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A Preliminary Report: Which Patients May Be Candidate For Intrathecal Baclofen Pump?

Atilla Yilmaz[1], Mustafa Turgut Yildizgoren[2*]
[1]Assistant Professor, Department of Neurosurgery, Mustafa Kemal University, Faculty of Medicine - Hatay Turkey
[2]Assistant Professor, Department of Physical Medicine and Rehabilitation, Mustafa Kemal University, Faculty of Medicine - Hatay Turkey

Original Research Article

***Corresponding author**
Mustafa Turgut Yildizgoren

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Abstract: Our aim is to emphasize appropriate patient selection for intrathecal baclofen (ITB) therapy in those suffering from severe spasticity despite various non-pharmacological and pharmacological interventions. The study included 10 patients (6 males, 4 females; mean age 31.5±10.8 years, range, 13 - 41 years) with spasticity that had undergone ITB therapy, and did not respond adequately to conventional physical therapy, medical therapy or focal treatments. The 10 patients enrolled in the study comprised 6 (60%) males and 4 (40%) females, with a mean age of 31.5±10.8 years. Three (30%) patients had spinal cord injury (SCI), 3 (30%) patients had multiple sclerosis (MS), and 4 (40%) patients had cerebral palsy (CP) history. The mean MAS score decreased from 3.6±0.5 to 1.0±0.0 ($p < 0.001$); the mean VAS score decreased from 38.0±12.0 to 20.0±8.1 at the final follow-up ($p=0.001$). Expanded Disability Status Scale (EDSS) scores in the patients with MS were 5.0, 6.5, and 7.0 points at baseline and the final visit. ITB is a safe and effective therapy for reducing spasticity and pain, and it improves function via implantation. Indications for ITB are as follows: diffuse or regional spasticity (if MAS score or PFSF score was > 2), ambulatory MS patients (if EDSS $\leq$ 5.5), non-ambulatory MS patients (if EDSS $\geq$ 7.0), non-ambulatory CP patients with global spasticity (if GMFCS Level 5), diplegic CP patients with severe hypertonia (if GMFCS Level -5).
Keywords: Acquired brain injury, Cerebral palsy, Intrathecal baclofen, Multiple sclerosis, Spinal cord injury.

INTRODUCTION

The definition of spasticity states it to be a velocity-dependent increase in muscle tone because of increased excitability of the muscle stretch reflex. Spasticity can occur whenever there is a lesion in the upper motor neuron pathway [1]. In neurological conditions such as multiple sclerosis (MS), cerebral palsy (CP), acquired brain injury (ABI) and spinal cord injury (SCI), spasticity is often seen as a major problem. It is estimated to affect up to 80% of patients with upper motor neuron diseases [2, 3]. Although spasticity can be used to the patient's advantage, such as enabling walking, standing, transfer in the paretic limb, and protection against deep venous thrombosis, it is a serious problem that can lead to disability and complications such as decubitus and severe muscle contractures [4]. In addition, if spasticity is an obstacle to functional goals, hygiene, and skin integrity, treatment should be started [5].

A wide range of non-pharmacological and pharmacological interventions can be used to treat spasticity [2, 6]. Stretching, electrical stimulation, cryotherapy, superficial or deep heat, whole-limb/body vibration, extracorporeal shock-wave therapy, use of assistive devices, complementary and alternative medicine (acupuncture, cannabis and cannabinoids, nutritional supplements, massage, chiropractic, exercise, yoga) are non-pharmacological interventions. If these measures prove inadequate, oral medication (baclofen, tizanidine, benzodiazepines, dantrolene sodium) can be added to the treatment. Furthermore, patients with localized or multifocal spasticity may obtain benefit from botulinum toxin or phenol injections [6, 7]. If patients have generalized spasticity despite combined pharmacological and non-pharmacological treatment, it may be managed more effectively with intrathecal baclofen (ITB) implantation [2, 4].

The purpose of the current study was to report our experience of continuous ITB therapy in 10 spasticity patients. It was also aimed to identify patients suffering from severe spasticity despite

various non-pharmacological and pharmacological interventions, and to emphasize appropriate patient selection for ITB.

MATERIALS & METHODS

The study was conducted at the Neurosurgery and PM&R clinics of Mustafa Kemal University, between 2014 and 2017. The study included 10 patients (6 males, 4 females; aged between 13 and 41 years with a mean age of 31.5±10.8 years) with spasticity that underwent intrathecal baclofen (ITB) therapy, due to insufficient response to conventional physical therapy medical therapy or focal treatments. The local ethics committee approved this study and all subjects gave written informed consent.

The indications for ITB are the presence of global or regional spasticity (± dystonia), a modified Ashworth scale (MAS) or Penn Spasm Frequency Scale (PSFS) score > 2, spasticity affecting two or more limb regions, including both lower and/or one or both upper limbs, either unilaterally or bilaterally, and if the duration of spasticity is longer than 6 months [8].

The ITB trial protocol started with the administration of test-doses preferably at L3-4 level. An intrathecal bolus injection of 50 mcg Baclofen was administered initially. In pediatric cases, the dose was 25 mcg. If no response was obtained to the standard dose, then 75-100 mcg was administered. An interval of 24 hours was left between the bolus doses. Muscle tone assessments in the hip flexors, hip adductors, knee flexors, knee extensors, and ankle plantar flexors using the MAS were conducted by a physiatrist at pre injection, and at 2, 4, 6, 8 hours after the ITB trial dose. The decision to perform ITB surgery was made on the basis of this examination, with the observation of objective reductions in MAS score of ≥ 1 or PSFS score of >1 in at least two affected limb regions after the ITB trial dose, it was concluded that the patient would benefit from ITB.

Under general anesthesia in the operating theatre, a Synchro Med II infusion pump (Medtronic Inc, Minneapolis, MN, USA) was implanted in the subcutaneous tissues outside the anterior abdominal wall and the catheter was implanted into the intrathecal space at the desired spinal level. After the surgery, all patients received daily standard physiotherapy in addition to appropriate patient education. The dose titration was performed via telemetry according to the clinical response. Demographic and clinical features, including diagnosis, disease duration, indication for ITB, functional levels, mobilization, duration of ITB, all medications, baseline and final MAS for the lower or upper limbs, VAS scores, side effects or complications were recorded.

STATISTICALLY ANALYSIS

All statistical analyses were applied using SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). The values were expressed as mean with minimum and maximum values and expressed as percentages. Paired comparisons were examined using the Wilcoxon signed rank test at baseline to final follow-up. A value of $p < 0.05$ was accepted as statistically significant in all analyses.

RESULTS

A total of 10 patients underwent ITB implantation between 2014 and 2017. The baseline and final clinical features of the patients are summarized in Table-1. Three (30%) patients had spinal cord injury (SCI), 3 (30%) patients had multiple sclerosis (MS), and 4 (40%) patients had cerebral palsy (CP). Six (60%) of these patients were paraplegic, and 4 patients were (40%) tetraplegic.

Four (40%) of these patients required continuous manual contact during ambulation, and 6 (60%) were non-ambulatory. The Functional Ambulation Classification (FAC) was FAC-Level 1 in 3 patients, FAC-Level 2 in 1, and FAC-Level 0 in 6. Of the total 10 patients, 8 (80%) were wheelchair-bound, and 2 (20%) were mobilized with long-leg orthosis and a walker (Patients 5 and 9).

The mean age of the patients was 31.5±10.8 years (range, 13 - 48 years). The mean disease duration was 15.4 ±10.0 years (range, 2 - 39 years). Before ITB, the mean oral baclofen dose was 57.0±14.9 mcg/d (range, 30 - 80 mcg), and the mean tizanidine dose was 12mg/d. All the CP patients had received daily intensive physiotherapy, while the others received home-based exercise therapy. Spasticity-related pain was present in 3 patients (2MS, 1SCI) (Patients 5, 6, 8). The mean baclofen test dose was 55.5±15.8 mcg (range, 25 - 75 mcg). The mean duration of ITB follow-up was 22.2±35.6 months (range, 3 – 120 months). The mean final ITB dose was 152.0±102.1 mcg/d (range, 50-340 mcg/d).

The mean MAS score decreased from3.6±0.5 to 1.0±0.0 ($p <0.001$); the mean VAS score decreased from 38.0±12.0 to 20.0±8.1 ($p=0.001$) at the final follow-up. The baseline and final Expanded Disability Status Scale (EDSS) scores of the MS patients were 5.0, 6.5, and 7.0.

During the follow-up, there was no reported transient hypotension, infective complication, pump-related complication or early pump revisions. Subcutaneous cranial cerebrospinal fluid collection occurred in Patient 2 and Patient 5. Patient 7 had excessive somnolence during a routine ITB refill that reversed completely when the ITB dosage was reduced. Patient 4 received routine ITB battery replacements at approximately the 8th year of pump life.

Table-1: Baseline and final clinical features of the patients with spasticity who implanted intrathecal baclofen pump (ITB)

No	*Diagnosis*	*Age/ Sex*	*DD (year)*	*Reason of ITB*	*Functional status*	*VAS for pain (mm)*		*Mobilization*	*Medications before ITB*	*Test Dose mcg*	*Clinical features after ITB*	*Side effects due to ITB*	*Baclofen Dose mcg/d*		*Dur (mo)*	*Spasticity (Modified Ashworth Scale)*	
						Baseline	*Final*						*Baseline*	*Final*		Baseline	Final
1	CP-total	13/M	13 y	Spasticity	GMFCS-IV	25	20	Wc, FAC=0	Baclofen 30 mg	25	Improvement in spasticity	-	150	120	12	UL: Ash 4 LL: Ash 4	UL: Ash 1 LL: Ash 1
2	CP-total	39/F	39 y	Daily Care, spasticity	GMFCS-IV	30	20	Wc, FAC=0	Baclofen 50 mg	50	Improvement in spasticity	Subdural CSF collection	150	96	3	UL: Ash 4 LL: Ash 4	UL: Ash 1 LL: Ash 1
3	CP-total	31/M	21 y	Daily Care, Spasticity	GMFCS-V	30	20	Wc, FAC=0	Baclofen 60 mg	50	Improvement in spasticity	-	300	270	5	UL: Ash 4 LL: Ash 4	UL: Ash 1 LL: Ash 1
4	CP-total	16/M	16 y	Spasticity	GMFCS-IV	40	20	Wc, FAC=0	Baclofen 50 mg	50	Improvement in spasticity	Battery replacements	350	340	9	UL: Ash 3 LL: Ash 3	UL: Ash 1 LL: Ash 1
5	PP-MS	41/M	17 y	Spasticity, Spasm	EDSS= 5,0	50	40	L-LO, FAC=1	Baclofen 80 mg, Tizanidin 12mg, Botox 300IU	75	Improvement in spasticity and pain	Subdural CSF collection	230	275	120	LL: Ash 4	LL: Ash 1
6	RR-MS	48/F	9 y	Pain, Spasticity	EDSS= 7,0	60	20	Wc, FAC=1	Baclofen 50 mg, Tizanidin 12 mg	50	Improvement in spasticity and pain	-	150	99	32	LL: Ash 3	LL: Ash 1
7	PP-MS	33/F	5 y	Spasticity	EDSS= 6,5	20	10	Wc, FAC=1	Baclofen 80 mg, Tizanidin 12 mg	50	Improvement in spasticity	Vomiting, Somnolence	200	100	18	UL: Ash 2 LL: Ash 4	UL: Ash 1 LL: Ash 1
8	SCI	25/M	15 y	Spasticity	T7 AIS A	40	10	Wc, FAC=0	Baclofen 50 mg, Tizanidin 12 mg	50	Improvement in spasticity and pain	-	200	70	18	LL: Ash 3	LL: Ash 1
9	SCI	34/M	17 y	Spasticity	T12 AIS C	40	20	Forearm Crutch, L-LO, FAC=2	Baclofen 60mg, Tizanidin 12 mg	75	Improvement in spasticity	-	250	50	3	LL: Ash 3	LL: Ash 1
10	SCI	35/F	2 y	Spasticity	T11 AIS A	45	20	Wc, FAC=0	Baclofen 60mg, Tizanidin 12 mg	75	Improvement in spasticity	-	100	100	3	LL: Ash 4	LL: Ash 1

AIS= ASIA Impairment Scale, CP=Cerebral Palsy, MS=Multiple Sclerosis, SCI=Spinal Cord Injury, ITB=Intrathecal Baclofen Pump, GMFCS=Gross Motor Function Classification System, EDSS=Expanded Disability Status Scale, FAC= Functional Ambulation Category, Wc=Wheelchair, L-LO= long-leg orthosis, DD= disease duration, LL= lower limb, UL=upper limb

DISCUSSION

In this paper, the details are reported of 10 spasticity patients who were treated with ITB. The results of this study show that a favorable clinical response was obtained with ITB in baclofen resistant or intolerant spasticity patients.

The general aim of ITB is to treat those individuals whose spasticity is not adequately controlled by conservative treatment including physiotherapy and/or oral medication. If MAS and/or PSFS scores are >2, they are potential candidates for ITB [7]. A decrease of 1 to 2 points in the MAS and/or a reduction of at least 2 points in the PSFS constitute a positive response to the trial.

Multiple Sclerosis (MS): In the current study, 3 of the 10 patients were MS (2 primary progressive-MS; 1 relapsing remitting-MS).There was no deterioration or improvement in the EDSS scores in any of the 3 patients after the ITB treatment. The EDSS scores of Patients 5, 6, and 7 were 5.0, 7.0 and 6.5, respectively. All the MS patients had severe spasticity, and 2 had painful spasms. In addition, 2 patients were wheelchair-dependent, and 1 patient was mobilized with a walker and long-leg orthosis. After the ITB, the painful spasms and the spasticity decreased in all patients.

In approximately 90% of MS patients, spasticity is a common symptom which progressively impairs function and quality of life as the disease worsens [9]. In literature, contrary to common opinion, although severe global spasticity was previously the major indication for ITB, it is currently also applied in selected ambulatory patients [10]. MS can be categorized into three levels of mobility impairment: ambulatory (EDSS ≤5.5), ambulatory with gait assistance device (EDSS 6.0 to 7.0), and non-ambulatory (EDSS >7.0) [11]. Patients with an EDSS score >7.0 can be successfully managed with ITB. There can also be successful ITB in selected individuals with EDSS 5.0–6.5. Thus, the decision for the application of ITB should be made according to needs on a case-by-case basis. Non-ambulatory patients are treated for symptomatic relief and to facilitate daily life, including personal care, seating and mobilization whereas ambulatory patients are treated with the additional aim of improving or preserving mobility. Patients who are ambulatory with assistive devices are weak candidates for ITB, because these patients have extensor rigidity when standing upright and walking. Therefore, it can be said that ITB therapy is effective in decreasing severe spasticity in non-ambulatory and selected ambulatory patients.

Cerebral Palsy (CP): In the current study, 4 of the 10 patients were CP. The functional level of 3 of these patients was GMFCS level IV, and 1 was GMFCS level V. The patients were aged between 13 and 39 years, so it was late for ITB. All of the patients had varying degrees of contracture and all were wheelchair-dependent.

CP has a prevalence of 2-3 per 1000 children. Approximately 7% of patients with spastic CP are appropriate candidates for ITB. ITB is the treatment of choice to reduce severe spasticity in a non-mobile child with tetraplegia and GMFCS level 5. ITB can also be used in diplegic with severe spasticity, GMFCS level 4, and to reduce lower and upper limb spasticity [12, 13]. ITB improves daily care, and quality of life for the child and careers. Thus, ITB therapy can be used effectively to reduce severe spasticity in total type CP, GMFCS level 5 and selected GMFCS level 4 patients.

Spinal Cord Injury (SCI): In the present study, of the 3 SCI patients, 2 were neurologically motor and sensory complete paraplegic (ASIA Impairment Scale [AIS] A), and 1 was incomplete (AIS C). One patient required continuous manual contact during ambulation (FAC=2) and 2 could not ambulate (FAC=0).

Spasticity is a serious complication for many SCI patients, and 40% - 60% of these patients have problematic spasticity resulting in a significant impact on daily living activities and patient independence [14]. *Sampson et al* [15] reported that 5% - 10% of SCI patients require ITB to treat excessive spasticity. *Taricco et al* [16] also showed that spasticity occurred much more frequently in SCI with Frankel grades of B or C, and more so in incomplete tetraplegics than in paraplegics, with a higher incidence of spasticity at cervical and upper thoracic level injuries than at lower thoracic and lumbosacral levels of injury.

Acquired Brain Injury (ABI): Previous studies have reported the prevalence of post stroke spasticity of both upper and lower limbs as 56% - 77% [17]. Thus, it may not be practical to use botulinum toxin injection alone for the management of spasticity in multiple muscles in multiple extremities, even if the recommended maximum dose of botulinum toxin injection is not exceeded. Previously, ITB was reserved for stroke patients with severe multilimb spastic hypertonia to facilitate hygiene, positioning, and comfort. Preferred candidates for ITB therapy include stroke survivors with spastic hypertonia which has not sufficiently responded to other treatment interventions or who cannot tolerate the adverse effects of other therapies [18].

As motor recovery varies with each individual and spasticity fluctuates over time, the ITB therapy may be deferred until several months after the onset of the underlying disease. In most cases, 3 to 6 months post-stroke is safe for ITB, because a considerable amount of neurological recovery has taken place by that time.

In the current study, there were no patients with acquired brain injury. Although the use of ITB for stroke patients was described in 2001 by *Meythaler et al* [18], the clinical use of ITB for stroke is not still widespread. Possible reasons for this may be the fear of complications such as surgical risks, risk of seizures, use of anticoagulation, risk of infection, pump/catheter malfunction, and other reasons including making the unaffected side weak, less effect on the upper limb, and a deterioration in ambulation [17]. However, ITB has also been shown to be effective in reducing severe post stroke spasticity.

There are some important limitations in this study that should be mentioned. The main weakness of this study was the small sample size. Therefore, acknowledging this as a preliminary study, there is a need for further studies of a long-term follow-up to determine the experiences at ITB.

CONCLUSION

Evidence suggests that not only can ITB reduce spasticity, but it can also improve function, prevent contractures, reduce pain, facilitate care and quality of life as well as improve gait in ambulatory patients.

Therefore, the criteria for ITB selection are based on:

- The presence of diffuse or regional spasticity
- MAS score >2 or PSFS score >2 (in two or more limb regions, including both lower limbs and/or including one or both upper limbs, either unilaterally or bilaterally; spasticity duration of >6 months)
- Non-ambulatory MS patients (if EDSS ≥ 7.0) are treated for symptomatic relief and daily care.
- Ambulatory MS patients (if EDSS ≤ 5.5) are treated with the additional aim of improving walking ability.
- Non-ambulatory CP patients with global spasticity (if GMFCS Level 5)
- Diplegic CP patients with severe hypertonia (if GMFCS Level 4-5)
- At least 3-6 months post stroke patients with unresponsive spasticity or who cannot sufficiently tolerate physical and medical therapy.

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