Catheter systems for intrathecal drug delivery

RICHARD D. PENN, M.D., MICHELLE M. YORK, R.N., AND JUDITH A. PAICE, PH.D., R.N.

Neuroscience Institute, Department of Neurosurgery, Rush-Presbyterian-St. Luke’s Medical Center, Chicago, Illinois

A prospective study of intrathecal catheter reliability was performed at Rush-Presbyterian-St. Luke’s Medical Center. All 102 patients who had baclofen administered chronically for spasticity via an implanted drug pump were included. Sixty percent of the patients had no catheter complications; the remaining patients had one to five complications over their course of treatment. Survival analysis demonstrated a steady rate of malfunction up to 80 months, with the mean time to first failure recorded at 20 months. Kinks, holes, breaks, dislodgments, and disconnections were the most common complications. On the basis of their research the authors conclude that the thin-walled silastic catheter does not perform well and that larger, thick-walled catheters should be used.

Key Words • catheter implant system • intrathecal drug infusion • baclofen • drug delivery • survival analysis • complications

The effectiveness of drug pumps for the treatment of spasticity and pain rests primarily on the reliability of all the components of the system, including the pump, connectors, and catheters. By far, the most vulnerable part of the system has proven to be the catheter, which is placed into the lumbar subarachnoid space. As noted in previous studies, these catheters are prone to dislodgment, kinking, tearing, and disconnection, affecting as many as 40% of patients who use these systems.1–6 These complications disrupt drug delivery and repair requires surgical intervention. To evaluate the performance of the delivery system (Medtronic, Inc., Minneapolis, MN), the only system approved by the United States Federal Drug Administration for intrathecal baclofen infusion, we have documented complications in 102 of the patients implanted with these systems for spasticity since the first trials of intrathecal baclofen 10 years ago. During this time period, several changes in the catheter systems have been made, and in this prospective study we report on the comparative complication rates and the problems encountered.

Clinical Material and Methods

Patient Population

All patients who had received intrathecal baclofen therapy at Rush-Presbyterian-St. Luke’s Medical Center were included in the analysis. This group included patients with multiple sclerosis, spinal cord injury, and other neurological disorders. A complication of the delivery system was suspected whenever its clinical efficacy was lost or an intermittent effect was encountered. A catheter malfunction was diagnosed only if the pump proved to be working properly and changing the catheter surgically restored the clinical response. Obvious problems such as dislodgments or disconnections could be found preoperatively by x-ray film studies, but often kinks, small holes, and fibrosis were detected only during surgery. Figure 1 illustrates the typical locations of each type of complication observed in our experience. In several cases, more than one complication was found for a single malfunction, such as a kink and a hole.

Intrathecal Drug Infusion System Tested

The prototype system that was implanted in the first 12 patients was a single thin-walled, one-piece, silastic catheter extending from the pump into the subarachnoid space. Following this model, the proximal portion of the catheter was modified to thick-walled tubing running from the pump to the lumbar incision (outer diameter 2.2 mm). The pump was attached to a small, thin-walled catheter extending into the lumbar subarachnoid space (outer diameter 1.2 mm), which could be introduced by a No. 16T Tuohy needle. This “standard” catheter system (model 8703, Medtronic) with its metal connector and U-shaped anchor was used in 76 patients. To try to improve the performance of the catheter system, a single silastic catheter (outer diameter 1.2 mm) with a titanium coil running down its full length (model 8704, Medtronic) was used on an investigational basis in eight patients. Most recently, a special custom-made distal catheter with a thicker wall (outer diameter 1.4 mm; inner diameter 0.54 mm) introduced by a No. 15T Tuohy needle, was tested in 15 patients.

Statistical Analysis

Survival curves (Kaplan–Meier) were constructed to analyze the time to first complication occurring within the total patient group and to compare time to complication between the two major catheter systems.7 Log-rank tests
were conducted to compare gender, diagnosis, and all catheter types. The data were analyzed using a standard statistical package (SPSS for Windows, version 6.0, SPSS, Inc., Chicago, IL).

Results

One hundred two patients have been followed for complications of the infusion system at our center. Eighty-two patients (80%) had severe spasticity due to spinal causes, divided almost evenly between multiple sclerosis (40 patients) and cord injury (42 patients). Twenty patients had spasticity or spasms due to other central nervous system (CNS) causes. The mean age of the patients was 43.6 years (range 12–77 years), and there were slightly more females (54 patients) than males (48 patients).

The mean follow-up time for the 102 patients was 31 months (standard deviation 27.2), with a range of 2 to 114 months. No catheter problems occurred in 60 of these patients. The remaining 42 patients had one to a maximum of five catheter complications. The mean time to first complication was 19.6 months. Ten of the complications occurred within the 30-day postoperative period. The mean time from the first complication to the second was 18 months in 23 cases. Six patients had a third complication, four a fourth complication, and one a fifth. The survival curve in Fig. 2 shows a close-to-linear rate of catheter malfunction up to approximately 80 months, at which time only a few patients were available for analysis.

No statistically significant differences in failure rates were found between gender (log-rank test; p = 0.956) or diagnosis (log-rank test; p = 0.518). Striking differences in failure rates were seen, however, with the different catheter designs. The survival curve in Fig. 3 demonstrates that the standard catheter (model 8703) performed much better than the one-piece catheter with a titanium coil for support (model 8704). Statistically, this difference did not quite reach significance (p = 0.069); however, this study was terminated early due to ethical concerns regarding the high failure rate.

The types of catheter complications encountered are listed in Table 1. Kinks and holes caused nearly half of the dysfunctions. In 20% of instances, the cause was not found at surgery, but replacing the distal catheter restored the clinical response to baclofen. No kinks or holes occurred in the thicker-walled, proximal catheter. This new custom-designed thicker-walled distal catheter has been used for the last 14 months in 15 patients and no complications have occurred, although the observation time is too short for valid comparisons to be drawn.

Discussion

Previous studies of intrathecal delivery systems have found catheter malfunction occurring at rates varying from 10% to 40%. Because the length of observation or the time at risk for malfunction is critical to any analysis, survival curves provide the best way to view the performance of the catheter system. The results in Fig. 2 provide a benchmark for any future catheter designs. As Fig. 3 clearly demonstrates, the “improved” design using a single catheter with an inner titanium coil was much worse,
and this became obvious by 20 months. Future designs intended to increase longevity can similarly be compared to the reliability of the standard catheter (model 8703) by using survival analysis.

The types of complications that were documented could have been predicted from the materials used and the small connectors. In over 50% of those patients experiencing system failure, the thin silastic tubing kinked, broke, or tore, creating a hole. Repetitive stress due to movement at the point of tethering most likely accounts for much of the problem. Adding barium to silastic to make it visible on x-ray film also makes the catheter weaker. In defense of this design, it should be noted that no injury to nerve roots or spinal cord occurred; the soft, pliable catheter was very safe and well tolerated by the patients. No kinks, breaks, or holes were found in the proximal larger, thick-walled catheter, but it was not intended for subarachnoid placements because of its larger size. A special distal catheter with a larger outer diameter and smaller inner diameter has been used for the last 14 months without a single failure in 15 patients. More time and patients are needed to determine if it is better, but the results so far are encouraging.

Disconnections, dislodgments, and fibrosis are less common complications but need to be addressed. One problem is the high torque on the catheter system due to body movement. Silastic provides some elasticity, but the sudden repetitive force on the connection points can lead to a disconnection. A single catheter with a much more solid connection to the pump might be more durable. Dislodgment from the subarachnoid space can occur because of repetitive pulling movements on the catheter as the patient moves. Better anchoring at the entrance to the subarachnoid space might be helpful in avoiding this problem. Fibrosis around the catheter tip in the subarachnoid space is relatively rare. It is a natural response to silastic and if severe enough, envelopes the entire catheter and blocks flow. Coating the catheter tip with material that is less reactive might minimize the problem.

Intrathecal baclofen provides the best measure of performance of the drug delivery system. When baclofen delivery stops, the patients experience clear signs and symptoms of their spasticity. Restoration of delivery always restores the clinical effect. The most difficult problem to diagnose is slow loss of efficacy due to fibrosis or a small hole in the catheter. The clinician may think that baclofen tolerance has occurred and may not recognize the cause as a catheter malfunction. Furthermore, a hole can be missed on a flow study that uses a bolus injection because the high pressure and flow rate in a bolus will drive the fluid past the hole, so it is not detected. A direct intrathecal dose of baclofen given by lumbar puncture will demonstrate responsiveness; alternatively, an assay of baclofen from the lumbar intrathecal space can be performed. The approximate cerebrospinal fluid baclofen concentration value should be 0.13 μg/ml for every 100 μg/day of infusion. If a different drug were infused that had a less obvious clinical response, recognizing a delivery problem would be much more difficult. Patients with chronic pain are an example. Lack of delivery could easily be missed because increased pain could be interpreted as the result of tolerance, changes in the pain state, or psychological factors.

Patients benefit so much from intrathecal baclofen that they are willing to have repairs made in the delivery system, even if it requires an operation. In a 10-year period, less than 8% of our patients withdrew from long-term treatment for any reason. The 60% success rate for 31 months for the thin, silastic catheters may be viewed as a reasonable success rate or as a too-high failure rate. In any case, improvements in the catheter system should be encouraged. Unfortunately, regulations on devices by the Food and Drug Administration inhibit the evolution of these systems, so that each change usually requires long, expensive trials. Now that a benchmark life expectancy is known, new systems can be measured against this standard and improvements can be made more rapidly. The same type of survival analysis used in this study should be done for any implanted systems, and comparison studies should also be performed on shunts for hydrocephalus.

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References


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Address reprint requests to: Richard D. Penn, M.D., Neurosciences Institute, Department of Neurosurgery, Rush-Presbyterian-St. Luke’s Medical Center, 1725 West Harrison, Suite 755, Chicago, Illinois 60612.

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Catheter systems for intrathecal drug delivery

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<th>Table 1: Complications in catheter systems in 42 patients</th>
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<td>Type of Complication</td>
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* Study focused on a total of 102 patients; 60 patients had no complication at mean follow-up period of 51 months.