

# CONTINUAL INFUSION OF INTRATHECAL BACLOFEN (ITB): LONG TERM EFFECT ON SPASTICITY

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## Abstract

*Background:* Spasticity is a disorder of muscular function causing muscular tightness or spasm which occurs when there is damage to the central nervous system whether it is of spinal cord or brain origin. This insult could be either pathological or traumatic.

*Method:* Thirty-three patients had intrathecal Baclofen pumps implanted for severe spasticity. These patients either did not respond to or tolerate oral medications.

*Results:* All patients showed significant improvement in their spasms following the procedure. Improvement was noted not only in spasticity, but also in pain, management of sleep disturbance, activities of daily living, indoor and outdoor mobility and behavior.

*Conclusion:* The number of complications was acceptable, and generally were not life-threatening. Infection was the significant complication in two patients and this led to explantation of their pumps. Patient satisfaction was very high and was related to improvement in the quality of life for the patients.

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## Introduction

Spasticity is a disorder of muscle function causing muscle tightness or spasm which occurs when there is damage to the central nervous system. Spasticity is a major disorder characterized by a velocity-dependant increase in tonic stretch reflex (muscle tone) with exaggerated tendon jerks resulting from hyperexcitability of the stretch reflexes as one component of the upper motor neurone syndrome<sup>1</sup>. This damage may result from spinal cord injury, traumatic brain injury, stroke, tumour, cerebral palsy or multiple sclerosis<sup>2,3,4,5,6,7</sup>.

In a clinical setting severe spasticity not only reduces rehabilitation goals but produces ailments such as joint contractures leading to bad posture, pressure sores, detrusor-sphincter dyssynergia and impaired motor function. Some workers have reported 25-35% rates of such seriously effected patients<sup>8</sup>. Spasticity can be debilitating and causes suffering in many ways such as muscle spasms, limited functional movement, impaired functional capacity, scissoring (involuntary crossing of legs), altered personal hygiene and pain. The pain may be neuropathic, resulting from deafferentation, central collateral sprouting or neural disinhibition. The pain may also be nociceptive/somatic directly due to muscle spasm.

Uncontrolled spasticity causes multiple problems, for example orthopaedic deformities, such as hip dislocation, contractures or scoliosis. It impairs personal hygiene and effects many other activities of daily living. In addition to all of the above, spasm can interfere with sleep and can result in depression.

Spasticity is usually managed by a combination of oral medication with antispastic agents such as Baclofen, Tizanidine or Diazepam and physiotherapy and rehabilitation.

Most of the mild to moderate spasticity cases are effectively managed with the conservative measures and available oral therapy mentioned, but cases of severe spasticity are less responsive.

Since unacceptable CNS effects often occur when high doses of Baclofen are taken orally the therapeutic effect usually cannot be improved by an increase in dose. Sedation, somnolence, ataxia and respiratory and cardiovascular depression are the drug's CNS

depressant properties.

When spasticity cannot be managed efficiently, some of the associated problems can be dealt with in a number of ways, in addition severe, late and long term spasticity could be managed with periodic injections of Botulinum toxin or Phenol into the spastic muscle, or implantation devices like intrathecal pumps. Surgery is also indicated and performed in very severe and late cases.

The most effective treatment, with the least side effects is intrathecal Baclofen (ITB) and this therapy can be used if oral medications fail and this consists of long term delivery of Baclofen to the intrathecal space. It was first carried out by Penn and Kroin in 1984<sup>2</sup>. ITB therapy gained US FDA approval for managing severe spasticity of spinal origin in 1992, and for severe spasticity of cerebral origin in 1996. Since then, several studies supporting this have been published by various authors<sup>9,10</sup>.

The abundance of GABA-B receptors in the superficial layers of spinal cord means that intrathecal administration of Baclofen results in a greater than four-fold increase in the cerebrospinal fluid level with 1% of the oral dose<sup>3</sup>. This treatment can be very effective. The benefits of ITB typically include reduced tone, spasm and pain and also increased mobility. The use of ITB therapy as a treatment for spasticity requires a four phase approach: (1) patient selection, (2) screening, (3) implantation, and (4) dose adjustment and maintenance.

## Materials and Methods

Between April 2004 until June 2009, 33 patients with severe spasticity had intrathecal Baclofen pumps implanted.

Thirty-three patients out of the 45 tested proved positive to the intrathecal Baclofen drug test, 9 female and 24 male, ages ranging from 12 to 57 years. There were 18 spinal injury patients, 6 with demyelination disease and 9 with brain insult.

The pumps implanted were all Medtronic and we used 5 pumps of 20cc Synchronomed II, 27 of 40cc Synchronomed II and one of 20cc Synchronomed L.

When patients have persistent and uncontrollable spasticity despite oral antispasmodic medications, they

will be offered implantation of intrathecal Baclofen pumps. As mentioned, selection of patients is the first step to plan screening and see if intrathecal diagnostic tests will be of benefit to the patient. If this is successful then the next step is implantation and later on dose adjustment.

In our institute we give a bolus dose of 50-100µg of Baclofen injected intrathecally in the diagnostic phase and spasticity is assessed over the next 10 hours, although the significant effect of intrathecal Baclofen would occur four hours after injection.

The spasticity is assessed according to the Ashworth Score and when the Score improved (reduced) by around two scales then the patient was considered eligible for implantation.

There are two choices of pump size, 20ml and 40ml capacity, depending on the size of the patient and also on the anticipated daily dose of intrathecal Baclofen and the estimated refill intervals.

When the decision is made to implant the Baclofen pump, the patient is usually put under general anaesthesia and with the patient on his side, a catheter is tunneled through a needle inserted through the L3-4 space, preferably in a paramedical approach and the catheter is guided upwards to the higher thoracic vertebrae and checked on fluoroscopy. The catheter which will be connected to the pump is then tunneled beneath the skin around the flank of the patient to the subcostal area. The pump is then implanted just beneath the skin in the subcutaneous fatty tissue which lies above the abdominal muscles of the lower abdomen.

Usually the pump is prepared and filled with Baclofen before implantation and the surgical incision closed properly in layers and the patient given prophylactic antibiotic cover for 48 hours.

## Results

All 33 patients who passed screening, showed significant improvement following pump implantation. The mean preoperative Ashworth Scale was reduced from 3.9 to 1.7. In addition to improvement of spasticity, there was significant clear improvement in patient behavior and activities of daily living. Also bladder and bowel functions were improved. It was noticed that after initiation of intraspinal treatment

most patients had an immediate reduction of muscle tone to normal levels and spontaneous spasms were eliminated. Many patients experienced less discomfort, significant pain relief, and daily activities were more easily accomplished.

In our group of patients the intrathecal daily dose after adjustment was variable, between 50 and 850µg per day. We noticed small doses were needed for patients with demyelination disease, whereas larger doses were necessary to control spasticity in those with brain insult. One patient had Morphine and Baclofen mixed in the pump for both spasticity and pain.

The pumps in two patients were explanted due to infection, one after three months and the other after four years. One patient had a damaged (broken) intrathecal catheter which was replaced. Other complications were minor, headache, swelling and pain at the site of the pump, but these were resolved within a few days.

We found a definite improvement after the use of intrathecal Baclofen in patients with supraspinal spasticity and this has been reported by others<sup>11,12,13</sup>.

## Discussion

The site of action of Baclofen in the spinal cord is not clear and Baclofen was first used in humans in 1974<sup>14</sup>. It is a gamma-amino butyric acid (like GABA) analogue that binds to the GABA-B receptor resulting in inhibition of calcium influx at pre-synaptic terminals and thus suppressing release of excitatory neurotransmitters. These GABA receptor sites occur widely throughout the central nervous system<sup>15,16,17</sup>.

As complications are related to operator inexperience it is recommended that specific personnel or a specific centre should perform this procedure, where protocols can be standardised and long term results properly evaluated. Therefore the programme requires specific team designated leadership and identified co-ordination to ensure smooth transition between the different stages of therapy and effective long term follow up. Rehabilitation therapists, particularly Physical and Occupational Therapists are essential team members who can help monitor patients' response to treatment and changing functional status over time. The team also involves a very experienced surgeon who should be actively involved with the

team for system-related problems which could arise at any time. ITB therapy could replace a number of orthopaedic and neurosurgical interventions for those cases suffering with irreversible, severe spasticity-with or without contractures.

There are several risks involved with placement of Baclofen pumps. A comprehensive study of ITB complications in a survey of 40 centres with a total of 1002 test doses and 936 pump placements was published<sup>17</sup>. Common test dose complications were nausea/vomiting (2.6%) and sedation (2.2%). Pump complications included CFS collection (3.3%), constipation (2.9%) and headache (2.4%). Common long-term complications were catheter kink or migration (4.5) and infection (1.2%).

Other studies showed that complication rates ranged from 20-50%<sup>18,19</sup>.

Even with safe surgical techniques, some common complications of Baclofen pump implantation still occur. Excessive swelling may be a sign of developing seroma, sometimes requiring percutaneous drainage. CSF leak may be detected by spongy swelling on the incision site on the back.

Intrathecal use of Baclofen does not completely eradicate the central risks. The most frequent drug-related side effects of ITB include drowsiness, dizziness, constipation and muscle hypertonia.

Baclofen withdrawal is a serious risk if there is an abrupt decrease in drug infusion; causes include catheter failure (eg-obstruction, fracture or dislodging of the intrathecal catheter), pump malfunction or low pump reserves. Symptoms include pruritis without a rash, hyperthermia, hypertension, changes in mental status and aggravation of spasticity, immediate and active intensive treatment and care should be instituted with doses of Benzodiazepines and try to recommence intrathecal Baclofen infusion.

In our study there were 2 out of 33 pumps explanted due to infection, and one patient needed significantly increasing doses; this was diagnosed as

catheter breakage and the catheter was replaced after three years of implantation. We had four patients with headache and dizziness after the test dose and implantation, but these side effects were temporary and were resolved easily.

Intrathecal Baclofen is approximately 100 times more effective than oral alternatives and produces fewer side effects than large oral doses which can lead to drowsiness, sedation, ataxia, weakness and fatigue due to Baclofen crossing the blood-brain barrier.

Although Intrathecal Baclofen is an alternative method requiring considerable initial outlay for the start up course, this can be reduced in the long term<sup>20</sup>. Nursing care and mobilization after Baclofen pump implantation become much easier with improvement in activities and daily living<sup>2,21</sup>. It also resulted in a decrease in the average length of subsequent hospitalisations<sup>21</sup>.

As a whole, IBT can improve the quality of life in carefully selected patients and can be cost effective<sup>22,23</sup>.

In our study we have demonstrated that ITB is an effective technique for relieving spasticity in patients who do not respond to conventional therapy.

## Conclusion

Spasticity secondary to spinal cord injury and other central nervous system damage is common with clinical manifestations of hypertonicity, spastic paralysis and hyper-reflexia. Multimodal treatment should be aimed at preventing exacerbating factors, daily physical therapy with stretching, medications, contracture release and denervation of the motor neuron endplate. The most effective oral therapy for spasticity is Baclofen, Diazepam and Tizanidine, though all have limitations. Denervation of the motor neuron endplate with Phenol or Botulinum toxin can be effective, but the most effective treatment, with the least side effects, is intrathecal Baclofen, which should be considered when conservative methods fail.

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