

## SHORT COMMUNICATION ΒΡΑΧΕΙΑ ΔΗΜΟΣΙΕΥΣΗ

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# Intrathecal baclofen administration for the treatment of spasticity Clinical considerations

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Ενδορραχιαία χορήγηση βακλοφαίνης  
για την αντιμετώπιση της σπαστικότητας:  
Κλινικοί προβληματισμοί

Περίληψη στο τέλος του άρθρου

**Key words:** Baclofen pump, Intrathecal baclofen, Multiple sclerosis, Spasticity

Patients with severe spasticity experience considerable difficulty in activities of daily life and often have pain at rest due to continuous muscle spasms.<sup>1</sup> Baclofen [4-amino-3-(4-chlorophenyl)-butanoic acid], an analog of gamma-aminobutyric acid (GABA), is currently the most effective and widely used oral agent for treatment of spasticity of spinal cord or cerebral origin. Intrathecal administration of baclofen offers a significant advancement in drug delivery that obviates some of the limitations of oral baclofen treatment.<sup>1,2</sup> Severe spasticity is rarely controlled by oral baclofen, although some relief of symptoms is possible.<sup>1</sup> The supratentorial central nervous system (CNS) side effects profile of baclofen puts an upper limit on oral baclofen dosage.<sup>1</sup> Suppression of the abnormal spinal segment reflex activity in severe spasticity may require a high oral dose, resulting in clinically hazardous levels of sedation. The most

successful solution to this dilemma has been the direct delivery of baclofen into the lumbar subarachnoid space by means of an intrathecal pump. Baclofen is only slightly lipid soluble; it persists in the cerebrospinal fluid (CSF), with a relatively long half-life of 90 minutes.<sup>3</sup> Furthermore, the slow rostral perfusion of baclofen along the subarachnoid space results in relatively high concentrations of the drug in the spine compared to the brain. Implantation of a pump for drug administration enables continuous infusion into the lumbar subarachnoid space, making possible the maintenance of an antispasmodic baseline.

### METHOD

Three patients were selected for treatment, all of whom were suffering from debilitating spasticity due to multiple sclerosis (MS). They were all males, aged 39, 48 and 49 years, with a history of MS of 19, 12, and 20 years, respectively and according to their degree of rigidity and severity of disability they were all categorized as 4 on the Ashworth scale (the most widely used scale for spasticity) (tab. 1). The oldest patient had also been paraplegic for the past 8 years following a spinal cord injury (burst fracture of T12) for which he had undergone a thoracolumbar fusion procedure (T11–L2). All patients responded positively to an intrathecal baclofen therapy (ITB) test (i.e., bolus intrathecal infusion of the agent) at an initial dose of 50 µg.

Implantation of the intrathecal baclofen pump and catheter is a relatively straightforward surgical procedure. The continuous-infusion pump and spinal catheter system was inserted under general anesthesia with the patient placed in the lateral position, and with administration of appropriate perioperative antibiotics. Intrathecal catheter placement was performed with the aid of fluoroscopic guidance, using a percutaneous technique, in which a 14- or 15-gauge Tuohy needle was introduced into an appropriate lower lumbar interspace to avoid the conus.

The catheter placement of the continuous-infusion pump itself is a matter of individual choice.<sup>1</sup> The standard placement has been in the lower abdominal wall, in a suprafascial pocket no more than 1 inch from the surface of the skin for ease of refilling. This standard placement position was chosen for our patients. Consideration must be made for patient comfort because the pump may abut

**Table 1.** Characteristics of 3 patients treated for spasticity with pump implantation for intrathecal administration of baclofen.

Patient	Gender, age	Primary disease	Duration of primary disease	Ashworth scale
1	Male, 39	MS	19 years	4
2	Male, 48	MS	12 years	4
3	Male, 49	MS T12 fracture	20 years (MS) 8 years (traumatic paraplegia)	4 (paraplegia)

MS: Multiple sclerosis

on either the lower ribs or the iliac crest in a mobile patient capable of assuming a seated position.

### RESULTS AND DISCUSSION

With use of the pump, all 3 patients reported improvement of their rigidity and diminution of the frequency and severity of spasms, and on examination they were evaluated as grade 2 on the Ashworth scale. In this series, optimal dose adjustment was accomplished within the first two weeks in all 3 patients, at a daily dose of baclofen of 45, 110 and 80 µg/24h, respectively.

This improvement has persisted unchanged in the follow-up period of 5, 6 and 5 months, respectively. No serious complications have been reported. The second patient had a headache in the immediate postoperative period (2 weeks) which was relieved with simple analgesics. The third patient presented inflammation of the abdominal surgical site at four months follow-up (fig. 1), which was effectively treated by the administration of antibiotics.

Although implantation of an intrathecal catheter and baclofen pump is usually well tolerated, it constitutes an invasive surgical procedure that must be thoroughly evaluated before being undertaken. Care must be taken in patient selection, surgical implantation, and postop-

erative management. Several selection criteria have been developed<sup>2</sup> for the ideal candidates (tab. 2), the most important of which are the failure of oral antispasmodic medication to control the symptoms (treatment-resistant spasticity), a positive ITB trial test and the absence of serious comorbidity factors.

A positive response to the ITB test consists of a significant decrease in muscle tone, frequency of spasms, or severity of spasms.<sup>1</sup> Patients with suboptimal responses may be rescreened after a rest period of 24 hours with 75 µg baclofen (100 µg if necessary, but a higher intrathecal dosage is rarely, if ever, indicated).<sup>1</sup> Some patients have clear, classic signs and symptoms of spasticity that have always been known to respond. In such cases, the ITB screening test may be omitted at the discretion of the physician.<sup>1</sup>

The placement of baclofen pumps is not without risk. Stempien and Tsai published the single most comprehensive study of ITB complications in a survey of 40 centres, with a total experience of 1,002 test doses and 936 pump placements.<sup>4</sup> Common test-dose complications were nausea/vomiting (2.6%) and sedation (2.2%). Pump complications included CSF collection (3.3%), constipation (2.9%), and headache (2.4%). Common long-term complications were catheter kink or migration (4%) and infection (1.2%).

A special note should be made about the risks of infection. Normal hallmarks of infection such as warmth or redness around the incision site should be monitored closely. The most common offending bacteria are *Staphylococcus aureus* and *S. epidermidis*.<sup>1,4-6</sup> The intrathecal administration of baclofen does not completely eradicate the risks associated with CNS toxicity. A bolus dose that is too high can result in rostral progression of hypotonia, followed by brainstem toxicity of ITB, including drowsiness, dizziness, constipation, and muscular hypotonia.<sup>4</sup> Brainstem effects include respiratory depression, hypotension, bradycardia, and coma. In the case of severe overdose, the pump should be stopped immediately. Simple airway, breathing, and circulation considerations must be addressed first, with mechanical ventilation, intravenous fluids and administration of vasopressors as supportive measures.



**Figure 1.** The position of the abdominal pocket for insertion of pump for intrathecal administration of baclofen (3rd case). The surgical site was complicated with inflammation, which was successfully treated with antibiotics.

**Table 2.** Patient selection criteria for programmable baclofen pump implantation for treatment of spasticity.

Inclusion criteria	Exclusion criteria
Age 13–65 years (older patients treated on compassionate use basis)	Pregnancy (for females of childbearing potential)
Ability to give informed consent (legal guardian for children)	Implanted programmable device (e.g. cardiac pacemaker)
History of severe chronic spasticity (at least 12 months)	History of stroke, impaired renal function, severe hepatic or gastrointestinal disease
Spasticity refractory to oral drugs (including baclofen) or unacceptable side effects to oral drug treatment	Hypersensitivity to baclofen
Positive response to intrathecal baclofen (dose $\leq 100 \mu\text{g}$ ) and no response to placebo	Cerebrospinal fluid blockage (e.g., on pyelography).

From Coffey RJ et al<sup>2</sup>

The primary benefit of ITB is the relief of severe spasms and spasticity. Overall, patients report increased independence and mobility and improved self-care ability. Apart from the objective findings, the patients in this case series, as those in the relevant literature, report better quality of living, and specifically a better sleep pattern, less day fatigue and improvement in urinary control. This constitutes an important element of overall patient satisfaction, even if it is difficult to assess objectively.<sup>1,7</sup>

Baclofen appears to be effective in patients suffering from spasticity of either spinal or cerebral origin.<sup>8,9</sup> Meythaler and colleagues studied 17 patients with stroke who had chronic spasticity lasting longer than 6 months,<sup>8</sup> in whom the Ashworth lower-extremity scores were reduced by an average of two points during screening. Zahavi and colleagues studied the long-term effects of intrathecal baclofen in patients with severe spasticity of spinal origin and concluded that intrathecal baclofen, delivered by an implantable programmable pump, results in improved clinical efficacy, but no improvement in disability or perceived health status.<sup>10</sup>

Optimal pump programming is personalized to each individual patient, and the dose ultimately depends on the severity and location of symptoms.<sup>1,2</sup> Optimal dosage can usually be attained with constant-flow pump titration in 2 to 6 adjustments over a period of 1 to 6 months. Tolerance is a risk that deserves special attention and progressively higher doses of ITB may be required in certain situations,<sup>1,2</sup> but the dosage depends not only on spasticity relief but also on overall patient satisfaction.

In conclusion, based on current documentation and the preliminary results in the cases reported here, intrathecal baclofen delivery via an implantable pump appears to be a safe and efficacious method for the treatment of spasticity of spinal and cerebral origin.<sup>11–13</sup> Appropriate patient selection and the implementation of a strict and

meticulous implantation technique are mandatory, because the complications of the method are neither rare nor negligible.<sup>13–15</sup> Adherence to selection criteria and perioperative management guidelines usually leads to a favorable outcome.

#### Ethical statement and conflict of interest

This study was conducted in accordance with the ethical standards of the Helsinki declaration of 1975, as revised in 2000. We declare no conflict of interest. We have no affiliation with any company whose products were used and absolutely no relationship (either economic or otherwise) is in any way implied by this paper. All medical equipment and technology used in our case series have undergone the standard approval procedure by the relevant fiscal committee of our hospital.

#### ΠΕΡΙΛΗΨΗ

##### Ενδορραχιαία χορήγηση βακλοφαίνης για την αντιμετώπιση της σπαστικότητας: Κλινικοί προβληματισμοί

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Η σπαστικότητα είναι κατάσταση του κινητικού συστήματος που χαρακτηρίζεται από μυϊκή δυσκαμψία, δυσκολία στον έλεγχο των εκούσιων κινήσεων και αυξημένα τενόντια αντανακλαστικά. Η εμφύτευση αντλίας βακλοφαίνης για ενδορραχιαία χορήγηση είναι σήμερα η αποτελεσματι-

κότερη μέθοδος αντιμετώπισης της σπαστικότητας με προέλευση τον εγκέφαλο και το νωτιαίο μυελό. Παρουσιάζονται οι πρώτες περιπτώσεις που αντιμετωπίστηκαν στην Κλινική μας, περιγράφονται τα πλεονεκτήματα και τα μειονεκτήματα της μεθόδου και συζητώνται τα αποτελέσματα βάσει της εμπειρίας μας και της σχετικής βιβλιογραφίας. Τρεις ασθενείς (άρρηνες, ετών 39–49), με σοβαρή σπαστικότητα λόγω πολλαπλής σκλήρυνσης (μέση κλίμακα Ashworth: 4), εκτιμήθηκαν για τοποθέτηση αντλίας βακλοφαίνης. Οι ασθενείς αντιμετωπίζονταν για πολλαπλή σκλήρυνση >10 έτη και οι συντηρητικές μέθοδοι απέτυχαν να ελέγξουν τη συμπτωματολογία. Η δοκιμασία εφ' άπαξ χορήγησης βακλοφαίνης ήταν θετική και εμφυτεύθηκε προγραμματιζόμενη αντλία για συνεχή έγχυση. Παρατηρήθηκε σημαντική βελτίωση της κλινικής εικόνας των ασθενών (μέση κλίμακα Ashworth: 2). Μετά από αρκετές προσαρμογές της ημερήσιας εγχόμενης δόσης, παρατηρήθηκαν μόνο ελάχιστες επιπλοκές. Στη διάρκεια του κλινικού επανέλεγχου για ένα εξάμηνο, η βελτίωση παρέμεινε σταθερή. Η ενδορραχιαία χορήγηση βακλοφαίνης από προγραμματιζόμενη αντλία είναι μια ασφαλής και αποτελεσματική μέθοδος για επιλεγμένες περιπτώσεις βαριάς σπαστικότητας. Η προσεκτική επιλογή των ασθενών και ο λεπτομερής κλινικός επανέλεγχος είναι απαραίτητοι για την επίτευξη μακρόχρονων θετικών αποτελεσμάτων.

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**Λέξεις ευρητηρίου:** Αντλία βακλοφαίνης, Ενδορραχιαία βακλοφαίνη, Πολλαπλή σκλήρυνση, Σπαστικότητα

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