measures analysis to assess changes in tone, mobility, self-help skills and quality of life.

References for this article can be found on our web site at
www.acnr.co.uk/contents4-1.htm

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