

Intrathecal Baclofen Therapy For Spasticity: A Single-Institution Experience and Review of the Literature

Spastisitede Intratekal Baklofen Tedavisi: Bir Merkezin Tecrübesi ve Derleme

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Summary

Objective: The authors present their experience in the treatment of spasticity with intrathecal baclofen (ITB) by continuous pump infusion system. The features, advantages and complications of this treatment modality are discussed, demonstrated by the clinical results of 25 consecutive cases together with literature review on this topic.

Materials and Methods: Twenty-five patients suffering from spasticity secondary to cranial and spinal pathologies were treated by ITB and pump implantation between 2006 and 2010. Of these patients, 18 were male (72%) and 7 were female (28%), with a mean age of 34.4±11.2 years (range: 12-52 years). The mean preoperative Ashworth score was 3.8±0.49. The average follow-up period was 20.3±10.2 months (range: 3-52 months).

Results: The mean postoperative Ashworth score was 2.44±0.86. The final evaluation of the patients revealed decrease in Ashworth score by 3 points in 2 patients (8%), 2 points in 9 patients (36%), 1 point in 10 patients (40%) and no change in 4 patients (16%). Excluding the patients whose pumps were removed, the final infusion rates ranged between 55 and 250 µg/day (mean: 134.6±62.8). Complications were seen in 6 patients (24%). The most common complication was catheter dysfunction, which was seen in 3 patients (12%). Pump infection requiring removal of the pump and antibiotic therapy occurred in 2 patients (8%).

Conclusion: Intrathecal baclofen delivered through an implanted catheter and pump system represents a significant advancement in the management of adult and pediatric spasticity. The procedure is generally safe and well-tolerated. Most important, intrathecal delivery maximizes spinal effect while minimizing cerebral side effects. Indeed, ITB offers perhaps the best option in many patients with severe spasticity refractory to medical management. *Türk J Phys Med Rehab 2011;57:1-7.*

Key Words: Baclofen pump, intrathecal baclofen, spasticity

Özet

Amaç: Bu çalışmada yazarlar spastisite tedavisinde uyguladıkları infüzyon pompa sistemi intratekal baklofen (İTB) terapisi ile ilgili tecrübelerini sunmaktadır. Yazarların 25 hastadan oluşan serisi sunularak bu yöntemin özellikleri, avantajları ve komplikasyonları tartışılmaktadır.

Gereç ve Yöntem: Kranyal ve spinal patolojilerine sekonder olarak spastisite tanısı olan yirmi beş hasta 2006 ile 2010 yılları arasında İTB pompası ile tedavi edilmiştir. Bu seride 18 erkek (%72) ve 7 kadın (%28) hasta bulunmuştur. Hastaların yaşı 12 ile 52 yaş arasında idi (ortalama= 34,4±11,2 yaş). Preop ortalama Ashworth skoru 3,8±0,49 olarak bulunmuştur. Hastaların ortalama takip süresi 20,3±10,2 ay idi (3 ile 52 ay arasındadır).

Bulgular: Postop ortalama Ashworth skoru 2,44±0,86 olarak bulunmuştur. Hastaların son değerlendirilmesinde Ashworth skorunda 2 hastada (%8) 3 puan düşüş, 9 hastada (%36) 2 puan düşüş, 10 hastada (%40) 1 puan düşüş ve 4 hastada (%16) değişiklik olmadığı saptanmıştır. Pompası çıkarılmış olan hastalar dışlandığında, son baklofen infüzyon dozu 55 ile 250 µg/gün idi (ortalama 134,6±62,8). Altı hastada (%24) komplikasyon görüldü. En sık görülen komplikasyon katater disfonksiyonu olup 3 hastada (%12) görülmüştür. Pompa enfeksiyonu 2 hastada (%8) görülmüş olup pompaları çıkarıldıktan sonra antibiyotik ile tedavi edilmiştir.

Sonuç: Katater ve implante edilen pompa sistemiyle uygulanan intratekal baklofen yetişkin ve pediatrik spastisiteye yönelik çok etkin bir tedavi yöntemidir. Pompa yerleştirme işlemi genel olarak güvenli ve hasta tarafından iyi tolere edilebilmektedir. İlacın intratekal verilme şekli omurilik üzerindeki etkinliğini arttırmakta olup beyin üzerindeki yan etkileri azaltmaktadır. *Türk Fiz Tıp Rehab Derg 2011;57:1-7.*

Anahtar Kelimeler: Baklofen pompası, intratekal baklofen, spastisite

Introduction

Spasticity, of both spinal and cortical origin, is associated with considerable morbidity, particularly in severely debilitated patients. Intrathecal baclofen (ITB) has been increasingly used as a relatively specific treatment modality for spasticity. Baclofen, a gamma-aminobutyric acid (GABA) agonist, works to inhibit the excitatory activity at the spinal reflexes (1). ITB therapy increases the inhibitory effects of GABAB receptors in the spinal cord and eliminates the side effects of oral antispasmodic agents (2). The primary benefit of ITB is the relief of severe spasms and spasticity. Overall, increased independence, mobility, ability to perform self-care and life quality are documented in successfully treated patients (3,4). Adequate patient assessment for ITB pump implantation is necessary to determine if surgical intervention is a viable option. Screening requires a complete physical examination and neurological assessment, including full history of spasticity and prior treatment regimens. Baclofen pump implantation is simple and safe, however, several risks are involved with the placement of the pump (3). Although ITB therapy is frequently associated with complications, such as infections, catheter malfunctions, and cerebrospinal fluid leaks, the benefits of therapy appear to outweigh the risks.

Table 1. Summary of the data of our patients.

Patients	Age/Sex	Primary Pathology	Preoperative Ashworth Score	Final Ashworth Score	Complications and Management	Final infusion dose ($\mu\text{g/day}$)
1	36 / F	MS	3	3	-	60
2	38 / M	spinal injury	4	4	No benefit - pump removed	0
3	38 / F	CP	5	2	Catheter dysfunction and revision	200
4	49 / F	spastic paraparesis	3	2	-	120
5	17 / M	MS	3	3	Infection and pump removal	0
6	18 / M	CP	4	2	-	220
7	36 / F	MS	4	2	-	150
8	23 / M	Spinal injury	4	4	Infection and pump removal	0
9	35 / F	Operated cervical tumor	3	1	-	60
10	42 / M	Head injury	4	3	-	160
11	12 / M	CP	4	2	Wound detachment - hyperbaric therapy	140
12	27 / F	Operated dorsal tumor	3	2	-	160
13	40 / M	MS	3	1	-	55
14	43 / M	Operated dorsal intramedullary tumor	3	1	-	70
15	37 / M	Spinal injury	4	2	-	220
16	52 / M	Spastic paraparesis	4	3	- Postoperative respiratory dysfunction and ICU follow-up, - Catheter dysfunction and revision	100
17	34 / M	Spastic paraparesis	3	2	-	90
18	18 / M	MS	4	2	-	200
19	46 / M	MS	3	2	-	80
20	44 / M	Spinocerebellar syndrome	5	2	-	225
21	20 / M	Spinal injury	5	4	-	145
22	45 / M	MS	3	2	-	100
23	38 / M	MS	4	3	-	56
24	50 / F	MS	5	2	Catheter dysfunction and revision	250
25	23 / M	NF II	5	4	-	100

(M: male, F: female, MS: Multiple Sclerosis, CP: Cerebral palsy, NF II: Neurofibromatosis type II)

In this article, the authors present their experience and results in the management of spasticity with ITB based on a review of 25 consecutive cases. Our data are evaluated in comparison to other major centers, and possible factors that might influence the treatment outcome are discussed, combined with detailed review of the literature on this topic.

Patients and Methods

Patients' General Informations

Twenty-five patients suffering from spasticity secondary to cranial and spinal pathologies were treated by ITB and pump implantation between 2006 and 2010. Of these patients, 18 were male (72%) and 7 female (28%) with a mean age of 34.4 ± 11.2 years (range: 12-52 years). The average follow-up period was 20.3 ± 10.2 months (range: 3-52 months). Patient consent forms were signed by all participants for agreement to treatment and free use of their clinical information by the physicians. All values were entered and analyzed in a Microsoft Excel spreadsheet (Redmond, WA, USA). All data were provided as the mean \pm standard deviation (SD), and statistical analyses were performed using the Wilcoxon test. Probability values of less than 0.05 were considered to be statistically significant. The data of the patients are summarized in Table 1.

Primary Pathology and Clinical Picture

In our series, there were 9 patients (36%) with the diagnosis of multiple sclerosis (MS), 4 (16%) with spinal trauma, 3 (12%) with cerebral palsy (CP), 3 (12%) with idiopathic spastic paraparesis, 3 (12%) with spastic paresis after spinal intramedullary surgery, 1 (4%) with head trauma, 1 (4%) with spinocerebellar syndrome and 1 patient (4%) with neurofibromatosis type 2 (Figure 1).

Ashworth Scale (scores 1-5) was used for assessment of 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). According to Ashworth Scale, there was no patient with a score less than 3 in our series. The Ashworth score was 3 in ten patients (40%), 4 in ten patients (40%) and 5 in five patients (20%). The mean preoperative Ashworth score was 3.8 ± 0.49 .

Patient Selection

One set of reasonable criteria for inclusion in an ITB trial includes the following items: 1) severe chronic spastic hypertonia in the lower extremities lasting at least 6 months, with Ashworth scores of at least 3 in an affected extremity, 2) failure to respond to maximum recommended doses of antispasmodic medications, including baclofen and possibly diazepam, clonidine, tizanidine, or dantrolene sodium, and 3) patients should demonstrate a positive clinical response to an ITB injection bolus. Patients not meeting these criteria were excluded from the ITB trial.

Screening involves a 50 µg-bolus injection of baclofen, diluted to 50 µg/ml, into the intrathecal space by barbotage over a period of not less than 1 minute. The patient is then observed over a period of 4 to 8 hours. A positive response consists of a significant decrease in muscle tone, frequency of spasms, or severity of spasms. During the test, the response was also evaluated by the physiotherapist. The final score was given after discussion and agreement between all examiners. Patients with suboptimal responses may be rescreened with 75 µg baclofen after a rest period of 24 hours. Higher intrathecal doses were not needed in our patients.

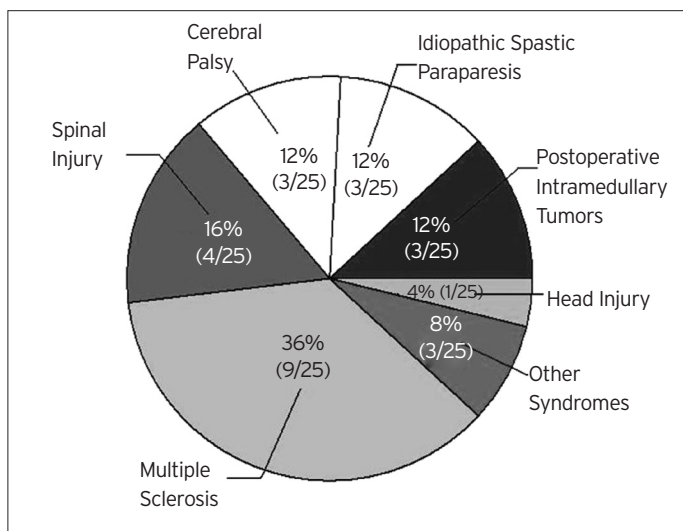


Figure 1. Graphic drawing showing the primary pathologies in our series and their percentages.

Surgical Technique and Dose Adjustment

Under general anesthesia and full monitoring, the procedures were performed with the patients lying on their sides at first placement of the posterior catheter. The intrathecal catheter was introduced through a needle into the intrathecal space between L1 and L5, mostly L3-4 interlaminar space, under fluoroscopic control. The position of the spinal catheter was based on the clinical goals. If the goal was to obtain only relaxation of the legs, T8 to T10 level placement was chosen. If the goal was to obtain some upper-extremity relaxation but mainly lower-extremity relaxation, T3 to T6 level placement was used. In children with severe upper-extremity spasticity or opisthotonic posturing, T5 to C5 level placement was chosen. After insertion of the catheter, fluoroscopic control was done again to control the position of the catheter tip and exclude any kinks in the catheter. Medtronic SynchroMed® II programmable pumps (Medtronic Inc, Minneapolis, MN) were implanted subcutaneously or under the fascia of the anterior rectus muscles and external oblique muscle in young or thin patients. The site of implantation was determined by the surgeon and depended on the amount of subcutaneous tissue (Figure 2).

Pump loading and drug infusion were started immediately after operation or on postoperative day 1. The initial infusion rate was 50 µg/day for all patients. Infusion rate was gradually increased by 10% every 5-7 days until clinical improvement without side effects was observed by the surgeon and the physiotherapist in the patients. During this period, the usual oral medication was reduced gradually to avoid the development of acute withdrawal syndrome. During the early postoperative period, minimal physical therapy is performed for 2-3 weeks, with avoidance of trunk rotation.

Results

At the time of this review, the final evaluations of the patients were performed and the postoperative neurologic status, course and complications were documented; the mean follow-up period was 20.3 ± 10.2 months (range: 3-52 months).

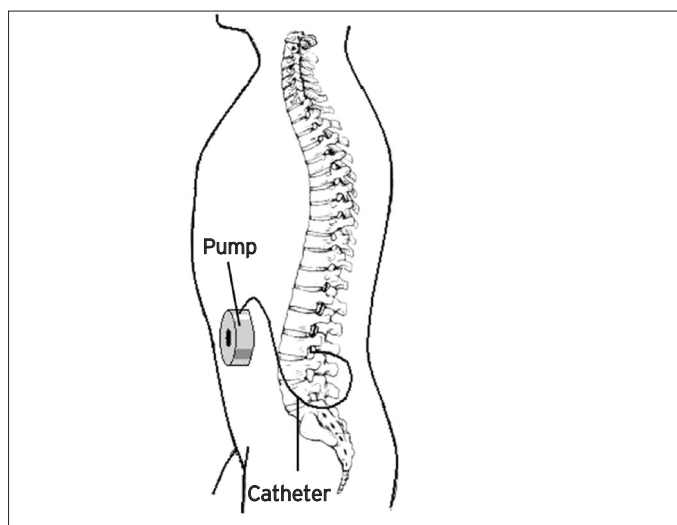


Figure 2. A schematic drawing demonstrating the pump implantation site and catheter insertion.

Clinical Outcome

The mean postoperative Ashworth score was 2.44 ± 0.86 . Ashworth score was found 1 in 3 patients (12%), 2 in 13 patients (52%), 3 in 5 patients (20%), and 4 in 4 patients (16%) (Figure 3). The final evaluation of the patients revealed decrease in Ashworth score by 3 points in 2 patients (8%), 2 points in 9 patients (36%), 1 point in 10 patients (40%), and no change in 4 patients (16%). Two patients of the group with no change in their score actually demonstrated initial benefit from the pump and improvement in their score, however, the pumps were removed due to later complications of the system. Also, 1 patient in this group showed decrease in the spasm-related pain despite the unchanged Ashworth score.

Caregivers were questioned regarding their ability to care for the patient after pump placement on the basis of the changes in their efforts to mobilize the patients, their amount of assistance in routine daily tasks and the contentment of the patients. Twenty-one caregivers (84%) stated that the ability to take care of the patient had improved, and 4 (16%) stated that the care was unchanged. From the second group, 2 caregivers described initial improvement in the care ability, however, after removal of the pump due to infection, the care ability returned to the level in the preoperative period. No caregiver described worsening of the ability and no patients suffered decubitus ulcers after pump placement.

Infusion Rates

Excluding the patients whose pumps were removed, the final infusion rates ranged between 55 and 250 $\mu\text{g}/\text{day}$ (mean: 134.6 ± 62.8). These infusion rates were adjusted after the first documented improvement in the spasticity, and remained stable until the final evaluation of the patients before this review. No patient developed tolerance to the treatment, thus, the infusion rates were not increased. In our series, there was no significant correlation between therapeutic infusion rate and primary pathology.

Complications

In our series, we observed complications in 6 patients (24%). The most common complication was catheter dysfunction, which was seen in 3 patients (12%). Catheter dysfunctions were managed by reoperation and sequent improvement of the catheter function. One of these patients suffered from postoperative respiratory difficulty in the early postoperative period before pump loading, which required follow-up in the intensive care unit and later extubation.

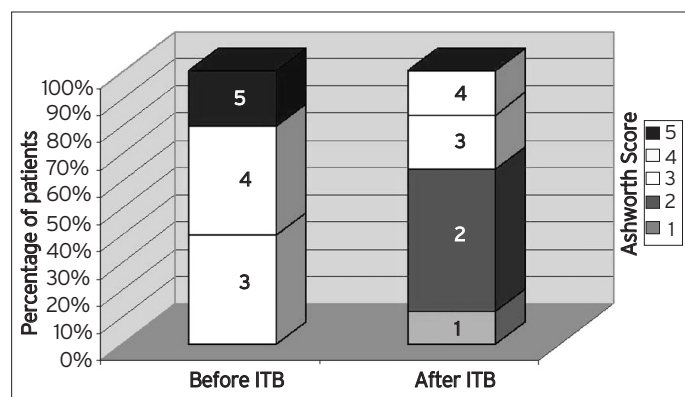


Figure 3. A bar graph comparing the Ashworth scores in our patients before and after intrathecal baclofen therapy (ITB) therapy.

This complication was unrelated to catheter dysfunction as it occurred before pump loading and drug infusion. Catheter dysfunction occurred later as a separate incidence. Pump infection requiring removal of the pump and antibiotic therapy was seen in 2 patients (8%). One patient developed wound detachment, which was managed and healed with hyperbaric therapy.

Discussion

Baclofen (4-amino-3-(4-chlorophenyl)-butanoic acid (Lioresal)) was approved in 1977 by the Food and Drug Administration (FDA) for the treatment of spasticity. Baclofen is an analog of GABA that is specific to the GABAB receptors (1). Oral GABA is a hydrophilic agent and is an ineffective antispasmodic drug, because it lacks penetration through the blood-brain-barrier (BBB) and is rapidly degraded by neural tissue. Baclofen is slightly more lipid-soluble and stable, thus, it crosses the BBB in significantly high concentrations without being taken up by cells. Baclofen has been found to bind to presynaptic GABAB receptors within the brainstem, dorsal horn of the spinal cord, and other central nervous system (CNS) sites (2). Baclofen administered to isolated spinal cord preparations inhibits both monosynaptic and polysynaptic reflexes (2). Presynaptic effects are believed to be secondary to decreases in calcium influx during an action potential, leading to reduced neurotransmitter release. The challenge with baclofen has been to develop a method of delivery that will minimize supraspinal side effects while maintaining efficacy. The supratentorial CNS side effect profile of baclofen provides an upper limit to oral baclofen dosing. The suppression of abnormal spinal segment reflex activity in severe spasticity can require oral dosing, which results in clinically hazardous levels of sedation caused by cerebral effects. The most successful solution to this issue has been direct delivery of baclofen into the lumbar subarachnoid space with an intrathecal pump. Intrathecal baclofen represents a significant advancement in drug delivery that bypasses several limitations of oral baclofen. Intrathecal delivery of baclofen overcomes the obstacles of the BBB and theoretically results in greater therapeutic efficacy concentrated at a spinal site of action (3). Moreover, baclofen is only slightly lipid soluble, thus, it remains within the cerebrospinal fluid, with a relatively long half-life of 90 minutes (5). Also, slow rostral perfusion of baclofen along the subarachnoid space creates a relatively high concentration of the drug in the spine compared with the brain.

Clinical Evaluation and Patient Selection

Adequate patient assessment for ITB pump implantation is necessary to determine the relevance of the surgical intervention. Screening requires a complete physical examination and neurological assessment, including detailed history of spasticity and prior treatment trials. Ashworth Scale (scores 1-5) was used to evaluate the 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). Ashworth Scale is a short and practical scale, which can be easily used by the physician for assessment of the spasticity, with good correlation with severity and treatment response (6). The indications for ITB therapy include: 1) presence of severe chronic spastic hypertonia in the lower extremities lasting at least 6 months, with Ashworth scores of at least 3 in an affected

extremity, 2) failure to respond to maximum recommended doses of antispasmodic medications, including baclofen and possibly diazepam, clonidine, tizanidine, or dantrolene sodium, and 3) patients should demonstrate a positive clinical response to an ITB injection bolus. These were the standard inclusion criteria used for patient selection for ITB in our series.

Screening involves a 50- μ g bolus injection of baclofen diluted to 50 μ g/ml into the intrathecal space by barbotage over a period of not less than 1 minute. The patient is then observed by the surgeon and the physiotherapist over a period of 4 to 8 hours. A positive response consists of a significant decrease in muscle tone, frequency of spasms, or severity of spasms. Patients with suboptimal responses may be rescreened after a rest period of 24 hours with 75 mg baclofen (100 mg if necessary). Intrathecal doses higher than 75 mg were not needed in our patients.

Pump Characteristics and Dose Adjustment

For chronic ITB infusion, all patients in our series were implanted with SynchroMed II (Medtronic, Inc.), which is 87.5 mm in diameter, 26 mm thick, has a capacity of 40 ml, and weighs 215 g when full. This infusion system consists of an intrathecal catheter, pump, and external computer programmer (Figure 4). The pump is based on systems that are also used for intrathecal/epidural delivery of morphine for chronic pain, intravascular delivery of chemotherapeutic agents and antibiotics. The pump is powered by a permanent lithium battery that cannot be recharged in situ; consequently, the pump must be surgically explanted and a new one inserted every 4 to 6 years with normal use. Normal refill intervals are usually between 2 and 3 months. Optimal pump programming depends on the patient, and dosing ultimately depends on the severity and location of symptoms, catheter position, and the patient's sensitivity to baclofen. Further adjustments may be made after evaluation of the response profile of the patient. Our protocol included starting of pump loading and drug infusion after the implantation or on postoperative day 1. The initial infusion rate was 50 μ g/day for all patients. Infusion rate was gradually increased by 10% every 5-7 days until clinical improvement without side effects was observed in the patients. This observation is performed by the surgeon and the physiotherapist. During this period, the usual oral medication of the patients was reduced gradually to avoid the development of acute withdrawal syndrome. The most critical time is the initial stabilization period, with dose adjustments made at subsequent refills. Recent 1-year mean daily doses reported in the

literature have ranged from 175 to 477 mg/day (7). In our series, we documented lower final infusion rates ranging between 55 and 250 μ g/day (mean: 134.6 ± 62.8), but with significant improvements achieved with these doses. In our series, there was no significant correlation between therapeutic infusion rate and primary pathology. It is necessary to remember that dosing depends not only on spasticity relief but also on overall patient satisfaction.

Van Schaeybroeck et al. (8) reported a blind dose-reduction test conducted in patients with CP that demonstrated subjective functional deterioration in five, but increased Ashworth Scale scores in only two patients, suggesting that spasticity is only a single component of the benefit to patients from ITB. It has been also suggested that subjective functional evaluations are influenced dramatically by baclofen related reduction in spasticity-related pain. Other complicating factors in optimal dosing are the complexity of the clinical syndromes (especially in supraspinal spasticity conditions like CP) and fluctuating external influences on the patient's condition (9).

ITB Benefits

The primary benefit of ITB is the relief of severe spasms and spasticity. Overall, patients report increased independence, mobility, and ability to perform self-care (3).

Reflexes have been found to be particularly improved. Latash, et al. (10) observed mono- and polysynaptic reflexes and voluntary movements in the lower extremities in patients with chronic refractory spasticity treated with a single bolus of ITB. Responses on EMG studies to joint movements, H-reflexes, ankle clonus, and defensive reactions in the lower extremities were significantly reduced within 30 to 45 minutes and almost completely suppressed by 2 hours. There was also improvement in selective voluntary activation of leg muscles in those with residual motor control. Because ITB exerts an almost purely spinal effect with little or no supraspinal effect due to its concentration gradient, this evidence suggests that supraspinal central motor commands may be somewhat intact despite long-term spasticity in some patients. Some patients report that they have a more consistent sleep pattern at night; renewed ability to have sexual intercourse, improved urinary function as detrusor hyperreflexia and bladder contractions are curtailed, and decreased muscle pain and fatigue accompanying spasm, partly because of the reduction in spasms, and possibly also because baclofen acts as an antagonist to substance P in suppressing central pain (11). Spasticity interfered with sleep in 82% of patients with incomplete lesions and in 50% of patients with complete lesions. Baclofen infusion improves sleep by reducing these spasms (12).

Baclofen appears to work in patients suffering from spasticity of either spinal or cerebral origin. Ordia et al. (13) studied 59 patients suffering from severe spasticity of spinal cord origin that was refractory to oral baclofen. In this series, the mean Ashworth score significantly decreased, from 4.3 to 1.4 and the spasm frequency score decreased from 3.6 to 0.5. Meythaler et al. (14) reported that the mean Ashworth score in the lower extremities after pump implantation had declined at 1 year from 3.7 to 1.8 in patients with stroke and from 3.4 to 1.5 in patients with CP (15). In our study, the overall mean Ashworth score (for spasticity of both cranial and spinal origin) decreased from 3.8 to 2.4. The final evaluation of the patients revealed decrease in Ashworth score by 3 points in 8%, 2 points in 36%, 1 point in 40% and no change in 16% of the patients. Two patients of the group with no change in their score actually demonstrated initial benefit from the pump and

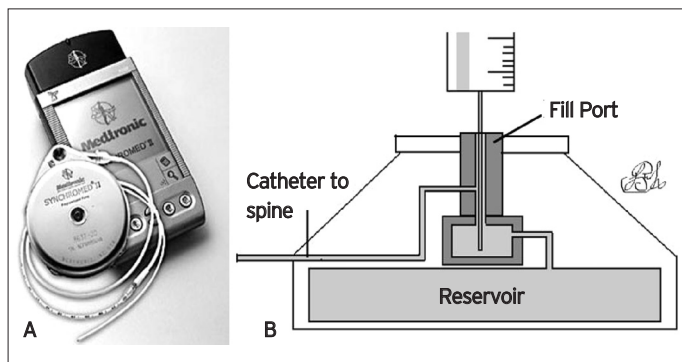


Figure 4. A) A photograph of the SynchroMed II (Medtronic, Inc.) pump used in our series. B) A schematic drawing demonstrating the structure of the pump.

improvement in their score, however, the pumps were removed due to later complications of the system. Also, our study showed that 84% of the caregivers achieved improved ability to take care of the patient, and 16% stated that care was unchanged. From the second group, 2 caregivers described initial improvement in the care ability, however, after removal of the pump due to infection, the care ability return to the level in the preoperative period. The other 2 patients did not gain benefit from the pump from the beginning. No caregiver described worsening of the care ability. Moreover, ITB appears to be cost-effective at an institutional level. Ordia et al. (13) found a reduction in the length of hospital stays but no change in overall use of outpatient resources during the 1st year after pump implantation. Patients reduced their mean hospital stays of 7.9 days/year preimplantation to 5.7 days/year in the 1st year postimplantation.

ITB Complications

Several risks are involved with placement of baclofen pumps. In the product manual, Medtronic warns of specific risks related to the pump itself. Heating of local tissue has been shown to elevate temperatures and cause baclofen overinfusion. Sources of electromagnetic interference like magnetic resonance imaging (MRI) will temporarily stop the pump motor's rotor due to the magnetic field of the imager, leading to brief disruption of intrathecal therapy (3). However, Diehn et al. (16) recently reported a study on clinical safety of magnetic resonance imaging in patients with implanted SynchroMed EL® model programmable infusion pumps (Medtronic, Inc., Minneapolis, MN). Increases in environmental pressure have been found to lead to slower infusion rates. Conversely, lower pressures will lead to higher infusion rates. Patients participating in extended high-altitude activities or stays may therefore require readjustment (3). In our cases, we do not restrict entering the MRI machine. However, the patients should inform us in such cases before the imaging in order to control and reprogram the pump immediately after the imaging procedure.

Stempien and Tsai (17) published a study of ITB complications in a survey of 40 centers with a total experience of 1002 test doses and 936 pump placements. Common test-dose complications were nausea/vomiting (2.6%) and sedation (2.2%). On the other hand, we did not observe significant side effects during the test-dosing in our series. Stempien and Tsai (17) also reported pump complications including CSF collection (3.3%), constipation (2.9%), and headache (2.4%). Common long-term complications were catheter dysfunction (4%) and infection (1.2%). In our series, 3 patients (12%) had catheter dysfunction and were successfully managed by surgical revision with no further complications. Normal hallmarks of infection such as warmth or redness around the incision site should be observed and monitored closely. More significant signs, such as purulent drainage, should be dealt with on an emergency basis, because severe infections may lead to meningitis. Pump removal and intravenous antibiotic drugs appropriate for the infecting bacteria are then indicated. In general, infection rates for baclofen pumps implanted to deliver the drug in an effort to treat spasticity appear to range from 0.7 to 1.7% (17,18). Meningitis in patients with implanted pumps ranges from 0 to 0.7% (19). In our series, 2 patients developed pump infections and were managed by removal of the implant and intravenous antibiotic trial. Meningitis was not seen in our series. Motta et al. (20) described low infection rate in their series after changing the surgical protocol, which included prophylactic antibiotic use 48 hours before surgery and use of subfascial (instead of subcutaneous) pump implantation. Reported infections appear to involve the perioperative period after

placement of the pump. The most common infective organisms are *Staphylococcus aureus* or *S. epidermidis*. Repeated percutaneous refills appear to carry a little risk of infection. One theory suggests that the host-derived albumin coating of the pump pocket reduces the risk of colonization (21). There are also reports of colonization of implanted pump reservoirs by bacteria and fungus without clinical infection (22).

Intrathecal use of baclofen does not completely eradicate the central risks. The most frequent drug-related side effects of ITB include drowsiness, dizziness, constipation, and muscular hypotonia (23). A bolus dose that is too high can result in rostral progression of hypotonia, followed by brainstem toxicity as the baclofen is carried up the neuraxis by rostral bulk CSF flow. Brainstem effects include respiratory depression, hypotension, bradycardia, and coma. Although baclofen has no direct antagonist, drowsiness and respiratory depression may be reversed with 1 to 2 mg of intravenous physostigmine over 5 to 10 minutes. Continuous infusion generally has a safer profile than bolus infusion. Malfunctions in prototype pumps have also been noted in the literature, resulting in milligram levels of baclofen release and leading to coma, although newer pump models have not shown this defect (24,25). In cases of severe overdose, the pump should be stopped immediately. Simple airway, breathing, and circulation considerations must be addressed, with mechanical ventilation, intravenous fluids, and vasopressors as supportive measures. In cases in which pump malfunction is the cause, the device should be turned off if necessary. A 20-ml syringe and 22-gauge Huber needle may be used for access to the fill port for removal of medication (25).

Baclofen withdrawal is a serious risk if there is an abrupt decrease in drug infusion. Causes include catheter failure, pump malfunction, or low pump reserves. Symptoms include pruritis without a rash, diaphoresis, hyperthermia, hypotension, changes in mental status, and aggravation of spasticity (26). Continued withdrawal may result in rhabdomyolysis or multiple organ failure, or it may mimic autonomic dysreflexia, sepsis, malignant hyperthermia, or neuroleptic-malignant syndrome. Management involves adequate evaluation of recent painful stimuli, listening for pump alarms, pump interrogation, abdominal and/or spine x-ray films, or indium infusion studies to evaluate for catheter fracture and baclofen extravasation. Once a diagnosis is made, oral baclofen may be administered if tolerated. In severe withdrawal, intrathecal baclofen administration through lumbar puncture may be necessary. Additional intravenous benzodiazepine therapy titrated according to effect may prove useful. Interestingly, both overdose and withdrawal of baclofen appear to induce seizures, especially in cases of supraspinal spasticity. Rates of seizure activity in patients receiving boluses of intrathecal baclofen are as high as 10.3% in cases of spasticity with supraspinal origin (27). Overdose-related seizures may be caused by rostral baclofen bulk flow to supraspinal tissue. Withdrawal seizures may occur as baclofen is eliminated from lipid stores and brain tissue (28). The seemingly paradoxical anti- and proconvulsant effects of baclofen may depend on the location of GABA_B-related inhibition (for example, on excitatory or inhibitory neurons in traumatized neuronal tissue). In each case, sudden drug level changes seem to have been most critical in the seizure-related activity.

Tolerance is another risk that deserves special attention. Several factors may require progressively higher doses of ITB. Tolerance requires increasing doses of medication, but it can be limited on occasion by a drug holiday. Some centers report success with intrathecal morphine or fentanyl during this holiday (29).

Progressive disease, decubitus ulcers, and infections (urinary or systemic) may also require readjustment of dosing.

In our series, the infusion rates were adjusted after the first documented improvement in the spasticity and remained stable until the final evaluation of the patients before this review. No patient developed tolerance to the treatment, thus, the infusion rates were not increased.

Conclusion

Intrathecal baclofen therapy is an excellent alternative for patients with spasticity whose disease is refractory to medical therapy. Our study showed that most patients will respond to an intrathecal test dose and will then be candidates for a pump and catheter system implant. Implants are safe, with a low morbidity rate. These results are similar to and support the previous reports of ITB. The most important factor to achieve the best results is the proper selection and follow-up of the patients. This requires a team work with multidisciplinary approach.

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