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Original Research Paper

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INTRATHECAL BACLOFEN PUMP FOR SPASTIC HYPERTONIA FOLLOWING PENETRATING BRAIN INJURY

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ABSTRACT Management of severe spasticity following penetrating brain injury is often a difficult problem. Orally administered medications generally offer limited benefits. Intrathecally administered baclofen has been shown to be effective in patients with spasticity caused by spinal cord injury and stroke, however, the effectiveness of ITB for spasticity related to penetrating brain injury is not well established. We reported two cases of spastic hypertonia following gunshot injury to brain with brief review of literature upon role of intrathecal baclofen pump (ITB) in cortical spastic hypertonia.

KEYWORDS : Penetrating brain injury, Intrathecal baclofen pump, Spasticity

INTRODUCTION

Gunshot wounds to the head become the leading or second leading cause of head injury in many developing countries. The clinical condition of the patient depends mainly on the mechanism (velocity, kinetic energy), anatomical location of the lesions, and associated injuries [4]. It frequently results in the major long-term disability in terms of motor weakness on one or both side of body. Further impairing mobility and function in this patient population is spastic hypertonia. This abnormal, excessive muscle tone can cause many problems, including pain, loss of free movement of a limb, and interference with the ability to walk and perform daily activities, such as bathing or dressing [13] . Management for spastic hypertonia included physiotherapy, anti-spastic drugs and ablative procedures including phenol injections. These procedures generally require repetition and have been associated with permanent weakness, dysesthesias, and causalgia [13]. Intrathecally administered baclofen has been shown to be effective in patients with spasticity caused by spinal cord injury and stroke [13]. However, the effectiveness of ITB for spasticity related to penetrating brain injury is not well established.

We reported two cases of spastic hypertonia following gunshot injury to brain with brief review of literature upon role of intrathecal baclofen pump (ITB) in cortical spastic hypertonia.

Case 1

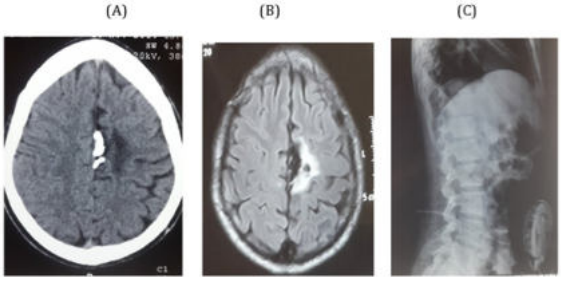
A 32-year-male was presented with spastic paraparesis. He had sustained a gunshot injury six years back during assault with paraparesis in both lower limbs, following which he underwent primary debridement with closure of scalp wound and cranioplasty for scalp defect after 6-month post injury.

Patient recovered from gunshot injury well but he developed spasticity in both lower limbs and become bedridden. Over a period of 6 years, the patient had been given local anesthetic injections, oral baclofen, diazepam, and gabapentin, all with minimal therapeutic effect. Bilateral lower limb manipulation under a general anesthetic and physiotherapy had failed to reach a satisfactory long-term outcome. Over time, the patient's spastic posturing and associated pain became more persistent and resistant to management then the patient was referred to rehabilitation center and Neurosurgery department for management of spastic paraparesis. On examination he was conscious, his power in right lower limb was 3/5, and in left lower limb 4/5, tone increased in both lower limb (Table 1). Bladder and bowel dysfunction was absent. NCCT head revealed midline hyper density at parasagittal region at left high parietal region suggestive of retain bony fragments **(Figure 1A).** Magnetic Resonance imaging (MRI) brain revealed hypo-intensity on T1 and T2 images **(Figure 1B)** at parasagittal region at left high parietal region with encephalomalacia. MRI of the spine was unremarkable.

Management

Patient and their relatives were explained about the possibility of ITB. After there consent the patient was consider for percutaneous ITB injection of 50 microgram to test its efficacy, 50 mg, on trial basis resulted in successful reduction in spasticity in both lower limbs (Table 1); the Physiotherapist, independent of the medical practitioners, confirmed these findings. Following multidisciplinary team discussion between the neurosurgeon, pain medicine specialist, physiotherapist, we decided to consider the offer of an ITB pump. This trial gave us the confidence to offer the placement of a permanent drug delivery system in the form of a TRICUMED IP 2000V infusion pump **(Figure 1C)**.

Figure 1: (A) NCCT head, (B) MRI Brain T2 image, (C) Postoperative LS x-ray



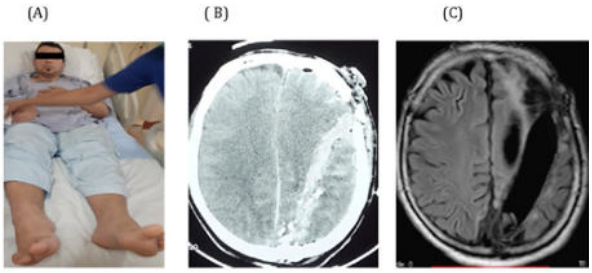
The pump was filled with 20 mL of 500 mg/mL of baclofen and the infusion rate of the pump was set to 75 microgram/day. After implantation of the infusion device, patients received follow-up care on an outpatient basis for refilling and dosage adjustment. The maximum refill interval currently recommended by the manufacturer is 80 days. Post operatively patient had significant improvement in the spasticity of both lower limb, now he is able to stand with support and able to carryout his daily routine activity.

Case 2

A 27-year male had gunshot injury 2 year back followed by hemiparesis on right side. Initially he was managed with wound debridement and ICU care. Patient recovered from event and become conscious after 3-month but he had severe spastic hemiparesis on right side of body. Over a period of one and half years, the patient had been managed with physiotherapy, oral baclofen, and gabapentin; but spasticity was resistant to all conservative management. On admission

patient was conscious with severe spasticity on right upper and right lower limbs **(Table 1)** with normal (5/5) power on left upper and lower limbs **(Figure 2A)**.

Figure 2 :(A) Pre-operative image showing functional status of patient.(B)NCCT Head ,[C]MRI Brain T1 image: Showing tract of perforating brain injury over left cerebral hemisphere



His CT head revealed tract of perforating injury over left cerebral hemisphere with retained bony fragments along its path **(Figure 2B).** His MRI brain revealed tract of perforating injury with encephalomalacic changes **(Figure 2C).** After discussion of risk and benefit patient were planned for trial ITB 50 microgram. Trial ITB shows reduction in hypertonia in both right upper and right lower limbs **(Table 1).**

Table 1: The summarized clinical data

Clinical profile	Case 1	Case 2
Age/ sex	34/ M	32/M
Symptoms	Spastic paraparesis	Spastic hemiparesis
MRI Brain	Gun shot wound with retain bony fragments at motor cortex	Perforating gun shot wound left motor cortex
SPASTICITY (Modified Ashworth Scale)		
Preoperative	Both Lower limbs: 3	Right UL- 2 Right LL- 2
After trial injection	Both Lower limbs: 0	Right UL-1 Right LL-0
Immediate post operative	Both Lower limbs: 1	Right UL-1 Right LL-0
Follow up	Both Lower limbs: 1	Right UL-1 Right LL-0
MUSCLE POWER (MRC Grade)		
Pre operative	Bilateral Lower limb 4/5	Right Upper Limb overall - 2/5 Elbow flexor-2/5, Extensor-0/5 Wrist 1/5, Hand gripping- 0/5 Right Lower Limb-3/5
After trial injection	Same	Same
Immediate post operative	Same	Same
Follow up with Physiotherapy	Bilateral Lower limb 4/5	Right Upper limb Shoulder-2/5 Elbow flexors-2/5,Extensor-1/5 Wrist 1/5, Hand gripping- 0/5 Right lower Limb-4/5
DTR		
Preoperative	Exaggerated, Clonus absent	Exaggerated, Clonus absent
Follow up	Normal	Normal
Preoperative Mobility Status	Bedridden	Bedridden
Postoperative 3 month follow up with Physiotherapy	Able to walk with support of Walker	Able to walk independently with Tripod Cane

Based on trial results patient under done continuous infusion placement of a permanent drug delivery system in the form of a TRICUMED IP 2000V infusion pump. The pump was filled with 20 mL of 500 mg/mL of baclofen and the infusion rate of the pump was set to 50 microgram/day. Post operatively patient had significant improvement in the spasticity of both upper and right lower limb, now at follow up at 3 month he is able to stand with support and able to walk carryout his some daily routine activity (Figure 2D).

DISCUSSION

Management of spastic hypertonia included physiotherapy, anti-spastic drugs such as baclofen and dantrolene sodium, botulism toxin injection, continuous intrathecal baclofen infusion and surgical interventions such as myelotomy and cordotomy or cordectomy [12]. The functional objectives of treatment were to improve gait, hygiene and other activities of daily living; pain relief; decreasing the frequency of spasms [6].

Oral Baclofen is mainstay of treatment for spasticity. It is structurally similar to GABA and binds to presynaptic GABA-B receptors within the brain stem, dorsal horn of the spinal cord, and other CNS sites. In the brain, baclofen delivered orally has some supraspinal activity, which may contribute to clinical side effects such as drowsiness, confusion, and memory or attention problems at the dosages required to reduce spasticity [8,12,13,]. Other central effects of the drug have included hallucinations, ataxia, and memory impairments [15,16]. Sudden withdrawal of orally delivered baclofen may lead to seizures and hallucinations [15,17]. Oral anti-spastic drugs are ineffective in controlling severe spasticity of cerebral origin than caused by spinal cord damage because of the patient`s increased susceptibility to adverse side effects and their limited ability to cross the blood-brain barrier[12,13].

Intrathecal baclofen (ITB) is suited for individuals with severe spasticity who either do not benefit from the oral form or do not tolerate the adverse effects. On the basis of electrophysiology and preclinical studies, the mechanism of the antispasticity effects associated with intrathecal baclofen is believed to result from hyperpolarization of motor horn cells [7]. The side effects noted with oral baclofen are largely averted via delivery of ITB. The delivery system for ITB therapy consists of a subcutaneously placed pump with a reservoir attached to an intra-spinal catheter. This delivery method concentrates the medication within the spinal sub- arachnoid CSF in the thoracolumbar and sacral spinal regions at a much higher level than that attainable via the oral route [11,12]. From there the CSF flows to the arachnoid villi for reabsorption, avoiding a baclofen effect on the cerebral hemispheres [11,12]. Only low levels of the medication have the potential to reach the brain stem or cerebrum [9,12,13]. This manner of delivery avoids the cognitive side effects of oral delivery; such as drowsiness and lethargy. We have not noted any complication in our two cases.

Use of ITB was associate with reduced spasticity and deep tendon reflexes (DTR) in spastic limbs following gunshot injury in our two cases. Role of ITB in acquired brain injury was detailed study by Meythaler JM et al [12]. In his double- blind, placebo-controlled trial (1999) reported continuous infusion of intrathecal-administered baclofen demonstrated that this drug is capable of significantly decreasing spasticity and dystonia in patients with acquired brain injury. Broseta, et al.

[1] reported on 14 patients receiving continuously infused intrathecal baclofen, including four adults with severe spasticity secondary to traumatic head injury and one child with cerebral palsy. Tone as measured by the Ashworth Scale was improved in all five and global ratings were excellent in two, good in one, and fair in two patients. Use of ITB was not associated with reduction in motor power in spastic limbs and in normal limbs. Meythaler JM et al [12,13] noted similar findings; according to him decrease in motor strength rarely occurs after administration of therapeutic doses of intrathecal baclofen. On the contrary, an increase in functional motor strength has often been reported. The increase in functional strength in these patients is believe to be caused by a reduction in motor tone, which is often so high before treatment that it effectively reduces the voluntary motor capacities of the hypertonic extremities. In an another study, Francisco and Boake [5] using a case-series design with 10 subjects, examined functional gains following ITB administration and found improved walking speed, functional mobility ratings, and spasticity while maintaining the muscle force in the uninvolved extremities.

Effect of ITB was more noted in lower limbs compare than upper limb with regards to muscle tone, spasm, and DTR. Meythaler JM et[13] al in his double- blind, placebo-controlled trial on stroke patients (2001) reported continuous infusion of intrathecal administered baclofen demonstrated better effect in lower limbs than upper limbs. Probable explanation for variable effect is higher concentrations of drug at lumber sub-arachnoid space, this finding supported by Kroin and Penn[9], who demonstrated a lumbar-to-cisternal drug cerebrospinal concentration of 4.1:1 after ITB. While moving the catheter more cephalad up to mid thoracic or above may improve spasticity in upper limb.

The intrathecal dose of baclofen is approximately 1% of the oral dose [2]. Dosing typically is initiated at an infusion rate of 25 μg/d and titrated up to an average of 400 to 500 μg/d. However, complications such as infection, impaired wound healing, catheter dislocation, and pump malfunction exist. Catheter complications have been reported to be as high as 62%[10], but the rate is between 20% and 25% in most clinical studies [3]. Pump malfunction resulting in overdose can result in respiratory depression, decreased cardiac function, and coma; abrupt stoppage of drug administration can result in withdrawal [14].

CONCLUSION

These reports provide modest support for the use of continuously infused intrathecal baclofen for severe spasticity following PBI. This reduction in tone will allow more freedom of movement and the potential for improved function when combined with a therapy program after ITB pump placement. More experience is required before deciding whether the benefits of this treatment justify its use. This experience will have to be gathered in a carefully controlled manner to evaluate the benefits of treatment effectively.

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