CASE REPORT

Intrathecal Baclofen Therapy to Reduce Spacticity in Two Patients with Traumatic Central Nervous System Injury

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Spasticity is a common sequela in patients with spinal cord injury (SCI) or traumatic brain injury (TBI). Conventional oral baclofen therapy in large doses may induce gastrointestinal discomfort and neuropsychiatric symptoms. Intrathecal baclofen (ITB) is a relatively new modality for treating spasticity of spinal cord origin. Herein, we present our experience with ITB therapy for treatment of SCI- and TBI-related spasticity. Case 1 involves a 21-year-old man with SCI at the C3-C4 region accompanied by a traumatic herniated intervertebral disc, resulting in incomplete tetraplegia. Case 2 involves a 19-year-old man with a localized brain contusion and acute subdural hematoma in the left frontal-temporal-parietal lobe. Both patients underwent ITB implantation after preoperative and ITB screening 28 months and 29 months, respectively to treat severe spasticity. Functional independent measure scores and mean modified Ashworth scores were calculated preoperatively and postoperatively in both patients to evaluate outcome of ITB therapy. Overall, both patients exhibited a good response. Mean modified Ashworth scores decreased soon after ITB implantation and adequate dosage adjustment in both patients. Functional independent scores improved gradually during the follow-up periods. There were no complications, and no overdose or withdrawal symptoms at 3-month postoperative follow-up in case 1 and at 7-month postoperative follow-up in case 2. ITB therapy is effective in reducing spasticity in patients with SCI and in patients with TBI. **(Mid Taiwan J Med 2009;14:34-40)**

Key words

brain injury, intrathecal baclofen, rehabilitation, spasticity, spinal cord injury

INTRODUCTION

Spasticity is a common sequela in patients with spinal cord injury (SCI) and in those with traumatic brain injury (TBI). Alternations in the balance of inputs from reticulospinal and other descending pathways to the motor and interneuronal circuits of the spinal cord combined with an impaired corticospinal system lead to muscle tone increase and spasticity. Therapies for spasticity include oral form anti-spastic medication, phenol intramuscular neurolysis, botulinum toxin A injection, orthopedic surgery, and selective dorsal rhizotomy. Although these therapies are effective in reducing spacticity, oral baclofen therapy can cause many unwanted symptoms, such as gastrointestinal discomfort (nausea, vomiting, diarrhea and constipation) and neuropsychiatric symptoms (confusion, asthenia, depression, somnolence and vertigo). Headache, dry mouth, weakness, and hypotension have also been reported [1]. These adverse effects are prominent particularly when large doses of

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baclofen are administered. If severe spasticity cannot be controlled by oral baclofen administration, intrathecal baclofen (ITB) therapy is advocated as an alternative choice [1].

Common indications for ITB therapy include cerebral palsy, brain injury, spinal cord injury, multiple sclerosis, and ischemic and hemorrhagic stroke. Before ITB implantation, a screening test is mandatory in order to evaluate whether the patient is suitable for ITB therapy. A 50 μg bolus injection of baclofen is delivered through the lumbar cistern. If the mean modified Ashworth scale (MAS) score decreases by more than one point, the patient is suitable for ITB implantation. If the mean MAS score decreases by less than one point, another 75 μg bolus injection will be administered the following day. If the decrease in mean MAS score is still less than one point, a maximal 100 μg bolus injection will be administered on the third day. If the mean MAS score does not decrease by more than 1 point after the maximal bolus injection, the patient is not suitable for ITB therapy. In Taiwan, ITB therapy is not commonly administered because of its high cost and, therefore, few studies on this treatment modality in Taiwan have been reported [2,3]. Herein, we present our experience with ITB therapy to control spasticity associated with spinal cord injury and traumatic brain injury.

CASE REPORT

Case 1

A 21-year-old male student was brought to the emergency department following a motor vehicle accident. He was unconscious upon arrival. The patient had no specific medical history. Upon arrival, his Glasgow coma scale was E1M5V1. Cervical spine magnetic resonance image revealed a region of high signal intensity at the C4 to C5 level. The patient's condition was managed conservatively. Upon discharge, muscle power in both limbs was grade 2 from C5 to T1 and grade 0 below the L2 level. There was only a mild sensation deficit, but numbness below the C5 level. His total functional independence measurement (FIM) score was 48 (Self Care: 6, Sphincter: 2, Mobility-Transfer: 3, Locomotion: 2, Communication: 14, Social Cognition: 21). Severe spasticity (the MAS scores of 4 limbs were all grade 3) was poorly controlled with baclofen (80 mg/day) and tizanidine (6 mg/day) upon discharge.

The patient required long-term catheterization because of poor self-voiding function after the accident. As a result, several urinary tract infection episodes occurred during hospitalization and after discharge. Six months after the accident, video urodynamic studies (VUDS) revealed a hypersensitive urinary bladder complicated by poor detrusor contractility. The patient was hospitalized and underwent a suprapubic cystostomy. At this admission the patient's total FIM score was 53.

Thirteen months after the accident, diluted botulinum toxin A (BOTOX®) was administered to control severe spasticity. It was injected into 2 sites in each head of the gastronemius and hamstring muscles bilaterally (total dosage was 400 U). One week after the botulinum toxin A injection his total FIM score improved to 65. However, severe clonus and spasticity still interfered with the patient's ability to perform daily activities.

Twenty-eight months after the accident, the patient received an ITB evaluation via a lumbar drainage tube that had been inserted at the L4/L5 level after induction of local anesthesia. Prior to the test, the mean MAS score was 2.28 in the right limbs and 2.7 in the left limbs. A single dose of 50 μg baclofen was injected. After an hour, the mean MAS score in the right limbs decreased to 1.6, while that in the left limbs decreased to 1.4. Six hours later, the mean MAS score in the right limbs decreased to 0.4 and that in the left limbs to 0.1. Eight hours later, the mean MAS score in the right limbs was 0.7 and that in the left limbs was 0.55. The mean MAS score decreased by 2 points after the test (Table). There were no adverse effects. Thereafter, the patient underwent intrathecal baclofen pump implantation (Medtronic®, SynchroMed). The tip of the catheter was placed at the T4-5 level, and the starting dose of intrathecal baclofen was 75 μg /day.

Table. Variations of mean MAS score in these two patients

Case 1	Initial mean MAS score (before 50 μg ST)	1 hour after 50 μg BBI	6 hours after 50 μg BBI	8 hours after 50 μg BBI	3 months after ITB-i (DD: 450 μg /day)
	R: 2.3	R: 1.6	R: 0.4	R: 0.7	R: 1.0
	L: 2.7	L: 1.4	L: 0.1	L: 0.6	L: 1.0
Case 2	Initial mean MAS score (before 75 μg ST)	1 hour after 75 μg BBI	6 hours after 75 μg BBI	8 hours after 75 μg BBI	3 months after ITB-i (DD: 200 μg /day)
	R: 1.7	R: 0.5	R: 2.1	R: 2.3	R: 1.2
	L: 2.1	L: 0.6	L: 2.3	L: 2.0	L: 1.1

MAS = Modified Ashworth Scale; ST = screening test; BBI = baclofen bolus injection; DD = daily dose; ITB-i = ITB implantation.

Three months after ITB implantation, the patient exhibited an obvious decrease in spasticity in both lower limbs after the daily dose of baclofen had been increased to a maintenance dose of 450 μg per day (starting at 75 μg, and then increased by 25 μg every 5 or 7 days in the outpatient department). The mean MAS had decreased by 1 point, and muscle power of both legs had improved. He was able to transfer from bed to wheelchair with minimal assistance. Ambulation was achieved with suspension and bilateral hip-knee-ankle-foot orthoses.

Case 2

A 19-year-old man was brought to the emergency department following a vehicular accident. Computed tomography (CT) revealed diffuse brain edema with uncal herniation, transtentorial herniation, and acute subdural hematoma (SDH) in the left frontal-parietal-temporal (F-T-P) lobes. The SDH was evacuated and an intracranial pressure monitoring device was implanted. Cranioplasty was performed four months after the accident to repair the skull defect. Twenty-six months later, intermittent jerky movements were noted and brain CT scan revealed hydrocephalus. A ventriculoperitoneal (V-P) shunt was inserted. The patient exhibited right spastic hemiplegia and his symptoms could not be controlled with baclofen (40 mg/day). Twenty-eight months after the accident, he underwent ITB screening. A single dose of 50 μg baclofen was administered. One hour later, the mean MAS score in his right limbs decreased from 1.8 to 0.6, while that in the left limbs decreased from 1.4 to 1.3. The following day, another baclofen screening test with a single 75 μg dose was performed. After 1 hour, the mean MAS score in his right limbs further decreased from 1.7 to 0.5 and that in the left limbs decreased from 2.1 to 0.6. Based on the patient's response, ITB therapy was indicated and the patient underwent surgery 1 month later. The intrathecal catheter tip was placed at the T9 level. The initial dose of baclofen was 75 μg /day. The decrease in mean MAS score was unsatisfactory 3 days after surgery, so the ITB dose was increased to 100 μg /day. Ten days after the operation, his ITB dose was adjusted to 80 μg /day. The mean MAS score at this time was 2.1 in his right limbs and 2.3 in his left limbs. His total FIM score was 46 (Self Care: 11, Sphincter: 8, Mobility-Transfer: 3, Locomotion: 2, Communication: 10, Social Cognition: 12). Twenty days after the operation, dry cough and increased spasticity were noted.

The ITB dose was adjusted to 90 μg and then increased again to 110 μg because the mean MAS scores in his right and left limbs had increased. He was discharged 35 days after the operation. At the time of discharge, the mean MAS score in his right limbs was 2.3 and that in his left limbs was 2.0. The total FIM score was 62 (self care: 17, sphincter: 8, mobility: 6, locomotion: 4, communication: 12, social cognition: 15). The ITB dose was increased gradually because of persistent lower limb spasticity. The ITB dose reached a plateau of 175 μg /day 2 months after the implantation of the ITB device. Four months after surgery, no complications or discomfort was observed. The

maintenance dose of ITB reached 200 μg /day 7 months after surgery and the mean MAS score for his right limbs was 1.2 and that in his left limbs was 1.1 (Table).

After implantation of the ITB pump, proper dose adjustment, and adequate rehabilitation training, these 2 patients have shown significant improvements in walking ability and activities of daily living (ADL). In addition, there were no technical complications or wound infections. The mean MAS scores fluctuated after ITB therapy due to baclofen dose adjustments and several episodes of infection (upper respiratory infections and urinary tract infections). After undergoing ITB therapy, both patients showed improvement in FIM scores, particularly in mobility and transfer skills.

DISCUSSION

We found that ITB therapy was effective in lowering mean MAS scores, decreasing painful spasms, and improving activities of daily living and functional status in patients with spinal cord or brain injury. ITB therapy not only effectively decreases painful spasticity, but also improves quality of life, sphincteric control, and FIM scores of patients [4-6]. Furthermore, it can prevent adverse effects due to other oral anti-spastic agents, such as baclofen, tizanidine, diazepam, clonidine, and dantrolene. The therapy is also useful in relieving autonomic disorders in patients with traumatic brain injury [7].

Although ITB therapy is not used widely in the early stage of disease, its application has been proven to reduce spasticity and autonomic disorders in the early stage among patients with severe traumatic brain injury [7]. Furthermore, ITB therapy is also recommended for patients with brain injury, strokes, anoxia or trauma in a subacute stage within 1 year after disease onset. ITB effectively decreases the mean MAS scores without adverse effects [8]. In this study, the 2 patients received ITB implantation 28 and 29 months, respectively, after undergoing ITB screening and careful evaluation. The effects of therapy did not interfere with rehabilitation programs or ambulation training. Francisco et al [9] emphasized that ITB therapy can help TBI patients even 14 years after an accident.

Another application of ITB therapy is to control spasticity in patients who have the ability to walk before undergoing the therapy. Aside from the numerous advantages cited, the therapy also leads to improvement in urinary system function, general quality of life, and sleep quality [10]. There have been reports of improvement in FIM scores in motor and cognitive aspects after therapy, as well as improved COPM (Canadian Occupational Performance Measure) scores for performance and satisfaction [11]. In addition, both cerebral and spinal-induced spasticity decrease after ITB therapy [11,12]. In this study, ITB therapy resulted in reduced spasticity, improved gait, greater independence in activities of daily living and did not interfere with ambulation.

Despite the positive outcomes, technical problems can occur, such as catheter separations, obstruction, migration, twists, catheter and pump reservoir separations, pump membrane damage, and leakage [13]. Other adverse effects of ITB include blurred vision, inability to ejaculate, poor memory, drowsiness, speech disturbance, dizziness, nausea, constipation, and disorientation [1]. Tolerance, overdose, and withdrawal symptoms have also been documented [14]. The 2 patients in this study did not suffer from any complications resulting from catheter use or from other technical incidents. However, general weakness or increased spasticity was documented both during admission and at OPD follow-up. These symptoms may be attributed to dose adjustment of ITB. Overdose or withdrawal symptoms were not exhibited in the two patients. Both showed improvements in their MAS and FIM scores.

The initial and maintenance doses of ITB have not been defined. Usually twice the effective bolus injection dose will be used as the starting dose [4] In our 2 patients, the effective screening doses differed between the 2 patients but the initial ITB dose was 75 μg /day in both patients.

Administering twice the effective ITB bolus-screening dose was not initiated in our patients. Instead, the dose was determined by clinical evaluation, along with the subjective feelings of the patients or their caregivers. In these 2 patients, general weakness was observed after adjusting the dose to 100 μg /day 3 days after the operation, which was less than twice the effective test dose. The difference in the initial dose might be due to individual variations. Further studies on the proper starting dose are, therefore, needed. Likewise, conservative administration is recommended.

The maintenance doses in the 2 patients were 450 μg /day and 200 μg /day, respectively. The doses were adjusted according to mean MAS scores, the FIM scores, or other objective evaluations and subjective feelings of the patients. They were not adjusted based on the cerebrospinal fluid baclofen concentrations because there is no proven correlation between CSF baclofen concentration and ITB dosage. CSF baclofen concentration may be influenced by personal variations, differences in CSF clearance rates or differences in catheter tip levels [15]. The maintenance dose in our 2 patients was reached after 3 months and 7 months, respectively. During the adjustment period, it was found that sporadic infection episodes, such as upper respiratory infection, led to increased spasticity. This, in turn, resulted in the increase in the ITB dose. Sometimes, the patient felt better yet at other times, weaker. However, there was no change in mean MAS scores or muscle power. This means that evaluation methods other than FIM or mean MAS scores are needed to adjust the dose.

In conclusion, ITB therapy is an effective alternative treatment for intractable spasticity. However, the cost-effectiveness and the interval of hospitalization and complications related to spasticity should be evaluated among a larger cohort of patients. Further studies on ITB dose among patients of different ethnic groups should also be conducted.

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使用椎管內Baclofen注射療法降低脊髓損傷或創傷性腦傷患者的張力

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張力的形成在脊髓損傷或創傷性腦傷的患者十分常見。傳統的口服劑量較大的baclofen療法常常會引發許多副作用，像是腸胃不適以及精神和神經系統的症狀。在這種情況之下，椎管內baclofen注射療法常常扮演另一種有效的選擇。在台灣因爲沒有發表相似的報告應用在脊髓損傷或創傷性腦傷的患者，所以我們發表這篇病歷報告分享我們的椎管內baclofen注射療法的經驗和兩位患者接受椎管內baclofen注射療法後的成效。在這篇病例報告中第一例病患是一位21歲的男性，診斷是頸椎第三第四節的創傷性脊髓損傷併有頸椎第三第四節的椎間盤突出，導致四肢不完全的癱瘓。第二例病患是一位19歲的男性，診斷是腦挫傷併有左側額葉顳葉以及頂葉的硬腦膜下出血。這兩位病患分別於受傷後28個月和受傷後29個月接受椎管內baclofen注射療法幫浦的植入，手術前皆有經過詳細的術前評估和成功的椎管內baclofen注射療法的篩檢測試。術前和術後都有使用生活功能獨立程度量度表和修正版艾許沃斯評分來做評估和紀錄。兩位病患接受完椎管內baclofen注射療法後都得到良好的成效。修正版艾許沃斯評分在手術完調整是當劑量之後有明顯的下降。在術後門診追蹤的紀錄，兩位患者的生活功能獨立程度量度表皆有持續明顯的進步。第一位位者在術後追蹤了三個月，而第二位患者在術後追蹤了七個月。兩位病患在後續的醫療追蹤紀錄裡並未發生任何的併發症，藥物過量或藥物戒斷的症狀。椎管內baclofen注射療法在這篇報告中顯示，對於脊髓損傷及創傷性腦傷的患者，證實可以有效的降低患者的張力。（中台灣醫誌 **2009;14:34-40**）

關鍵詞

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