Intrathecal Baclofen Therapy for Spasticity

Spasticity is defined as a motor disorder characterised by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks resulting from hyper-excitability of the stretch reflex, as one of the components of the upper motor neurone syndrome.[1] For some patients neurolysis or chemodenervation with botulinus toxin or phenol may be useful, particularly for focal spasticity. The intrathecal administration of baclofen (ITB) offers a safe and effective alternative to oral medications that may be ineffective in some patients with severe diffuse spasticity due to a variety of causes including multiple sclerosis, cerebral palsy, traumatic and hypoxic brain injury, and spinal cord injury. It is also effective in the management of spasticity resulting from cerebral palsy in children.[11] Several studies from North America have also shown considerable economic benefits resulting from reduced in-patient costs and related fees.[2,8,9]

Intrathecal Baclofen (ITB)

ITB involves the continuous delivery of baclofen from an implanted pump, situated subcutaneously in the anterior abdominal wall, connected to a catheter whose distal end lies within the lower dorsal subarachnoid space (Figure 1). ITB therapy is a good alternative when physical methods and oral medication (including muscle relaxants and oral anti-spasticity drugs) fail to produce satisfactory control of spasticity or are poorly tolerated.[4] Baclofen is an agonist to a bicuculline-insensitive variety of GABA receptors, known as GABA-B. A possible explanation for its effect on spinal cord functioning is triggering of a cascade of events that includes neuronal hyperpolarisation, with prevention of calcium influx and thus facilitation of potassium conductance and inhibition of release of excitatory neurotransmitters. This eventually leads to pre-synaptic inhibition with reduction of both mono- and poly-synaptic reflexes and motor activity. As a consequence abnormal muscle tone and stretch reflex hyperexcitability are reduced, bringing about reduced spasticity.

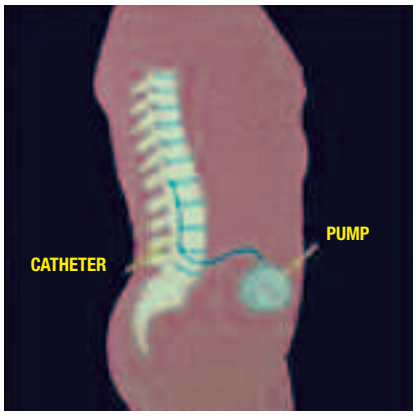

Figure 1: Diagram of implanted programmable pump.

Since baclofen is hydrophilic it crosses the blood-brain barrier poorly, leading to low CSF concentrations when administered orally. Intrathecal delivery circumvents this property and intrathecal doses are typically 100 – 1000 times smaller than oral doses to achieve the same effect. The negative effects on arousal and cognition can thus be avoided. The effects of ITB are reversible and the treatment does not involve destruction of neural tissue.

Inclusion criteria for ITB therapy

After a multidisciplinary assessment, treatment goals are agreed. Motivation and commitment of patients, families and caregivers should be taken into consideration. Clinical, functional and psychosocial factors may also have a bearing on the suitability of a patient for ITB therapy.[5] It may also be helpful to discuss alternative treatment options in advance, in the event that ITB therapy proves to be ineffective or poorly tolerated.

Contraindications to ITB therapy

Relative contraindications include unmasking of poor trunk control due to latent weakness of muscle groups following resolution of spasticity. Patients on anticoagulant medication should have this stopped temporarily during the intrathecal baclofen trial and for the subsequent implantation of the pump.

ITB therapy is absolutely contraindicated in patients with active infection, allergy to baclofen, and in pregnancy (since baclofen may be teratogenic).[5]

Chart 1: Contraindications to ITB therapy

Relative contraindications
- *Poor trunk control with reduced spasticity*
- *Pre-existing bladder problems*
- *Anticoagulation therapy*

Absolute contraindications
- *Active infection*
- *Allergy to oral baclofen*
- *Pregnancy*

Benefits of ITB therapy

Objective improvements are seen in the form of reduced muscle tone, spasms and pain with increased mobility, and improvement in speech, sleep quality, bladder control and self-image. Improvements may also be seen in activities of daily living (ADLs), self-care, dressing, sitting tolerance, movement, transfers, orthotic wear and in overall comfort.[10]

Approach to ITB therapy

a. Patient selection
b. Screening
c. Pump implantation
d. Dose adjustment
e. Pump maintenance

a. Patient selection

The preferred approach involves a multidisciplinary assessment. Potential candidates for treatment will have severe spasticity which has been inadequately controlled by, or who have experienced significant side-effects with, standard drug treatments.

Chart 2: Indications for ITB therapy

- *Severe multiple joint spasticity, particularly in the lower limbs*
- *ADLs and mobility limited by spasticity*
- *Spasticity that interferes with nursing care and hygiene*
- *Spasticity refractory to other treatment modalities*
- *Severe side-effects with other treatment modalities*
- *Complications of spasticity (contractures, pressure sores)*
- *Painful spasms*
- *Clonus interfering with transfer and mobilisation*
- *Medical stability (infection-free, no unresolved medical issues)*

b. Screening trial – intrathecal testing

A variety of trial regimes may be utilised, the purpose being to ascertain if spasticity can be controlled with intrathecal baclofen, After establishing CSF access with a lumbar spinal drain we give an initial intrathecal test dose of 5 micrograms (mcg) of baclofen to exclude any allergic response. Thereafter incremental doses of

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baclofen are given twice daily with a dosage interval of at least eight hours, and increasing the dose by 25mcg each time. The response to each dose and any adverse effects are noted. With severe dystonia it can be helpful to undertake a trial of continuous infusion of baclofen.

The onset of action of a single dose of baclofen is about two hours, with a peak effect occurring usually in four to six hours. A positive response is on average a one point drop in the Ashworth scores in the affected limbs, but other factors to be noted include reduced pain or spasms, improvement in range of motion, positioning, and mobility.

Latent weakness may be uncovered after the baclofen and this may limit its usefulness in some patients. It is limited to about six to eight hours after a bolus administration. Excessive length of weakness may be seen in patients with multiple sclerosis.

c. Surgical implantation

Prior to implantation of the ITB pump the patient should be medically stable, infection-free, but may continue on oral spasmolytic medication (which can be gradually withdrawn in the early postoperative period).

The site of pump placement is evaluated and marked on the skin, taking into consideration factors such as the patient's belt line, the wheelchair armrest position, and any orthosis. It may also be necessary to consider the position of any stoma site since many of these patients may have a colostomy, urinary diversion or feeding gastrostomy. Ideally the positioning of the pump site should be agreed with the patient, family and carer. Informed consent should include a discussion about expectations of treatment with ITB, and the proposed arrangements for aftercare and the need for periodic refilling of the pump; and the need for the pump to be replaced after an interval of approximately five to seven years, the average battery life.

The pump is implanted under general anaesthesia. Incisions are made in the lower midline lumbar region and in the right hypochondrium, at the site selected preoperatively. A fine bore lumbar catheter is passed via a Tuohy needle such that its tip lies in the lower thoracic region and CSF flow is established. In passing the lumbar catheter care should be taken to pass it slightly off the midline to minimise the risk of late damage to the catheter by the 'scissoring' action of the adjacent lumbar spinous processes. From the abdominal incision a second catheter is tunnelled subcutaneously, attached to the lumbar catheter, and anchored

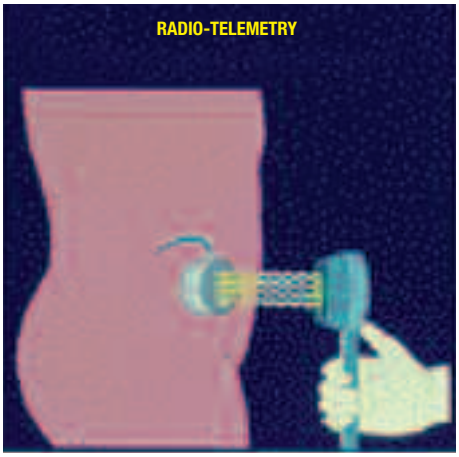

Figure 2: Diagram of telemetry wand.

Figure 3: The Synchromed II infusion system.

to the subcutaneous tissues. A subcutaneous abdominal pocket is now fashioned, just large enough to contain the pump, and passing distally far enough that the pump does not lie beneath the incision, thereby minimising the risk of wound dehiscence. The pump is now filled with baclofen and the proximal end of the catheter attached prior to placement of the pump within the pocket to which it is anchored with retaining sutures. The procedure usually takes about one hour. The pump can be programmed so that the catheter is flushed and a therapeutic rate of baclofen delivery is commenced at the end of the procedure.

Since the effectiveness of baclofen given intrathecally seems to be greater with continuous administration rather than with a single bolus dose, a simple guide to total daily administration is to set the pump to deliver 1.5 times the minimal effective bolus dose established during the ITB trial. The eventual rate of delivery will need to be established somewhat empirically over the next few days by titrating the dose to the observed response.

Postoperatively a pressure dressing may be applied to the abdominal wound and the patient should lie flat to minimise the risk of spinal headache due to CSF leakage and also to prevent development of fluid accumulation within the abdominal pocket.

d. Dose adjustment

If a manual pump has been placed (Cordis 'Secor' or Pudenz-Schulte system) patients can decide for themselves when to pump, although a daily routine is preferred. Once the pump has been activated it cannot be reactivated again until after a delay in order to prevent accidental or deliberate overdosage.

Constant-rate infusion systems have a pressurised gas-filled chamber deep to the reservoir; the gas is further compressed when the pump is refilled and, by virtue of the high resistance of the outlet tubing from the reservoir, the flow rate (and thus the delivery of drug to the CSF) remains constant until the pump is refilled. With such pumps (Therex 300 or Infusaid 400) dosage can only be adjusted by emptying the pump and refilling it with a different concentration of baclofen.

With programmable pumps (Medtronic SynchroMed range) the rate can be adjusted using an external programmer that interrogates and re-programmes the chip in the pump (Figure 2). The pump can be set to deliver at rates by day and by night – or even more frequent alterations. The SynchroMed Infusion System (Figure 3) consists of a small titanium disk about 7.5cm in diameter and 2.5cm thick which contains a refillable reservoir and a computer chip that regulates the battery-operated pump; and, in common with other systems, a fixable silicone catheter that serves as a pathway from the pump to the intrathecal space. Dosage should not be adjusted more frequently than every 24 hours in order to allow for stabilisation of the intrathecal baclofen concentration and incremental increases, if indicated, of 10-20% should be made for patients with spasticity of spinal cord origin, and of 5-10% for children and for adults with spasticity of intracerebral origin. Typical maintenance doses in our series of patients receiving ITB for spasticity from a wide range of causes is of the order of 100-200 mcg per 24 hours.

e. Pump maintenance

Periodic refilling of the reservoir with baclofen will need to be performed approximately every 6-12 weeks depending upon the rate of daily infusion. Dose titration can be further fine-tuned during this stage, the aim being to control (but not to abolish) spasticity to the point that the limbs can be managed easily and the

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patient is enabled to perform functional tasks. Careful re-assessment should be undertaken at regular intervals.

To refill the reservoir the pump is emptied and a new supply of baclofen (for intrathecal administration) is injected using a special refill kit supplied by the manufacturers. This involves the use of a non-coring 22-gauge, Huber-type needle to reach the reservoir through its silicone septum. The pump is then reprogrammed. The programmable pumps emit a low reservoir alarm sound if a preset level is reached (usually 2ml of their 18ml capacity).

The procedure is performed with sterile precautions in a clean environment. We have found it beneficial to have each patient allocated to a dedicated nurse trained in spasticity assessment and in pump maintenance. This not only gives a useful point of contact for the patient and their carer, but also reduces the infection risk that might arise with pump refilling being performed by less experienced staff undertaking the procedure on an occasional ad hoc basis.

Further rehabilitation after ITB pump placement

Since the problems caused by spasticity are numerous and multi-faceted a team approach for continuing management is required. Further treatment may involve stretching, strengthening, conditioning and motor retraining. Serial casting or tendon release procedures can also be undertaken to achieve maximum elongation after spasticity has been successfully treated.

Chart 3: Rehabilitation guidelines after ITB pump placement

- *Re-assess the patient as new*
- *Elongate shortened tissues through stretching and serial casting or tendon release procedures*
- *Initiate strengthening programme, knowing spastic muscles are weak*
- *Attempt to re-establish motor control and coordination*
- *Re-evaluate orthoses, adaptive equipment and seating systems*
- *Modify the home programme and family training*
- *Employ other antispastic medicines to optimise the functional outcome eg Botulinum toxin injections to treat residual focal spasticity*

Adverse effects of baclofen

ITB has CNS depressant properties causing sedation, somnolence, dizziness, drowsiness, ataxia and possible cardiac and respiratory depression.

Rapid reduction of baclofen administration may result in ITB withdrawal syndrome, a rare and life-threatening condition consisting of pruritus, rash, anxiety, disorientation, fever and cardiovascular instability.[7]

Complications of ITB therapy

Complications of ITB treatment are common and in most cases mild and reversible but some, particularly those related to the catheter, can be troublesome to diagnose even though ultimately fairly simple to rectify. It is important to explain to patients in advance of implantation that such complications may arise since once established ITB is generally well tolerated and can bring about considerable improvement in quality of life. Examples of the range of complications are given in Chart 5.

One of the commoner complications is catheter leakage, due to kinking or fracturing, and this usually presents as an apparent loss of efficacy of ITB with increasing spasticity or unpredictable variation in effectiveness of the drug.

Occasionally the spinal catheter tip can cause irritation of a lumbar nerve root with resulting unilateral sciatica. Re-opening of the lumbar incision under general anaesthetic and withdrawal of the catheter by 1-2cm usually results in complete resolution of this problem.

ITB has CNS depressant properties and sudden withdrawal may result in a rare but potentially life-threatening condition (see above). Baclofen overdosage can be dealt with by adjusting the rate of administration but with major overdosage the patient may become weak, apnoeic or unconscious. (Such a condition may arise if, for example, the patient is inadvertently placed in an MRI scanner, for which reason extreme caution should be taken before subjecting patients with implanted infusion devices to such investigation. Temporary explantation of the pump may even need to be considered if a strong indication for MRI scanning exists). Treatment of the condition requires intensive care unit admission where endotracheal intubation and assisted ventilation may be required. The pump should be stopped (or removed) and respiratory depression should be reversed with physostigmine 1-2mg intravenously.

Chart 4: Side effects and overdose symptoms of baclofen[6]

Common side effects

- *Drowsiness, tiredness*
- *Increased weakness*
- *Dizziness, lightheadedness*
- *Mild confusion*
- *Constipation*
- *Bladder disturbance*
- *Sleep disturbance*
- *Ataxia*

Symptoms of overdose

- *Drowsiness*
- *Lightheadedness*
- *Sudden onset of blurred vision of diplopia*
- *Vomiting*
- *Seizures*
- *Fever*
- *Coma*

Chart 5: Complications of ITB therapy

Patient-related
- *Hypersensitivity to baclofen*

Operator-related
- *Programming error*
- *Drug concentration error*

Complications of test doses
- *Nausea or vomiting*
- *Sedation*

Procedure-related
- *CSF leak and spinal headache; CSF collection*
- *Pump socket seroma*
- *Infection*
- *General anaesthesia risks*

Pump-related
- *Flipping of pump*
- *Failed pump*
- *Power failure*

Catheter-related
- *Kinking*
- *Fracture*
- *Occlusion*
- *Dislodgement*
- *Catheter tip fibroma*

Summary

Since its introduction in the 1980s long-term administration of ITB has proved to be a safe, well-tolerated and cost-effective treatment for severe spasticity in adults and children. It is of benefit in patients with spasticity due to cerebral or spinal causes and the beneficial effects tend to be maintained in the longer term. The reduction in spasticity leads to functional improvement and pain relief and, in patients with severe disability, ease of nursing care. Furthermore the reduction in severe diffuse spasticity in stroke patients is not accompanied by adverse effects on arousal or on cognition.[3] However there is a risk, particularly in ambulatory patients, of unmasking underlying muscle weakness. Although complications are relatively common these tend to be amenable to relatively simple measures.

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