INTRATHECAL BACLOFEN THERAPY FOR SPASTICITY: EXPERIENCE OF 48 CASES

SPASTİSİTEDE İNTRATEKAL BAKLOFEN TEDAVİSİ: 48 VAKALIK TECRÜBE

INTRATHECAL BACLOFEN FOR SEVERE SPASTICITY

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Öz

Amaç: Intratekal baklofen (ITB) tedavisi farklı etiyolojik nedenlere bağlı spastisitenin tedavisinde yaygın olarak kullanılmaktadır. Bir gama aminobutirik asidB (GABAB) reseptör agonisti olan baklofen, nöronal eksitabiliteyi düşürerek etki gösterir. Bu çalışmanın amacı kliniğimizde ITB tedavisi verilen hastaların sonuçlarını komplikasyonları ile birlikte sunmaktır. Gereç ve Yöntem: Kliniğimizde ağır spastisite nedeniyle 2005 ve 2016 yılları arasında ITB tedavisi uygulanan yaş ortalaması 36.45 yıl olan, 29 erkek ve 19 kadın olmak üzere toplam 48 hasta (6 pediatrik hasta) dahil edilmiştir. Spastisite düzeyi Ashworth skalası ile değerlendirilmiştir. Ortalama takip süresi 3.1 yıldır. Bulgular: Bu seride spastisite etiyolojisinde en sık multipl skleroz olduğu (n=18), bunu takiben serebral palsi (n=7) ve diğer nedenler (n=23) olduğu görüldü. ITB tedavisi öncesi ortalama Ashworth skoru 3.52 iken, uzun dönem takipte 162.66 mcg / gün ortalama ITB dozu altında Ashworth skorunun ortalama 2.0'a düştüğü bulundu. Uzun dönem takipte 6 hastanın Ahworth skorunun başlangıç ile aynı olduğu, toplam 9 hastada komplikasyon yaşandığı; ancak bunların sadece 3 tanesinde pompa çıkarılmasının zorunlu olduğu saptandı. Tartışma: Ağır spastisite hastalarının tedavisinde ITB tedavisi oldukça etkili olmakla beraber, ITB tedavisinde başarı, doğru hasta seçimi ve özenli hasta takibine bağlıdır.

Anahtar Kelimeler
Spastisite; İntratekal; Baklofen

Abstract

Aim: Intrathecal baclofen (ITB) treatment is widely used in various etiological conditions resulting in severe spasticty. Baclofen, used in the treatment of spasticity, decreases the neuronal firing by acting on gamma aminobutyric acid receptorB. The aim of this study is to present results and complications of 48 patients treated with ITB at our institution. Material and Method: In this study, 29 male and 19 female patients who underwent ITB pump implantation due to severe spasticity between 2005 and 2016 were included. Mean age was 36.45 years, where six of 48 patients were pediatric. Spasticity of each patient was evaluated according to Ashworth scale. Average follow-up period was 3.1 years. Results: The most frequent etiological factor was multiple sclerosis (n=18), followed by cerebral palsy (n=7) and others (n=23). Baseline mean Asworth score was 3.52 which decreased to 2.0, with an average ITB dose of 162.66 mcg/day at long term follow-up. Nine patients had complications; of which only 3 needed pump removal. Discussion: ITB, applied with adequate patient selection and cautious regular follow up, is an effective treatment modality in patients with severe spasticity.

Keywords
Spasticity; Intrathecal; Baclofen

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Introduction

Spasticity, characterized by velocity dependent increase in muscle tone, presents with difficulty in coordinated movements, painful spasms, rigidity and hyperactive reflexes [1]. Loss of inhibitory effect on alpha and gamma motor neurons following upper motor neuron damage results in spasticity. Main etiological factors for spasticity are multiple sclerosis (MS), stroke, traumatic brain or spinal cord injury and cerebral palsy (CP) [2]. Proper treatment of spasticity to lessen functional disability of the patients mandates multidisciplinary approach. Oral therapy, physical therapy, botulinum toxin injection, surgical interventions like dorsal rhizotomies or peripheral neurotomies and intrathecal baclofen infusion are current treatment options for spasticity.

Intrathecal baclofen (ITB) therapy is an effective and useful technique for management of spasticity [3,4]. Baclofen is an agonist of γ-aminobutyric acidB (GABAB) receptor, which is a transmembrane protein that affects calcium and potassium channels; and when activated it reduces the influx of calcium into the presynaptic terminals of afferent fibers which reduces the release of excitatory transmitters [5]. It has also effect at the postsynaptic membrane by increasing potassium influx, so that the membrane potential increases and neuronal firing becomes inhibited.

This study evaluates patients treated with ITB at our institution regarding the outcome and complications, and results were discussed.

Material and Method

This study includes forty-eight patients with severe spasticity who underwent ITB treatment at Cerrahpasa Medical Faculty Department of Neurosurgery between 2005 and 2016. There were 29 male and 19 female patients with a mean age of 36.45 (range:5-67) years. There were six pediatric patients with an age range of 5 to 18 years. Mean follow-up was 3.10 (range:1-11) years. Two patients were lost to follow-up. Muscle tone in lower extremities (including hip abduction, hip flexion, knee flexion, and ankle dorsiflexion) and upper extremities (including shoulder abduction, elbow extension, elbow flexion, and wrist extension) were examined. Level of spasticity was evaluated according to the Ashworth Scale.

All patients with severe spasticity lasting more than 6 months and failure in response to oral anti-spasmodic treatments were screened for ITB test bolus injections with a dose of either 25 or 50 mcg depending on age group, children or adult, respectively. Four to 6 hours after bolus injections, patients were re-evaluated by the same physician. The patient was considered as a candidate for ITB pump implantation if any improvement on Ashworth scale was Present. In cases of no improvement in Ashwoth scale, a repeat ITB test injection with a double dose was performed 24 hours later. Figure 1 shows workflow of the ITB pump patient selection applied at our institution. All patients or their legal caregivers signed the patient consent form. Details of the surgical procedure can be found in our previous study which covered the first 25 patients of our study population [6].

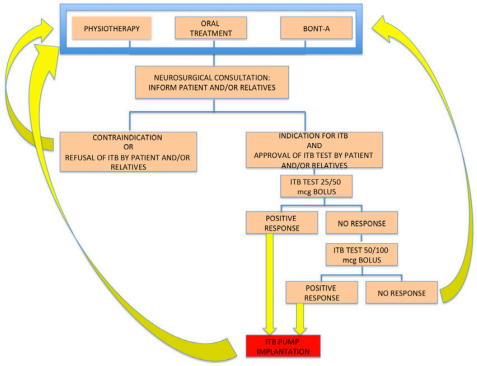

Figure 1. ITB patient selection algorithm used in our institution.
BONT-A: Botulinum NeuroToxin -A ITB: Intrathecal Baclofen

Results

Etiology of spasticity was MS in 18 cases followed by CP (n=7), and other factors (n=23) (Figure 2). Average Ashworth score of the patients was 3.52 and 2.0, before ITB treatment and at long term follow-up, respectively. Ashworth score was 0 in 1 patient, 1 in 17, 2 in 14, 3 in 9, 4 in 5 patients at the last outpatient visit. Improvement in Ashworth score was 3, 2 and 1 point in 6, 19, 15 patients, respectively. Six patientshad no change in Ashworth score at long term. Interestingly 3 of these six patients showed benefit in means of spontaneous spasms.

Catheter tip location was always checked at the early postoperative period with plain radiograms. Tip level was found between cervical C7 and T9 vertebrae throughout the series and in majority of cases it was located at T6-7 level.

Initial ITB dose was 50 mcg/day in majority of adult patients (n=36 patients) and 25 mcg/day in four of 6 pediatric cases. In order to maintain their ambulatory status, infusions were started at 25 mcg/day in two adult patients. Initial infusion rate was set to a higher dose in remaining four adult and two pediatric patients, since they responded to the double dose ITB test injection (second test). . Mean ITB daily infusion rate of the patients at last follow-up was 162.66 mcg (range: 25-600 mcg). We have experienced complications in 9 patients (18.75%). Catheter dysfunction or disconnection was present in 4 patients, which were treated by re-implantation of a new catheter. In another patient requiring a revision surgery due to a broken catheter, the new catheter was introduced through one upper level, since previous catheter could not be removed safely and left inside (Fig 3). CSF accumulation due to catheter

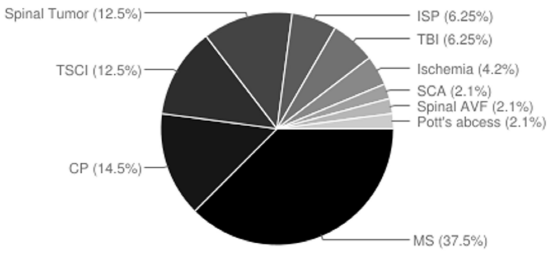

Figure 2. Etiological factors for spasticity of 48 patients
CP: Cerebral Palsy, MS: Multiple Sclerosis, ISP: Idiopathic spastic paraparesis, SCA: Spinocerebeller ataxia, TBI: Traumatic brain injury, TSCI: Traumatic spinal cord injury, Spinal AVF: Spinal arterio-venous fistula

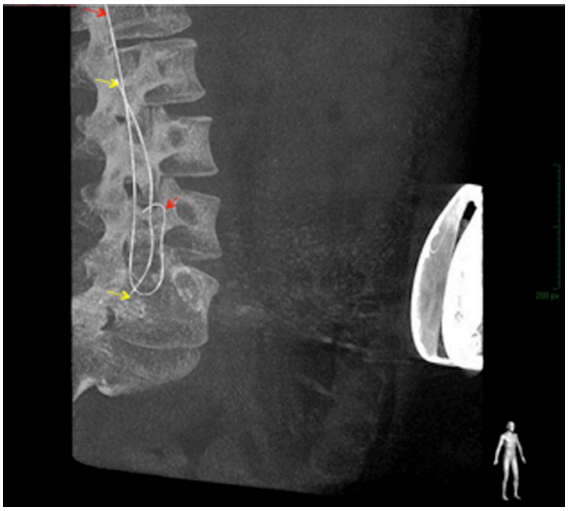

Figure 3. Three dimensinal radiographic image of the patient showing two spinal catheter, one of which could not be removed during revision surgery. The tip of the previous catheter marked with yellow arrows whereas the new one was marked with red arrows.

dysfunction around the pump was observed in a patient, which finally required new catheter replacement. One patient had experienced intrathecal baclofen toxicity after reservoir filling, which needed ICU care and eventually new pump replacement [7]. Wound detachment was observed in two patients. One of them treated by hyperbaric therapy whereas the other required reconstruction with a local flap (Fig 4). In two cases, the pump system was removed permanently due to infection and in one patient due to patient's own will. Although she had benefited from ITB, 6 months after the pump implantation she refused to have a foreign material.

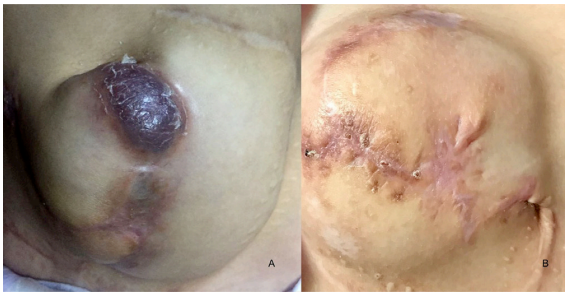

Figure 4. One of the pediatric patients in the series developed wound necrosis [A], which then reconstructed with local flap [B].

Discussion

Baclofen, an agonist of GABAB receptor, is approved by the Food and Drug Administration for the treatment of severe spasticity [8]. Baclofen binds to presynaptic and postsynaptic GABAB receptors at the dorsal horn of the spinal cord and inhibits mono- and polysynaptic reflexes [9]. ITB is a widely accepted treatment modality in severe spasticity [10]. Intrathecal administration of baclofen has some advantages over oral baclofen treatment such as obtaining higher concentrations at spinal cord level that cannot be provided by oral baclofen treatment without systemic side effects. Most important factors for favorable outcome for ITB treatment are patient selection and regular follow-up of the patients [6]. We believe that functional improvement as perceived by patients should be the main factor in evaluating the beneficial effects of ITB treatment, since outcome scales currently used in follow-up may not cover level of improvement in quality of life, while they focus mainly on spasticity and spasm levels [11, 12].Accordingly, three patients in our series have beneficial effect from ITB on spasms although they did not show a decrease in Ashworth score.

ITB is a treatment option of severe spasticity in both cerebral and spinal origins and there is no significant difference in the efficacy of ITB between paraplegic and tetraplegic patients [13,14]. Catheter tip level has no shown effect on outcome [14]. Moreover catheter tip level does not have any correlation with the maintanance dose of ITB and complications with catheter like migration, disconnection and infection [15]. Catheter tip level was around T6-7 in majority of patients in this study. Although catheter level is reported to be unrelated to outcome, we try to introduce the catheter as higher level as possible in spastic quadriplegic patients. In order to rule out downward migration and kinking of the catheter, we routinely take plain radiograms at early postoperative period. Then we check and compare the level of the catheter determined during surgery with the fluoroscopy.

Besides decreasing Ashworth score, ITB also improves pain score and self care of the patients with spasticity [16,17]. Fares et al. [18], reported that, with a mean follow up period of 52 months, patients are found to be still diminished in mean Ashworth score compared to the baseline, and mean ITB dose was reported as 137.81 mcg/day. In another study, daily ITB dose was compared on the basis of etiology, which had no significant difference between cranial and spinal etiological groups. However it has been reported that ITB dose needed to be increased significantly in long term[19]. In our series with a mean follow up of 3.1 years, average daily dose of ITB was 162.66 mcg. Patients showed a mean 1.52 points decrease in Ashworth score at long term follow up.

Complications related to ITB treatment was analyzed in a review of 558 complications reported in 1352 patients, with a mean 0.41 unwanted event per implant. Majority of these events were related to the catheter, which was followed by complications due to surgical procedure and pump device. Studies with a long term follow up, especially longer than 18 months, reported increased complication rates. It has been concluded that higher complication rates should be expected in centers that follow patients for a longer period of time [20]. We have experienced 9 complications in 48 patients; removal of the ITB device was needed only in 3 patient, where one was due to the patient's own will.

In order to minimize the complications, care should be taken not only during surgical procedure but also at follow up. Sterile conditions must be provided during refill procedure. Patients and their caregivers must be warned about the withdraval signs of ITB, which are rebound increase in spasticity, rigidity, tachycardia, piloerection, pruritis, seizure, halucinations, fever, sudden fluctuations in blood pressure, and change in conciousness. Regular follow up is the most crucial factor for proper and early management of complications. It should be kept in mind that

drug refills must be performed with 6 months intervals at most to prevent withdraval signs.

In conclusion, ITB is currently the best and effective treatment modality in patients with severe spasticity, when it is applied with adequate patient selection and cautious regular follow up.

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Competing interests

The authors declare that they have no competing interests.

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