One of the most disabling aspects of acquired brain injury is the development of spasticity and dystonia, often defined as spastic hypertonia. Spastic hypertonia can interfere with the use of remaining viable motor function, limit the range of motion in joints, cause pain, and is often disabling with respect to mobility, transfers, activities of daily living, sitting, and sleeping.4 Excessive muscle hypertonia has been linked to increased metabolic requirements in brain-injured patients.4 The incidence of contracture development for severely brain-injured patients who require inpatient rehabilitation has been reported to be as high as 84%,10 and the major cause of disfiguring contractures is spastic hypertonia.10

Spasticity is a motor disorder characterized by velocity-exaggerated increases in tonic stretch reflexes (muscle tone), with exaggerated segmental reflex responses, resulting from hyperactivity of the stretch reflex.11,12 Spasticity is part of the upper motor neuron injury syndrome and generally develops when the suprasegmental control of the spinal cord is lost in these segmental reflexes.1,12 Recent evidence indicates that descending tracts may directly modulate not only the peripheral segmental reflex arcs but also the anterior horn cells.8 With loss of this upper motor neuron modulating influence, the anterior horn cell may itself become hyperexcitable, with a resultant increase in activity by the extrafusal muscle fibers.

Spastic hypertonia in brain injury encompasses a variety of conditions that may contribute to increased tone or involuntary movement including dystonia, rigidity, myoclonus, muscle spasm, posturing, and/or spasticity.8 All of these conditions may contribute to the development of joint contractures frequently noted in severely brain-injured patients. Some of these conditions, particularly acquired dystonia, may be more disabling than spasticity in brain-injured patients. In general, spastic hypertonia due to brain injury is a more complex condition than the spasticity associated with pathological conditions of the spinal cord. The most significant clinical example of this difference involves the lack of success noted with oral medications in treating spastic hypertonia caused by acquired brain injury as compared to their relative success in treating spinal cord injury or multiple sclerosis.6,11,12

A recent double-blind, randomized bolus administration trial of intrathecally administered baclofen demonstrated that this drug is capable of significantly decreasing spasticity and dystonia in patients with acquired brain injury.7 These reproducible findings have led us to conduct a continuous infusion trial to study the feasibility of intrathecal baclofen administration as a means of sustaining reduced spasticity and dystonia among brain-injured patients. The present communication documents our preliminary experience with continuous intrathecal baclofen infusion in patients with severe spasticity following acquired brain injury and is the first report of its type that we are aware of in the medical literature.

Clinical Material and Methods

Patient Population

The study population consisted of 11 male and one female patients with acquired brain injury. Participants were between 17 and 39 years of age (mean 28 years) and had severe, progressive spasticity and dystonia refractory

---

**PROSPECTIVE ASSESSMENT OF CONTINUOUS INTRATECAL INFUSION OF BACLOFEN FOR SPASTICITY CAUSED BY ACQUIRED BRAIN INJURY: A PRELIMINARY REPORT**

**JAY M. MEYTHALER, J.D., M.D., ANNE MCCARY, R.N., M.S.N., C.R.N.P., AND MARK N. HADLEY, M.D.**

*Department of Physical Medicine and Rehabilitation, and the Division of Neurological Surgery, University of Alabama School of Medicine, Birmingham, Alabama*

Twelve consecutive patients with severe spasticity and hypertonia following acquired brain injury were treated with continuous intrathecal infusion of baclofen via an implanted, programmable infusion pump–catheter system for a minimum of 3 months. In every case intrathecal baclofen therapy resulted in a statistically significant reduction in upper- and lower-extremity tone, spasm frequency, and reflexes, contributing to improved functional abilities. There were no untoward side effects or complications associated with treatment.

This preliminary assessment indicates that intrathecal administration of baclofen is effective in treating the disabling spasticity caused by acquired brain injury in selected patients.

**KEY WORDS** • intrathecal drug infusion • baclofen • brain injury • spasticity • hypertonia • rehabilitation

---

**J Neurosurg 87:415–419, 1997**

**Prospective assessment of continuous intrathecal infusion of baclofen for spasticity caused by acquired brain injury: a preliminary report**

**JAY M. MEYTHALER, J.D., M.D., ANNE MCCARY, R.N., M.S.N., C.R.N.P., AND MARK N. HADLEY, M.D.**

*Department of Physical Medicine and Rehabilitation, and the Division of Neurological Surgery, University of Alabama School of Medicine, Birmingham, Alabama*

Twelve consecutive patients with severe spasticity and hypertonia following acquired brain injury were treated with continuous intrathecal infusion of baclofen via an implanted, programmable infusion pump–catheter system for a minimum of 3 months. In every case intrathecal baclofen therapy resulted in a statistically significant reduction in upper- and lower-extremity tone, spasm frequency, and reflexes, contributing to improved functional abilities. There were no untoward side effects or complications associated with treatment.

This preliminary assessment indicates that intrathecal administration of baclofen is effective in treating the disabling spasticity caused by acquired brain injury in selected patients.

**KEY WORDS** • intrathecal drug infusion • baclofen • brain injury • spasticity • hypertonia • rehabilitation

---

**J Neurosurg 87:415–419, 1997**
to maximum medical therapy, which interfered with their activities of daily living. Nine patients had suffered traumatic brain injuries and three had experienced anoxic acquired brain injuries. All participants were recruited consecutively.

Initial Evaluation Procedure

The following parameters (Table 1) were assessed to determine the general status of the patient prior to enrollment and to obtain baseline values: 1) complete physical examination and neurological assessment, including a thorough history of the patient's spasticity and the treatments and medications used to manage the condition; 2) the five-point Ashworth Scale (rigidity) to assess muscle tone in both the lower extremities (hip abduction, hip flexion, knee flexion, and ankle dorsiflexion) and the upper extremities (shoulder abduction, elbow extension, elbow flexion, and wrist extension); 3) a four-point scale reflecting the number of spontaneous sustained flexor and extensor muscle spasms per hour; and 4) a five-point scale documenting deep tendon reflexes at the biceps, patella, and Achilles.

Inclusion Criteria

After the initial screening evaluation, patients were enrolled in the study if they met all of the following criteria: 1) they were between 10 and 75 years old; 2) they had a diagnosis of severe chronic spastic hypertonia in the lower extremities (although the upper extremities could also be involved) of at least 6 months' duration that was defined by an average Ashworth Scale score of at least 3 in the affected extremities (two or more extremities) or an average spasm score of at least 2 in the affected extremities; 3) they failed to respond satisfactorily to treatment with oral antispasmodic medications (including baclofen and possibly diazepam, clonidine, and/or dantrolene sodium); or 4) they experienced unacceptable side effects at effective treatment dosages of these drugs.

### Table 1

<table>
<thead>
<tr>
<th>Score</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashworth Scale</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>no increase in tone</td>
</tr>
<tr>
<td>2</td>
<td>slight increase in tone, giving a “catch” when affected part is moved in flexion or extension</td>
</tr>
<tr>
<td>3</td>
<td>marked increase in tone, but affected part easily flexed</td>
</tr>
<tr>
<td>4</td>
<td>considerable increase in tone; passive movement difficult</td>
</tr>
<tr>
<td>5</td>
<td>affected part rigid in flexion or extension</td>
</tr>
<tr>
<td>spasm frequency</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>no spasms</td>
</tr>
<tr>
<td>1</td>
<td>mild spasms induced by stimulation</td>
</tr>
<tr>
<td>2</td>
<td>infrequent full spasms occurring &lt;1/hr</td>
</tr>
<tr>
<td>3</td>
<td>spasms occurring &gt;1/hr</td>
</tr>
<tr>
<td>4</td>
<td>spasms occurring &gt;10/hr</td>
</tr>
<tr>
<td>reflex</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>reflex absent</td>
</tr>
<tr>
<td>1</td>
<td>hyporeflexia</td>
</tr>
<tr>
<td>2</td>
<td>normal</td>
</tr>
<tr>
<td>3</td>
<td>mild hyperreflexia</td>
</tr>
<tr>
<td>4</td>
<td>3 or 4 beats clonus only</td>
</tr>
<tr>
<td>5</td>
<td>clonus</td>
</tr>
</tbody>
</table>

### Table 2

Clinical characteristics in 12 brain-injured patients undergoing treatment for spasticity

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)</th>
<th>Cause of Brain Injury</th>
<th>Average Tone+ Pre-treatment</th>
<th>Average Tone+ at 3 Mos Treatment</th>
<th>Baclofen Dosage at 3 Mos (μg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23, M</td>
<td>trauma</td>
<td>4.2</td>
<td>2.8</td>
<td>172</td>
</tr>
<tr>
<td>2</td>
<td>31, M</td>
<td>trauma</td>
<td>3.9</td>
<td>2.4</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>21, M</td>
<td>trauma</td>
<td>2.9</td>
<td>2.0</td>
<td>412</td>
</tr>
<tr>
<td>4</td>
<td>21, M</td>
<td>trauma</td>
<td>3.2</td>
<td>2.4</td>
<td>120</td>
</tr>
<tr>
<td>5</td>
<td>36, M</td>
<td>trauma</td>
<td>3.0</td>
<td>2.2</td>
<td>120</td>
</tr>
<tr>
<td>6</td>
<td>23, M</td>
<td>trauma</td>
<td>4.2</td>
<td>2.4</td>
<td>278</td>
</tr>
<tr>
<td>7</td>
<td>25, M</td>
<td>trauma</td>
<td>3.8</td>
<td>3.2</td>
<td>120</td>
</tr>
<tr>
<td>8</td>
<td>17, M</td>
<td>trauma</td>
<td>2.2</td>
<td>1.1</td>
<td>200</td>
</tr>
<tr>
<td>9</td>
<td>34, M</td>
<td>trauma</td>
<td>4.0</td>
<td>1.8</td>
<td>165</td>
</tr>
<tr>
<td>10</td>
<td>38, F</td>
<td>anoxia</td>
<td>3.9</td>
<td>2.9</td>
<td>230</td>
</tr>
<tr>
<td>11</td>
<td>28, M</td>
<td>anoxia</td>
<td>1.9</td>
<td>1.1</td>
<td>144</td>
</tr>
<tr>
<td>12</td>
<td>39, M</td>
<td>anoxia</td>
<td>5.0</td>
<td>1.6</td>
<td>144</td>
</tr>
</tbody>
</table>

* Ashworth Scale score.

Screening Methods

All patients were screened via a randomized, double-blind, placebo-controlled crossover evaluation. Patients were randomly assigned to groups receiving an intrathecal bolus injection of preservative-free normal saline or 50 μg of baclofen. A lumbar puncture was performed at either the L3–4 or the L2–3 interspace, and the 1-ml bolus was injected. The crossover phase of the trial evaluation occurred during a second outpatient clinic visit at least 48 hours after the initial drug administration. At that time, the opposite substance was injected in the same manner as before, with subsequent data collection the same as that which took place during the initial trial. Neither the patient nor the investigator knew which substance was injected until after the second trial phase was completed. Data for the Ashworth Scale, spasm, and deep tendon reflex scores were then collected by the same investigator at 1, 2, 4, and 6 hours postinjection as described previously.

Clinical Setting

Most patients (10 of 12) underwent screening in an outpatient rehabilitation clinic setting that was part of a single tertiary care university medical center, and two were screened as inpatients within the same university medical center. Consideration for continuous baclofen delivery via programmable pump and intraspinal catheter was given to those patients who had a reduction of muscle tone of at least 2 points on the Ashworth Scale in trial evaluations or experienced a reduction in the number of spasms in the affected limbs while receiving the active agent, as determined by the spasm frequency scale, with no untoward side effects.

Implantation Procedure

The continuous infusion pump and intraspinal catheter system were implanted while the patient was receiving a general anesthetic and was placed in the lateral decubitus position. The catheter was placed in the lumbar subarachnoid space at L3–4 via a percutaneous technique using a 14-gauge Tuohy needle. The intraspinal catheter was
Intrathecal baclofen for brain injury

Fig. 1. Graphs showing the average lower-extremity muscle tone according to the Ashworth Scale (left), spasm frequency (center), and reflex (right) scores for patients before treatment and after 3 months of continuous intrathecal drug administration. Bars ± 1 SD.

passed into the subarachnoid space for 25 cm in a cephalad direction. The intraspinal catheter was tunneled into the subcutaneous space to a separate small flank incision. The programmable pump was placed in a lower abdominal wall subcutaneous pocket above the rectus fascia. The pump catheter was tunneled to the separate flank incision as well, where it was connected to the intraspinal catheter, connecting the system and completing the procedure.

After implantation of the infusion device, patients received follow-up care on an outpatient basis for refilling and dosage adjustment. The maximum refill interval currently recommended by the manufacturer is 90 days; however, depending on the dosage, patients may be seen as frequently as every 30 days. During the first months of continuous therapy, many participants required frequent dosage adjustments as each patient adapted to changes in lifestyle and improved functional status without spasticity. Many patients have to learn to adapt mobility, transfer, and self-care techniques to the changes (reduction) in their spasticity. Patients typically require a period of intensive inpatient rehabilitation to benefit functionally from the decreased motor tone and/or increased voluntary motor control they experience with the intrathecal administration of baclofen.1,4 Dosage adjustments are made in small increments of 10 to 20% to achieve symptomatic improvement and can be performed as soon as 24 hours after the preceding dosage adjustment. The first follow-up evaluation is generally scheduled for 10 days after pump placement and as frequently as necessary to obtain optimum dosing. Dosage adjustments are determined by the caregivers and researchers, with the most basic goal being a decrease of 2 points in the tone or spasm frequency score in the affected limbs. Refill kits are available from the pump manufacturer. Medication refill is accomplished percutaneously using a sterile technique.

Statistical Analysis

The statistical study design was an A–B single case control design with individual patients serving as their own controls. Because muscle tone, spasm, and reflex scores were measured on ordinal scales, the Wilcoxon signed-rank test was also used to measure the significance of observed differences between baseline values and those observed after 3 months of continuous treatment. A two-tailed test was used, with probability values of less than 0.05 considered significant. Although nonparametric tests were used, the data are presented as the means ± the standard deviations (SDs) to facilitate the interpretation of the magnitude and clinical significance of the results. Rather than consider each muscle separately, scores for muscle tone, spasms, and reflexes were averaged for the upper or lower extremities in each patient.

Statistical analysis was performed using commercially available software for Macintosh (Stat View; Abacus Concepts, Inc., Berkeley, CA).

Protocol Review

The study protocol was reviewed and approved by The University of Alabama at Birmingham Health Sciences Human Investigation Committee (new drug and device investigations). Before testing, after being familiarized with the experimental method and the potential risks as well as the potential benefits of the procedure, each patient signed an informed consent form.

Results

The average Ashworth Scales scores for lower-extremity tone in each patient at baseline and after 3 months of treatment are shown in Table 2. The average dosage of intrathecal baclofen required to achieve this reduction was 183.8 µg/day, range 100 to 412 µg/day.

Lower Extremities

Overall, the average lower-extremity Ashworth Scale scores (Fig. 1 left) decreased 1.4 points from 3.5 ± 1.2 points before treatment to 2.2 ± 0.9 points after 3 months of treatment (p < 0.0001, Wilcoxon signed-rank test).

A similar response was observed for lower-extremity spasm frequency scores (Fig. 1 center). The average lower-extremity spasm score decreased 1.5 points from 1.8 ± 1.2 points before treatment to 0.2 ± 0.5 points after 3 months of treatment (p < 0.0001, Wilcoxon signed-rank test).

The average reflex score for the lower extremities (Fig. 1 right) decreased 2.5 points from 2.7 ± 1 point before treatment to 0.2 ± 0.6 points after 3 months of treatment (p < 0.0001, Wilcoxon signed-rank test).

Upper Extremities

Upper-extremity treatment responses were similar to lower-extremity responses, although of slightly smaller magnitude because the initial upper-extremity baseline scores were lower compared with those of the lower extremities (Fig. 2).
The average upper-extremity Ashworth Scale scores decreased 1.4 points from 3.3 ± 1.3 points before treatment to 1.9 ± 0.8 points after 3 months of treatment (p = 0.0033, Wilcoxon signed-rank test). The average upper-extremity spasm score decreased 1.2 points from 1.8 ± 1.3 points before treatment to 0.6 ± 1 point after 3 months of treatment (p = 0.0070, Wilcoxon signed-rank test). The biceps reflex score decreased 1 point from 2.7 ± 0.5 points to 1.7 ± 0.6 points over the same time frame (p = 0.0111, Wilcoxon signed-rank test).

Patient Outcomes and Complications

We noted significant reductions in joint contractures in seven patients, and in five others there have been functional improvements in gait and transfers. Two patients have progressed from being dependent in gait to independent walking with supportive devices. Research regarding the functional gains in these individuals is ongoing and will require follow-up review of patients after restorative therapies are discontinued to evaluate whether these functional gains can be maintained.

Complications from pump placement were minor in this population. Spinal headaches were noted in five patients and lasted up to 1 week after placement. There were three cases of postoperative atelectasis. One patient experienced catheter dislodgement caused by “tiddler’s syndrome.” This syndrome, as described by Medtronics Inc. (verbal communication, 1996), is associated with obsessive–compulsive patients who manipulate and spin their intrathecal delivery pumps by playing with them soon after placement.

Discussion

This work was accomplished using a Food and Drug Administration–directed investigational new drug (IND) treatment protocol to investigate the effectiveness of intrathecally administered baclofen in the treatment of spasticity and hypertonia caused by head injury. To our knowledge, this is the first report documenting the use of continuous intrathecal infusion of baclofen in the treatment of severe spasticity following acquired brain injury.

All patients treated with continuous intrathecal baclofen therapy in this study were first evaluated using a double-blind, placebo-controlled screening protocol. This avoided the effect of simple relaxation on spasticity and spasm frequency and allowed the identification of patients who showed a positive response to intrathecal baclofen with no adverse reactions to the drug.

In patients suffering from spastic hypertonia originating with spinal cord injury who have retained some residual motor function below the level of injury, experience shows that a decrease in motor strength rarely occurs after administration of therapeutic doses of intrathecal baclofen. On the contrary, an increase in functional motor strength has often been reported.2,3,5,9 The increase in functional strength in these patients is believed to be caused by a reduction in motor tone, which is often so high before treatment that it effectively reduces the voluntary motor capacities of the hypertonic extremities. To date, we have noted no reduction of voluntary motor function among brain-injured patients treated with continuously delivered intrathecal baclofen. This is true even among patients who have suffered a predominant hemiparesis.

Some patients with spastic hypertonia of any cause rely on reflex spastic hypertonia to assist them with functional activities. A reduction in the baseline hypertonia in these patients is of concern and could be a detriment. An untoward, complete loss of tone and functional ability is rare with intrathecal baclofen treatment and can be assessed in part during the bolus trial. However, an excessive loss of tone that occurs during the intrathecal baclofen screening trial is not a direct contraindication for continuous infusion therapy, because the pump can be programmed to modulate intrathecal baclofen administration, effectively titrating medication delivery to achieve an ideal balance between function and hypertonia.

Until recently there have been few evaluations of the effects of intrathecal baclofen on spastic hypertonia involving the upper extremities. A bolus trial study performed exclusively on brain-injured patients has demonstrated significant reductions in upper-extremity tone, spasm frequency, and reflexes.9 We have previously confirmed by postoperative x-ray studies that insertion of the intraspinal catheter in a cephalad direction 25 cm from the L3–4 intralaminar space results in a catheter tip location between the T-5 and T-7 levels. By directing the intrathecal catheter to a level more cephalad than T-10, we have accomplished an improved sustained response in upper-extremity tone with continuously infused intrathecal baclofen. These effects on the upper extremities appear to be more consistent than those noted during the bolus trial, in which the drug was introduced via a bolus injection into the lumbar cistern.
Intrathecal baclofen for brain injury

Although this is a preliminary report on 12 consecutive brain-injured patients with severe spastic hypertonia treated with intrathecal baclofen, the results are encouraging. We have documented statistically significant reductions in spasticity in these patients as determined by established tone, spasm frequency, and reflex scoring systems. These improvements have been maintained with minimum modulation of intrathecal baclofen delivery after the first 3 months of treatment. Although issues regarding the long-term effectiveness of intrathecal baclofen and drug tolerance have yet to be decided in brain-injured patients, the experience of several investigators suggests that patients with hypertonia caused by brain injury may actually require less intrathecal baclofen than patients with spasticity of spinal origin.10

Spastic hypertonia is a progressive motor disorder that can vary over time, particularly in the 1st year after neurological injury. It is our view that patients with hypertonia following brain or spinal injury should not be evaluated for intrathecal baclofen therapy for at least 6 months postinjury,9 in part because it has been hypothesized that γ-aminobutyric acid agonists may interfere with the early stages of recovery after central nervous system injury.7 We have found, however, that continuous intrathecal baclofen therapy initiated as early as 6 months postinjury appears to be effective in preventing the development of severe joint contractures that typically occur in these patients within the first 12 months after injury.

The presence of a ventriculoperitoneal shunt is not a contraindication for the use of intrathecal baclofen, a particularly relevant issue when dealing with brain-injured patients. We have implanted 24 pumps in our total series of patients, five of whom have ventriculoperitoneal shunts. In none of these patients (three of whom we have followed for more than 3 months) has there been any effect indicating upper central nervous system impairment caused by intrathecal baclofen therapy.

There is promising research in a variety of areas that may lead to improved neurological function among patients with acquired brain or spinal cord injuries. For this reason and others, our group generally avoids irreversible, neuroablative procedures for patients with disabling spastic hypertonia. A programmable continuous infusion delivery system for the administration of intrathecal baclofen allows the physician to customize treatment for the individual needs of the patient with spasticity, without irreversible consequences. This form of treatment has been of value to patients with severe spasticity caused by spinal cord pathology and has the potential for improving the quality of life in patients with spasticity caused by acquired brain injury. Our initial work suggests that if aggressive medical approaches to spasticity have been unsuccessful and if the dosage of intrathecal baclofen required to produce effective changes in spasticity does not create untoward side effects, intrathecal baclofen treatment can be of significant value for selected patients with severe hypertonia and spasticity after brain injury.

References
4. Joint Section on Trauma and Critical Care of the American Association of Neurological Surgeons and the Brain Trauma Foundation: Guidelines for the Management of Severe Head Injury, Park Ridge, Ill: American Association of Neurological Surgeons, 1995

Manuscript received December 23, 1996. Accepted in final form March 25, 1997.

This study was supported by Medronics, Inc., and used an FDA-approved IND treatment protocol, IND No. 39–327, and investigational device protocol No. G9110200.

Address reprint requests to: Mark N. Hadley, M.D., Division of Neurosurgery, University of Alabama at Birmingham, 511 MEB, 1816 Sixth Avenue South, Birmingham, Alabama 35294.