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Successful Control of Intractable Myoclonus in a Patient With Hypoxic Brain Injury After Intrathecal Baclofen Therapy: A Case Report

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HIGHLIGHTS

- Myoclonus after hypoxic brain injury (HBI) induces sleep disturbance causing generalized pain, which impedes quality of life.
- Few cases are reported for controlling myoclonus of bed-ridden patients with severe sequelae after HBI.
- Intrathecal baclofen therapy should be regarded as a substantial therapy for myoclonus after HBI.

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Conflict of Interest
The authors have no potential conflicts of interest to disclose.

ABSTRACT

Myoclonus is an abrupt arrhythmic condition with shock-like movements that can be triggered by sensory stimuli, affecting the trunk or limbs during voluntary movement. Since motor symptoms are often not easily treatable, various pharmacological treatment options have been suggested. We report a case of using intrathecal baclofen (ITB) therapy in a patient with hypoxic brain injury (HBI), leading to the alleviation of myoclonus. A 29-year-old woman repeatedly presented with generalized myoclonus and multiple joint contractures at both upper and lower limbs after resuscitation. She cried during intractable myoclonus events, making it difficult for her to maintain a good sleep pattern. Due to the persistent status of multiple joint contractures and intractable myoclonus, we offered an ITB trial to control her symptoms. After ITB, her total scores on the Unified Myoclonus Rating Scale progressively improved as the doses of baclofen increased. Therefore, ITB therapy should be considered as a substantial option in the management of intractable myoclonus in patients with HBI to prevent various complications and improve the quality of life.

Keywords: Myoclonus; Baclofen; Infusion Pumps, Implantable; Injections, Spinal; Hypoxic Ischemic Encephalopathy

INTRODUCTION

Myoclonus is an abrupt condition with jerky arrhythmic muscle movements that can be triggered by sensory stimuli, affecting the trunk or limbs during voluntary movement [1,2]. Lance-Adams syndrome (LAS) is a type of myoclonus associated with hypoxic injury to the brain, and myoclonus that occurs almost immediately after a hypoxic episode is called acute post-hypoxic myoclonus. Myoclonus that emerges after the resolution of a coma is diversely associated with dysarthria, ataxia, seizures, or consciousness disturbance. Furthermore, LAS significantly affects the functional level and the quality of life in patients with hypoxic brain injury (HBI), resulting in additional difficulties with motor control and pain. Since these motor symptoms are often considered poorly treatable, various pharmacological treatment options have been suggested, including anticonvulsants as monotherapy or in combination, but frequently with inadequate symptom control [3]. Previously, using intrathecal baclofen (ITB) therapy has reportedly been used to control myoclonus induced by HBI in few cases of bed-ridden patients with severe sequelae facing consciousness disturbances and functional decline. Although the benefits obtained by relieving myoclonus are scarce due to severe functional deterioration, the advantages in terms of resolving sleep disturbances and difficulty in maintaining posture caused by abnormal movement cannot be ignored. Herein is a report of a case of using ITB therapy in a patient with HBI to control myoclonus, leading to improved sleep maintenance and quality of life.

CASE REPORT

A 29-year-old woman apparently attempted suicide and was found hanging by a rope. She was unresponsive and in cardiopulmonary arrest at her home. Immediately, cardiac massage was started. She was transferred to the emergency department of our hospital, where an electrocardiogram indicated pulseless electrical activity. After approximately 10 minutes of intubation and attempts to revive her, she was resuscitated, and her heartbeat was detected. She was treated with targeted temperature management, maintaining hypothermia to reduce tissue injury following a lack of blood flow to the brain. After 48 hours of hypothermia, upward deviation of the eyeball occurred after sedative dosage was reduced. A diagnostic evaluation, including electroencephalography and computed tomography, showed unremarkable findings. Diffusion-weighted images of the brain showed symmetrical hyperintensities in the perirolandic areas, parieto-occipital cortices, putamina, and hippocampi, indicating a diffuse hypoxic injury (**Fig. 1**). Initially, the patient was treated with oral valproic acid. The next day, she presented with generalized myoclonus characterized by jerky and repeated involuntary contractions of muscles in both upper and lower limbs. She tended to cry during intractable myoclonus events, which made it difficult for her to maintain a good sleep pattern. Additional trials were attempted with clonazepam and levetiracetam, resulting in poor response. Excessive drowsiness and the elevation of amylase and lipase appeared after the administration of oral anticonvulsants, so they were discontinued. After approximately 2 months of hospital stay in the intensive care unit, she was transferred to the Department of Physical Medicine and Rehabilitation to continue comprehensive rehabilitation. A neurologic examination showed a minimally conscious status, representing

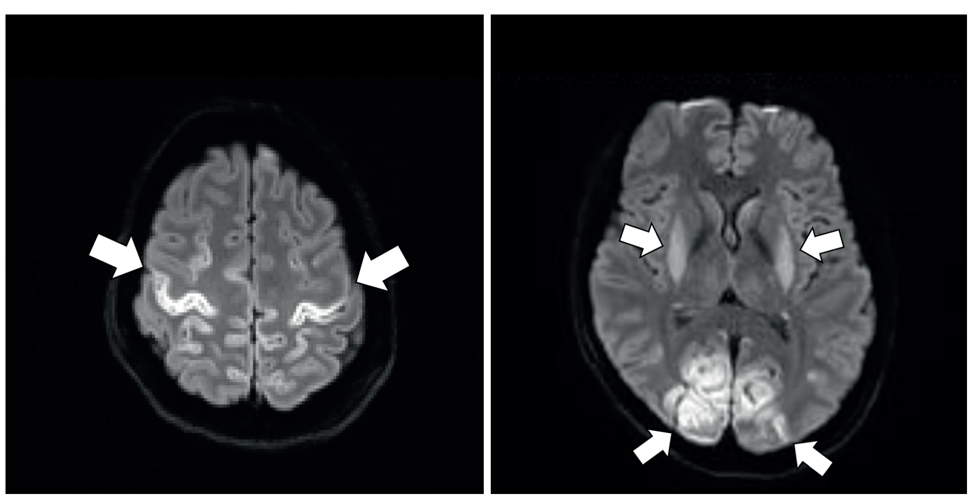

Fig. 1. Diagnostic evaluation of the patient. Hyperintensities of diffusion-weighted images are noted symmetrically in the perirolandic areas (arrows on the left), parieto-occipital cortices, putamina, and hippocampi (arrows on the right), indicating diffuse hypoxic brain injury.

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inconsistent responses to auditory and visual stimulation. Spasticity was assessed using the modified Ashworth scale (MAS), which scored grade 3 for both upper and lower extremities. Physical examinations showed that her major joints, including her shoulders, elbows, wrists, hips, knees, and ankles showed multiple contractures, which made it difficult for her to properly position herself. Continuous jerky and arrhythmic movements of both limbs and uncontrolled crying were observed (**Supplementary Video 1**). For abiding myoclonus and spasticity in all the extremities despite oral medication therapy, we offered the ITB trial to control her symptoms.

The patient was transferred to another hospital for ITB therapy. According to her medical record, she underwent a trial of lumbar bolus injection for 2 days to test its effectiveness. At the first day of trial, a bolus injection of 50 mcg of baclofen was performed. The heart rate, the respiratory rate, blood pressure, O_2 saturation, and the body temperature were monitored every 2 hours, and physical changes, such as range of motion (ROM) and spasticity, were checked. Spasticity gradually improved with the MAS score moving from grade 3 to grade 1+ for the upper extremities. On the second day of trial, 75mcg of baclofen were used. Gradual changes appeared after 4 hours of injection, showing improved spasticity status from MAS grade 3 to grade 2 for the lower extremities. Additionally, changes in myoclonus were not evaluated accurately in terms of scale including frequency and duration but crying response representing the patient's discomfort was decreased and sleep disturbance improved compared with before ITB trial. Her vital signs were stable during all the procedures. There was no significant difference regarding the effect for spasticity of the upper and lower limbs according to the position of the catheter tip [4,5]. Furthermore, due to her severe consciousness disturbance, the risk of fatal complications induced by central side effects, such as aspiration pneumonia, was high, which led to demonstrate the position of catheter tip to more caudal level [5].

As the baclofen trial was successful, an intrathecal drug administration system was implanted, and the catheter tip connected to the pump was placed at T10 vertebral level (**Fig. 2**). The initial ITB dose was 75 mcg/day, and it was gradually increased to 180 mcg/day after 2 weeks. After successful ITB therapy, she was transferred to our hospital to evaluate the effectiveness of the treatment and for comprehensive rehabilitation. The Unified Myoclonus Rating Scale

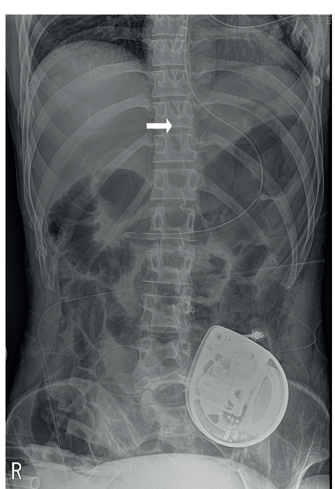

Fig. 2. An abdomen plain radiograph shows implanted intrathecal baclofen pump. The catheter tip placed at T10 vertebral level is indicated (white arrow).

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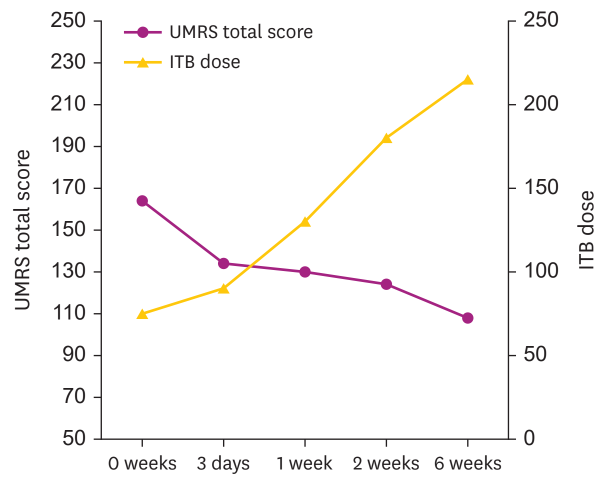

Fig. 3. UMRS total scores and ITB doses are illustrated. UMRS total scores progressively improved as doses of baclofen were increased.
UMRS, Unified Myoclonus Rating Scale; ITB, intrathecal baclofen.

(UMRS), a validated clinical rating instrument measuring the intensity of myoclonus, was used to evaluate her myoclonus before and after the therapy [6]. The total UMRS scores gradually improved as the doses of ITB were increased (**Fig. 3**). Myoclonus in the upper and lower limbs and the following crying episodes significantly decreased compared to the prior ITB trial in terms of amplitude and frequency (**Supplementary Video 2**). After the ITB pump insertion, she was admitted to the inpatient Department of Physical Medicine and Rehabilitation in our hospital again. Followed by a diminished degree of myoclonus, the sleep disturbance improved, and the crying response decreased. Improved sleep quality and the absence of jerky movements made proper bedside positioning possible, which elicited a satisfactory response from the caregivers. After 6 weeks of implantation, the ITB dose was gradually increased at follow-up outpatient visits to 215 mcg/day, which helped the patient to position herself more easily and minimize crying. Specific changes in passive ROM after the treatment are shown in **Table 1**. Spasticity was improved from grade 3 to grade 2 in bilateral elbow, wrist, and hip joints according to MAS. No significant changes were shown in bilateral knee and ankle joints. Compared to a successfully enhanced status of myoclonus, the patient showed little differences in terms of multiple contractures after ITB therapy. She will undergo tendon release and osteotomy for proper positioning in our hospital department.

The patient and her parents were informed that the data concerning the cases would be submitted, and they provided informed written consent for the publication of this case report and the accompanying images.

DISCUSSION

Myoclonus induced by various neurological abnormalities, such as severe hypoxic ischemic encephalopathy, spinal cord injury, and human immunodeficiency virus infection, still remains a challenging task. The control of movement abnormalities in LAS is chiefly achieved through the utilization of drugs such as anticonvulsants [1,3,7]. The possible mechanism of action in the case of clonazepam is the facilitation of gamma amino butyric acid (GABA)ergic transmission and a decrease in 5-hydroxytryptophan utilization in the brain [8]. Intrathecally

Table 1. Changes in passive ROM of major joints before and after ITB therapy

ROM (°)	Before ITB therapy		After ITB therapy	
	Right	Left	Right	Left
Shoulder joint				
Flexion	60	60	70	70
Extension	20	0	20	20
Abduction	70	70	80	90
Adduction	30	30	40	40
Elbow joint				
Flexion	60	40	150	70
Extension	0	0	0	0
Wrist joint				
Flexion	20	10	30	20
Extension	10	10	10	10
Hip joint				
Flexion	40	40	50	50
Extension	0	0	10	10
Abduction	30	30	40	40
Adduction	20	20	30	30
Knee joint				
Flexion	50	60	70	100
Extension	0	0	0	0
Ankle joint				
Dorsiflexion	10	10	10	10
Plantarflexion	30	30	30	30

ROM, range of motion; ITB, intrathecal baclofen.

administered baclofen acts at the level of the spinal cord, bypassing the blood-brain barrier, which is more effective in the management of complex movement disorders [9]. Several cases have been identified in which ITB therapy was attempted for myoclonus induced by mechanisms other than HBI. Chiodo and Saval [10] demonstrated cases of secondary myoclonus of spinal origin utilizing ITB in the treatment. Zhang et al. [11] reported on controlling painful muscles in a 38-year-old woman presenting with stiff-person syndrome.

The precise mechanism of post-hypoxic myoclonus is unclear. Animal studies indicate that selective vulnerability to hypoxia of purkinje cells in the cerebellar vermis leads to disinhibition of GABAergic fastigial nucleus, which in turn leads to cell death in parts of the motor thalamus and inducing neuronal injury cerebral cortex, the hippocampus, and the reticular thalamic nucleus [2,7]. As an exemplary GABAergic agent, the mechanism by which baclofen regulates myoclonus at the supraspinal level is that it stimulates the GABA-B receptor and imitates GABA effect in postsynaptic cells, resulting in maintaining stable status of GABAergic balance and controlling motor function [1]. Furthermore, it is believed that baclofen can influence dopamine metabolism in the central nervous system, inhibiting both nigrostriatal and mesolimbic dopaminergic neurons as well as substance P and decreasing the dopamine turnover rate, thereby boosting dopamine availability, and reducing dopamine receptor hypersensitivity [1,12]. ITB for myoclonus from spinal cord injury decreases inter-neuron inhibition leading to myoclonus, which might be a similar mechanism to that from HBI. It would be merely different in terms of administration doses, duration, and treatment response rate, associated with several factors such as drug concentrations in cerebrospinal fluid [10].

Previous reports of using ITB as a treatment of myoclonus in HBI have suggested that the improvement of myoclonus mainly occurs in patients with low functional decline. Birthi et al. [1] reported on a 25-year-old man who was treated with ITB therapy to control action myoclonus in HBI after cardiopulmonary arrest. The treatment showed less severe sequelae excluding

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consciousness disturbance and gait difficulty. In this situation, the improvement of functional ability was achieved by controlling action myoclonus using ITB therapy, which interfered with the enhancement of gait function. As illustrated in our case, ITB therapy has not been tried in myoclonus patients with prominent consciousness disturbances and functional impairments.

Evaluating the patient, establishing an individualized management plan, mobilizing early, and proper positioning are significant components of the proposed treatment to contribute to the survival and recovery benefits in an intensive care unit [13]. Improper positioning can cause a variety of symptoms that can afflict patients, such as multiple contractures and sleep disturbances, and negatively affect the neurological recovery after a severe brain injury. It is obvious that various movement disorders appearing after HBI are factors that cause generalized pain in a situation where multiple contractures exist. After controlling myoclonus via ITB therapy, generalized pain and sleep disturbances were reduced and a stable status was maintained, relieving the caregivers' burden. The significance can be found in that the control of myoclonus can induce positive effects concerning the prevention of various complications in patients with prominent functional decline.

In our case, the UMRS score was utilized to evaluate the severity and frequency of myoclonus prior to and after the ITB therapy. Each subscore is rated on a scale of 0 to 4, with greater scores allocated to myoclonus of greater severity or frequency [1,6]. It can objectively evaluate myoclonus in a resting position, action myoclonus, and the resulting functional deficits. Presenting severe sequelae after HBI, the effect in terms of functional gain after controlling myoclonus was insignificant, but our patient showed dramatic improvement in total UMRS scores, as myoclonus in the resting position improved, which resolved the issues of sleep disturbance and proper bedside positioning. Due to the patient's severe consciousness disturbance, the subscore of the questionnaire was calculated after an interview with her parents, who were the main caregivers.

In conclusion, our case report emphasizes that prompt management to control myoclonus after HBI might be a significant consideration. As an unsatisfactory effect of oral anticonvulsants for myoclonus after HBI has been identified, alternative therapy could be required. Our case demonstrated the possibility of ITB as an alternative therapy for myoclonus, in addition to its role in managing the spasticity of patients with severe brain injury. Hence, ITB therapy can be a noteworthy choice for the treatment of intractable myoclonus after HBI.

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SUPPLEMENTARY MATERIALS

Supplementary Video 1

Myoclonus of the patient prior to intrathecal baclofen therapy is presented. Myoclonus was most prominent in the proximal legs and arms,, which remained uncontrolled despite significant doses of oral anticonvulsants.

Click here to view

Supplementary Video 2

Bedside status of the patient after intrathecal baclofen therapy is illustrated.

Click here to view

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