Intravenous baclofen as an alternative to intrathecal baclofen for intractable spasticity or dystonia: outcomes and technical considerations

Clinical article

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Object. The aim of this study was to identify the benefits of intraventricular baclofen (IVB) therapy for the treatment of intractable spasticity or dystonia in a subset of patients who had experienced multiple revisions while receiving intrathecal baclofen (ITB) therapy.

Methods. The authors reviewed the charts of 22 consecutive patients with intractable spasticity or dystonia who initially underwent ITB therapy, subsequently suffered multiple revisions during ITB therapy, and ultimately received IVB therapy, all during a 12-year period from November 1998 to October 2010. The intraventricular catheters were positioned in the lateral ventricle, aided by stereonavigation.

Results. The surgical revision rate (the average number of surgical revisions per average number of follow-up years) during ITB therapy was 0.84, and was 0.50 during IVB therapy. The most frequent complication requiring surgical revision during ITB therapy was catheter occlusion, followed by pump malfunction/pump pocket issues, and infection. The most frequent complication requiring surgical revision during IVB therapy was infection, followed by catheter misplacement/migration. Four patients suffered infection that required removal of their intraventricular catheter, and currently have no baclofen system.

Conclusions. Some of these patients had a history of increasing revisions with increasing frequency during ITB therapy. Such a history puts them at risk for spinal arachnoiditis, a condition that complicates further ITB therapy. For such patients, the authors believe that IVB therapy may be a beneficial therapeutic option, given that the surgical revision rate was lower for IVB than for ITB. Intraventricular baclofen may be a cost-effective option for patients with mounting revisions during ITB therapy.

(http://thejns.org/doi/abs/10.3171/2012.6.PEDS11456)

Key Words • intrathecal baclofen • intraventricular baclofen • spasticity • cerebral palsy • functional neurosurgery

Since the mid-1980s, ITB has been used to treat medically refractory spasticity caused by various conditions, including cerebral palsy, traumatic brain and spinal cord injury, and multiple sclerosis.19,24–26 Subsequently, ITB became a therapeutic option for dystonia in the 1990s.3–5,15,16 Several studies have described beneficial outcomes from ITB systems, reporting patient satisfaction,11 patient goal attainment,34 and cost effectiveness.13 Nevertheless, ITB systems are associated with numerous catheter (fracture, occlusion), pump (malfunction, rotation), and wound complications (infection, dehiscence).22,32,33 These issues necessitate additional surgical intervention, leading to multiple revisions.

Recently, a few studies have reported the use of IVB in refractory spasticity or dystonia. Albright and Ferson19 reported the use of IVB for dystonia with favorable results. Haranhalli et al.19 used IVB in 2 patients after multiple complications from ITB. In the present study, the authors report the outcomes of a series of 20 patients who were treated with IVB therapy after increasing revisions during ITB therapy.
Methods

Patient Selection

We reviewed the charts of 22 consecutive patients with intractable spasticity or dystonia who initially underwent ITB therapy, subsequently suffered multiple complications from their ITB therapy, and ultimately received IVB therapy, all during a 12-year period from November 1998 to October 2010 (Table 1). We could not retrieve follow-up information for 2 patients, and their data were excluded from the study. The 20 other patients included 6 females and 14 males. The patients’ ages ranged from 4 to 65 years (mean 23 years) during the initial intrathecal catheter placement, and from 6 to 68 years (mean 27 years) during the initial intraventricular catheter placement. The causes of the spasticity/dystonia of the patients included cerebral palsy (n = 11), spinal cord injury (n = 4), traumatic brain injury (n = 2), cerebrovascular accident (n = 1), mitochondrial dystrophy (n = 1), and iron deposition disorder (n = 1). The follow-up period ranged from 0.5 to 121 months (mean 62 months) for ITB and from 2 to 57 months (mean 20 months) for IVB. Four patients (Cases 2, 6, 9, and 14) had a concomitant ventriculoperitoneal shunt, whereas 2 patients (Cases 19 and 20) had a history of spinal fusion.

Surgical Procedure for IVB

The patient was placed supine and a surgical navigation system was calibrated using tracer technology. An entry point in the right or left posterior parietal region was identified near Keen’s point. Subsequently, the abdominal incision over the previous ITB pump was reopened and dissected down to the old catheter, which was disconnected from the pump. The spinal segment of the previous ITB catheter was then ligated and returned to the pump pocket. A bur hole was then made at Keen’s point and the new catheter was tunneled subcutaneously between the bur hole and the abdominal incisions. The ventricular catheter was directed into the ventricle using stereotactic neuronavigation. Once good CSF flow was determined, the ventricular catheter was trimmed and connected to the other catheter, which was tunneled subcutaneously between the incisions using a connector. The other end of the catheter was attached to the pump. The pump was then programmed to prime the catheter.

Results

There were a total of 82 complications noted in these 20 patients while using ITB (Table 2). Catheter-related complications constituted 67.1% (n = 55) of the total complications, whereas pump-related complications constituted 32.9% (n = 27). Catheter-related complications included foreign body reaction (n = 23), pneumocephalus (n = 3), infection (n = 10), and failure to infuse (n = 1). Pump-related complications included catheter occlusion (n = 4), catheter disconnection (n = 1), and pump malfunction (n = 2).

TABLE 1: Characteristics of 20 consecutive patients with intractable spasticity or dystonia who initially underwent ITB therapy and eventually received IVB therapy*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex</th>
<th>Indication</th>
<th>Age (yrs)</th>
<th>No. of Revisions</th>
<th>F/U (mos)</th>
<th>Age (yrs)</th>
<th>No. of Revisions</th>
<th>F/U (mos)</th>
<th>Baclofen Dose (μg/day)†</th>
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<tr>
<td>1</td>
<td>M</td>
<td>CP</td>
<td>19</td>
<td>6</td>
<td>113.6</td>
<td>28</td>
<td>0</td>
<td>4.6</td>
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<td>2</td>
<td>M</td>
<td>CP</td>
<td>15</td>
<td>5</td>
<td>59.9</td>
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<td>4</td>
<td>6.9</td>
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<tr>
<td>3</td>
<td>M</td>
<td>IDD</td>
<td>4</td>
<td>4</td>
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<td>14</td>
<td>0</td>
<td>2.2</td>
<td>481.9</td>
</tr>
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<td>4</td>
<td>M</td>
<td>TBI</td>
<td>13</td>
<td>1</td>
<td>33.4</td>
<td>16</td>
<td>1</td>
<td>6.3</td>
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</tr>
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<td>M</td>
<td>SCI</td>
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<td>300</td>
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<td>M</td>
<td>CP</td>
<td>9</td>
<td>5</td>
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<td>1</td>
<td>46.9</td>
<td>762</td>
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<td>3</td>
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<td>24</td>
<td>1</td>
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<td>8</td>
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<td>26.3</td>
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<td>12</td>
<td>M</td>
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<td>34</td>
<td>2</td>
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<td>34</td>
<td>0</td>
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<tr>
<td>13</td>
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<td>CP</td>
<td>56</td>
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<td>F</td>
<td>CP</td>
<td>14</td>
<td>12</td>
<td>48.2</td>
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<td>0</td>
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<td>F</td>
<td>CVA</td>
<td>37</td>
<td>7</td>
<td>66.7</td>
<td>42</td>
<td>0</td>
<td>2.5</td>
<td>100</td>
</tr>
<tr>
<td>17</td>
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<td>CP</td>
<td>9</td>
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<td>0.5</td>
<td>9</td>
<td>1</td>
<td>2.2</td>
<td>644.5</td>
</tr>
<tr>
<td>18</td>
<td>M</td>
<td>MD</td>
<td>8</td>
<td>6</td>
<td>21.0</td>
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<td>3</td>
<td>6.5</td>
<td>180</td>
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<td>SCI</td>
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<td>6</td>
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<td>F</td>
<td>CP</td>
<td>28</td>
<td>5</td>
<td>107.9</td>
<td>37</td>
<td>0</td>
<td>11.4</td>
<td>170</td>
</tr>
<tr>
<td>average</td>
<td></td>
<td></td>
<td>22.65</td>
<td>4.35</td>
<td>62.0</td>
<td>27.25</td>
<td>0.85</td>
<td>20.4</td>
<td>554.4</td>
</tr>
</tbody>
</table>

* CP = cerebral palsy; CVA = cerebrovascular accident; F/U = follow-up; IDD = iron deposition disorder; MD = mitochondrial dystrophy; SCI = spinal cord injury; TBI = traumatic brain injury.
† Cases 2, 4, 14, and 19 did not have a final baclofen dose because their intraventricular catheters were removed.
A comparison of intraventricular and intrathecal baclofen

Table 2: Numbers and types of complications in each group

<table>
<thead>
<tr>
<th>Complication</th>
<th>ITB</th>
<th>IVB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheter occlusion</td>
<td>31</td>
<td>1</td>
</tr>
<tr>
<td>Pump malfunction/pocket issues</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>Infection</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>Catheter fracture/leak</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Catheter misplacement/migration</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Catheter kink</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Baclofen withdrawal</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Catheter disconnection</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Seroma</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>82</td>
<td>18</td>
</tr>
</tbody>
</table>

* Includes catheter tip loculations, subdural catheters, and catheter malfunctions without identifiable causes.

tuated 15.9% (n = 13). Spiral computed tomography with contrast injection, as outlined in our previous article, was used as indicated to diagnose some of these complications. The most common complication was catheter occlusion, followed by pump complications, infection, and catheter fracture. The average time before the first ITB system experienced any complication was 27.6 months. The average time between the last ITB revision and the initial intraventricular catheter placement was 12.9 months.

There were a total of 18 complications noted in 10 of 20 patients while using IVB. Catheter-related complications constituted 44% (n = 8) of the total complications, whereas pump-related complications constituted 16.7% (n = 3). The most common complication was infection, followed by catheter migration/misplacement. The first complication occurred, on average, 7.4 months after placement of the initial intraventricular catheter.

Overall, 87 surgical revisions occurred during ITB therapy and 17 during IVB therapy. The revision rate (the average number of surgical revisions per average number of follow-up years) during ITB therapy was 0.84, and was 0.50 during IVB therapy. Currently, 4 patients (Cases 2, 4, 14, and 19) have no IVB system due to infection. One patient (Case 15) received globus pallidus internus deep brain stimulation while under treatment with IVB.

Illustrative Case

This 28-year-old man (Case 1, Table 1) presented with a history of intractable spasticity secondary to cerebral palsy. The patient underwent placement of an initial ITB system when he was 19 years old. After that time, he had chronologically encountered 2 infections, a catheter extrusion, and 3 catheter occlusions (1 instance associated with a fracture). Due to his recurrent complications with ITB, it was believed that IVB would be a better alternative. After placement of the intraventricular catheter, the pump was programmed at 1442 μg/day, the same rate as when the patient was on ITB. On postoperative Day 1, the patient was very sleepy; he would respond to touch, but would nod off if he had no stimulation. For the next few days, the dose was decreased sequentially to 1161 μg/day and then to 1045 μg/day, at which point the patient became more responsive. At discharge, the patient was awake and alert. Currently, the patient has been on IVB therapy for 4.6 months with no complications.

Discussion

In the 1980s, Penn et al. first reported the usage of ITB in humans. Since that time, ITB has been employed to treat spasticity caused by spinal cord injury, multiple sclerosis, cerebral palsy, and traumatic brain injury. Benefits using ITB have also been attained for patients with dystonia. Sampson et al. determined that continuous ITB provided a suitable cost-benefit ratio for select patients who had not gained adequate relief from less invasive therapy, who were bedridden due to severe spasticity, or who were dependent on a wheelchair while suffering from severe spasm-related pain.

The percentage of patients with complications from ITB requiring surgical management has ranged from 16%–33% in various studies. Of these patients, 18%–47% suffered from more than 1 complication. Common issues included infection, catheter-related problems (catheter disconnections, fractures, and malfunctions), and CSF leaks. Our patients suffered from multiple complications related to continuous ITB; the majority of these complications were catheter- or pump-related.

A cost analysis of continuous ITB for severe spinal spasticity demonstrated that approximately two-thirds of the costs can be attributed to pump implantation and related hospitalization, while roughly one-fifth can be attributed to complications. Savings originated from withdrawal of oral medication, job preservation, and avoidance or delay of admission to a nursing home. Obviously, a method to reduce the incidence of these complications, especially for patients with a history of past complications, would effectively reduce the total cost of baclofen therapy. Our surgical revision rate was lower for IVB than for ITB, suggesting that IVB may be a cost-effective option for patients with increasing revisions during ITB therapy.

Recently, Albright and his colleagues reported the use of IVB for the treatment of 10 patients with either severe secondary generalized dystonia or degenerative dystonia. Their indications for IVB included a lack of response to ITB, spinal deformity, and/or clinical impression that IVB would elicit a better response than ITB. They noted that patients with a history of intraventricular hemorrhage or meningitis should undergo a flow study to assess the benefits of IVB. Haranhalli et al. reported on 2 patients with dystonia who underwent IVB therapy after multiple catheter-related complications from ITB therapy; the cause of these complications was linked to severe writhing from excessive truncal dystonic movements. Similarly, our indications for IVB therapy included spasticity refractory to ITB and/or a history of increasing complications.

Albright and colleagues endoscopically positioned the catheter within the third ventricle. Past studies have suggested that baclofen acts at the cerebral convexities when treating generalized dystonia, inhibiting the stimu-
lulation of the premotor and supplementary motor cortex.²⁰
Infusion into the lateral ventricles might introduce baco-
fen into regions of stagnate flow and cause regional
toxicities; on the other hand, infusion within the third
ventricle may disseminate with CSF via the aqueduct
and fourth ventricle, while maintaining a high concentra-
tion once CSF reaches the cerebral convexities.¹³

Albright and colleagues reported an average IVB
dosage of 303 μg/day, although a value of 2012 μg/day
was considered an outlier and consequently was excluded
from analysis.¹⁷ Moreover, 2 of the patients did not re-
spond to IVB infusion; they also had not responded to
high-dose ITB infusion. Our average IVB dosage was
554.4 μg/day (Table 1). One possible explanation for the
different values between the 2 studies may be the differ-
ent patient populations (patients with dystonia compared
with patients with spasticity). Albright and Ferson rea-
soned that IVB may be less efficacious for patients with
spasticity, because baclofen needs to reach the spinal cord
level, whereas it needs to reach the cerebral convexities
for dystonia. This theory would support the need for a
higher average dose among our patients. In another study,⁵
the ITB dosage was noted to be higher for patients with
generalized dystonia compared with those with spasticity.
Overall, there may not be a correlation between ITB dose
and corresponding CSF baclofen level,⁶ therefore, infer-
rings patterns from IVB dosages may be inconsequential.

Park²³ did caution against the potential toxicities of baclofen,
noting the deaths of 2 beagles at high doses of
IVB in a prior study.² Albright agreed that the deaths
were likely due to obtundation and profound systemic
hypotonia that occur with severe baclofen overdos ing.²³
Nevertheless, similar to our findings, Albright reported
that no patient exhibited any sign of overdose while on
IVB therapy.²³

Catheter occlusions constituted the majority of com-
plications during ITB therapy in our patient population.
Arachnoiditis may explain the high incidence of catheter
occlusions. Baclofen itself does not induce inflamma-
tion.¹⁴ However, our patients harbored preexisting neuro-
logical disease, infection, and trauma and had undergone
previous surgical spinal interventions, which are risk
factors for arachnoiditis.⁹ Recently, a rat model for spi-
nal cord injury demonstrated that inflammatory cells and
connective tissue could occlude chronic intrathecal tub-
ing in the setting of active inflammation.²⁰,²⁴ Placement
of the catheter within the spacious ventricle, a proximal
CSF site lined by ependyma, rather than within the spinal
canal and arachnoid-lined cavity, may decrease the risk
of arachnoiditis. Catheter occlusions by choroid plexus or
ependymal tissue have been reported.¹²,¹⁸,²¹

The high incidence of infection during IVB therapy
may be attributable to the presence of a ventriculoperito-
neal shunt. Five of the 7 infections associated with IVB
therapy occurred in 2 of the 4 patients with a concomi-
tant ventriculoperitoneal shunt. The same 2 patients cur-
cently do not harbor a baclofen system. Accurate catheter
placement—typically ipsilateral to the shunt catheter—is
a more prominent issue for IVB therapy. The ventricular
catheter had to be revised for migrations to the choroidal
fissure and perimesencephalic region. Catheter placement
was difficult for these patients due to their very small ven-
tricles, which may be a limiting factor for IVB therapy.
Of note, IVB dosing required some additional adjust-
ments for the patients who harbored a ventriculoperitone-
al shunt. This adjustment was necessary only during the
initial period of IVB therapy, and these patients’ baclofen
requirement reached a “steady state” after 1–2 months
similar to those of other patients without a ventricu-
loperitoneal shunt.

Our study has several limitations. We did not use a
standard score to assess the level of spasticity or dysto-
nia in our patients (such as the Ashworth scale and oth-
ers). Furthermore, the follow-up period for ITB was sig-
nificantly longer than that for IVB, affecting the rate of
complications detected in the 2 groups. With time, our
patients may endure more complications with IVB. In ad-
dition, with time, our threshold for considering IVB de-
creased; this phenomenon potentially provides a selection
bias in our series.

Conclusions

The patients reviewed in this series had a history of
revisions with increasing frequency during ITB therapy.
Such a history puts them at risk for spinal arachnoiditis, a
condition that further complicates ITB therapy. Accord-
ing to our data from this study, IVB therapy may afford a
lower surgical revision rate. For select patients, we believe
that IVB therapy may be a beneficial therapeutic option.

Disclosure

Dr. Turner serves as a consultant to Medtronic.

Author contributions to the study and manuscript preparation
include the following. Conception and design: Cohen-Gadol, Turner.
Acquisition of data: Cohen-Gadol, Turner. Analysis and interpreta-
tion of data: all authors. Drafting the article: all authors. Critically
revising the article: all authors. Reviewed submitted version of
manuscript: all authors. Approved the final version of the manuscript
on behalf of all authors: Cohen-Gadol.

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M. Turner, H. S. Nguyen, and A. A. Cohen-Gadol
A comparison of intraventricular and intrathecal baclofen


Please include this information when citing this paper: published online August 3, 2012; DOI: 10.3171/2012.6.PEDS11456.