Stereotactic endoscopic placement of third ventricle catheter for long-term infusion of baclofen in patients with secondary generalized dystonia

Technical note

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Continuous infusion of baclofen is a treatment option for severe generalized dystonia. Catheter insertion within the third ventricle has been described as an alternative to standard intrathecal placement to maximize intracranial concentrations of baclofen. The authors describe their experience with a novel technique for stereotactic endoscopic insertion of baclofen infusion catheters in the third ventricle in 3 patients with severe secondary generalized dystonia. Insertion was successful in all 3 patients, and all of them experienced significant improvement in dystonia scores on the Barry-Albright Dystonia Scale. Follow-up ranged from 5.5 to 7 months (mean 6 months), and no mechanical complications or CSF leaks were observed. The stereotactic endoscopic insertion of a baclofen infusion catheter into the third ventricle appears to be a safe method for continuous intraventricular baclofen infusion in patients with generalized secondary dystonia.

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Key Words • baclofen • dystonia • cerebral palsy • functional neurosurgery

SECONDARY dystonia is a prominent feature in 15%–25% of patients with CP and is often refractory to medical therapy.4,18 Secondary generalized dystonia is also a common sequela of traumatic and anoxic brain injury.5,18 Narayan et al.19 first described the use of intrathecal baclofen to treat secondary generalized dystonia in 1991. Since then, multiple studies have demonstrated its efficacy for children with secondary dystonias.4,5,8,10,18,21,26,27 Albright and colleagues4 demonstrated that a more cranial location of the catheter tip was associated with improved efficacy in secondary generalized dystonia. Electrophysiological studies have suggested cerebral sites of baclofen action in patients with dystonia, whereas the sites of action in spasticity are primarily spinal.9,23

Albright4 was the first to report the intraventricular administration of baclofen in 2 children with mixed spasticity and dystonia, with mixed results. On the basis of these observations, he performed experiments in dogs that demonstrated the safety of long-term intraventricular baclofen administration.2 A larger series of 10 patients with severe dystonia, including 9 with secondary generalized dystonia, demonstrated good results in all but 2 patients in whom high-dose intrathecal baclofen treatment had failed previously.6 To date, 13 cases treated with intraventricular baclofen infusion have been reported.1,6,25

We report the use of intraventricular baclofen in 3 additional cases and describe a novel surgical technique. All patients had severe, secondary generalized dystonia as the primary indication for baclofen therapy. The rationale for using intraventricular baclofen was based on data supporting improved efficacy of intraspinal baclofen for dystonia with a more rostral catheter tip,7 the cortical location of pharmacological targets in dystonic patients,9,23 the reported safety and efficacy of long-term intraventricular baclofen administration,1,2,6,25 and our institutional experience of poor control of dystonic symptoms with intraspinal catheters.

Methods

Patient Histories

Three children with a history of secondary generalized dystonia and spasticity (mean age 8.8 years, range 3.7–17 years) underwent placement of an intraventricular catheter and subfascial placement of a programmable pump for the continuous administration of baclofen (Table 1). Two patients underwent a preoperative baclofen

Abbreviation used in this paper: CP = cerebral palsy.
Surgical Procedure

One patient (Case 3) was previously treated with continu-
puncture, with significant improvement in muscle tone.
A trial consisting of a single intrathecal baclofen bolus dose
of 100 μg (Case 1) or 75 μg (Case 2) delivered via lumbar
puncture, with significant improvement in muscle tone.
One patient (Case 3) was previously treated with continu-
ous infusion of intrathecal baclofen.

The first patient was a boy whose age was 5 years and
10 months, in whom adrenoleukodystrophy and develop-
mental delay had been diagnosed. He had severe general-
ized dystonia. The patient in the second case, who was 3
years and 7 months old, had a near-drowning event re-
sulting in cardiac arrest. Despite successful resuscitation,
he suffered severe hypoxic-ischemic encephalopathy and
bilateral thalamic infarctions. He subsequently developed
quadriplegia and dystonia characterized by intermittent
axial posturing, including opisthotonos. He underwent
placement of the intraventricular catheter and pump 1
month after his accident. The third patient, a 17-year-old
boy with a history of CP, spastic quadriplegia, and prom-
inent dystonia, was previously treated with intrathecal ba-
clofen infusion for 4 years and 10 months. Dystonic post-
uring included intermittent hyperextension and rotation
of the neck and torso that significantly interfered with his
feeding and overall care. Some improvement in truncal
dystonia was achieved with an intrathecal infusion rate
of 852 μg/day via a high-thoracic catheter; however, his
cervical dystonia remained poorly controlled.

Surgical Procedure

After the induction of general anesthesia, the patients
were positioned supine with a gel roll elevating the right
shoulder and the head turned to the left and secured on
a doughnut pillow. Next, the Stealth AxiEM electromag-
netic navigation system (Medtronic, Inc.) was registered.
A straight incision was marked overlying the planned right
frontal entry point in the approximate location of the Ko-
cher point. The frontal horn of the lateral ventricle at the
foramen of Monro was selected as the target. A right retro-
auricular incision was marked to secure the tunneled cath-
ter. A standard right peribulbar abdominal incision
was also marked for subfascial implantation of a 20-
or 40-ml baclofen pump, as previously described.15 To mini-
imize the risk of infection, 30 mg/kg of cefazolin was
administered intravenously prior to the incision, chlorhexi-
dine was used to prepare the skin, and all surgical team
members were fully scrubbed and double gloved.14

First, the right frontal and retroauricular incisions
were sharply opened, and a subgaleal tract was tunneled
with a shunt passer. Next, we tunneled an 8709SC ba-
clofen infusion catheter (Medtronic, Inc.) from the cau-
dal to the cranial regions and wrapped it in bacitracin-
soaked laparotomy sponges. Through a standard 7-mm
bur hole at the right frontal entry point, we made a cruci-
ate opening in the dura mater. An electromagnetic stylet
(Medtronic) was placed within a 10-Fr blunt, peel-away
introducer (3.2-mm internal diameter; Aesculap). The
stylet was passed from the entry to the target in the lateral
ventricle by using AxiEM stereotactic navigation. After
the stylet was removed, the introducer was peeled back
and secured to the drapes with staples.

Next, the Neuropen endoscope (Medtronic) was ad-
vanced through the introducer sheath, and the foramen
of Monro was visualized. The infusion catheter was then
passed through the bur hole and sheath into the lateral ven-
tricle adjacent to the endoscope and, under endoscopic
visualization, through the foramen of Monro into the third
ventricle. The endoscope was then advanced through the
foramen of Monro to confirm the final position of the cath-
ter tip.

After the endoscope was withdrawn, the peel-away
introducer sheath was removed, and the catheter was se-
cured within the bur hole by using thrombin-soaked Gel-
foam and fibrin tissue sealant. Subsequently, a Silastic an-
chor was used to secure the catheter more caudally to the
galea beneath the retroauricular incision by using mul-
tiple 3-0 Nurolon sutures. After the peribulbar incision
was opened and the subfascial pocket developed, the cau-
dal end of the catheter was tunneled to the abdomen and
secured to a 20- or 40-ml Synchromed II infusion pump
(Medtronic). Before we connected the pump and catheter,
we injected 10 mg of vancomycin and 4 mg of gentamicin
into the catheter, as is our practice for CSF shunts.22

All incisions were copiously irrigated with bacitracin
and then closed in layers. The baclofen infusion was start-
ed at a rate of 50–100 μg/day. Postoperatively, the patients
were observed overnight in the pediatric ICU because of
concern for respiratory depression.2 On the 1st postop-
erative day, all patients underwent CT scans of the head
without contrast enhancement as well as lateral skull and
anteroposterior skull, chest, and abdominal x-ray studies
(Fig. I).

Results

In all 3 patients, insertion of the third ventricle cath-
ter and programmable pump was successful. None of
the patients experienced respiratory depression, and there
were no perioperative complications. All 3 patients expe-

trial consisting of a single intrathecal baclofen bolus dose
of 100 μg (Case 1) or 75 μg (Case 2) delivered via lumbar
puncture, with significant improvement in muscle tone.
TABLE 1: Summary of 3 cases of spastic quadriparesis and secondary generalized dystonia treated with
intraventricular baclofen infusion*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)</th>
<th>Diagnosis</th>
<th>Previous ITB</th>
<th>BAD Scale Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.8</td>
<td>adrenoleukodystrophy</td>
<td>100-μg test dose</td>
<td>Preop</td>
</tr>
</tbody>
</table>
| 2       | 3.7       | hypoxic-ischemic encephalo-
|          |     |   lopathy                 | 75-μg test dose          | 28   | 10    | 5.5     |
| 3       | 17        | CP                         | 852 μg/day (intrathecal pump) | 30   | 12    | 7       |

* BAD = Barry-Albright Dystonia; FU = follow-up; ITB = intrathecal baclofen.
Intracranial and extracranial infusion catheter and retroauricular Silastic anchor demonstrating the tip of the infusion catheter entering the third ventricle through the right foramen of Monro.

Discussion

Further study is required to compare benefits and complications of intraventricular and intrathecal baclofen infusion in the treatment of secondary generalized dystonia; however, it appears that intraventricular baclofen infusion is a promising approach that may be performed with minimal risk. These 3 cases bring the total number of reported cases of intraventricular baclofen infusion to 16, including 13 for dystonia.16,25

Presently available catheters are designed for intraspinal placement and are therefore flexible and require the use of an introducer for primary access to the ventricular system. Albright and Ferson6 also described an endoscopic technique. In this report, we describe a combined stereotactic endoscopic approach through a smaller introducer (the 10-Fr vs 19-Fr size). The use of navigation together with endoscopic visualization, although more expensive, increases the safety profile of access to the third ventricle in patients who commonly have distorted intraventricular anatomy.

Intrathecal baclofen infusion is a well-established treatment for severe spasticity and secondary generalized dystonia, especially among children with CP or those who have suffered severe traumatic or anoxic brain injury.3–5,8,12,18–20,29,27 It has also been successfully applied to other movement disorders, including cervical and focal hand dystonia10 as well as neuroleptic malignant syndrome.25 Standard catheter placement is in the low thoracic spine.17 Some authors have also described the use of cervical catheters in the context of previous spinal fusion,10,16 as a strategy to optimize efficacy in the upper extremities in quadriplegic spasticity,17 and for the control of cervical dystonia.10

The use of intrathecal baclofen infusion has rarely been described.1,6,25 Specifically, it has been suggested as a strategy to improve secondary generalized dystonia by increasing the concentrations of baclofen in the intracranial subarachnoid space.1,6,9,23 It has also been used effectively for the treatment of refractory neuroleptic malignant syndrome.25 All previous reports of intraventricular baclofen for dystonia have described catheter placement in the third ventricle to optimize symmetrical subarachnoid drug concentrations.1,6 Although intracranial catheter placement after hemispherectomy has been reported as a successful treatment for refractory neuroleptic malignant syndrome in 1 patient, different catheter positions within the ventricular system (for example, lateral vs third) have not been compared in patients with dystonia, and the comparative efficacies of intraventricular versus intraspinal baclofen infusion remain unknown.

The long-term administration of intraventricular baclofen appears to be safe although dose-related toxicity, including respiratory depression and temperature lability, was demonstrated in dogs.2 Complications are common with implanted baclofen infusion systems; in published reports they occur in between 5% and 40% of cases.18,26 Complications are more common in the pediatric population,24 and some studies suggest a higher frequency in patients treated for dystonia.25 It is possible that rarely reported complications of intrathecal baclofen, including amnesia,15 may become more common with intraventricular delivery; however, if similar efficacy can be maintained with lower baclofen concentrations because of a higher concentration of the drug in the intracranial subarachnoid space proximal to cortical targets, perhaps these complications can be avoided. Given our small series with short follow-up, we have not observed catheter malfunction or acute baclofen withdrawal. We do not yet have the clinical experience with intraventricular infusion to determine whether acute baclofen withdrawal is more
Intraventricular baclofen infusion

likely or more dangerous than what has been seen with long-term intraspinal infusion. Furthermore, we have no experience using this technique in patients with ventriculoperitoneal shunts, which would complicate attempts at intraventricular infusion.

Conclusions

We achieved significant improvement in dystonia as measured by Barry-Albright Dystonia Scale scores in all 3 of our patients, and similar results compared with previous reports of intraventricular baclofen and intrathecal baclofen. Stereotactic endoscopic placement of a third ventricle catheter for continuous infusion of intraventricular baclofen appears to be a safe and effective method that holds promise for the treatment of secondary generalized dystonia. Further study is required to determine the best candidates for this technique and to elucidate advantages in comparison with intrathecal baclofen administration.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Walker. Acquisition of data: all authors. Drafting the article: Bollo. 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: Walker. Study supervision: Walker.

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