Implanted continuous epidural morphine infusion system

Preliminary report

ROBERT E. HARBAUGH, M.D., DENNIS W. COOMBS, M.D., RICHARD L. SAUNDERS, M.D., MICHAEL GAYLOR, M.D., AND MARK PAGEAU, R.N.

Sections of Neurosurgery, Anesthesiology, and Behavioral Medicine, Dartmouth-Hitchcock Medical Center, Hanover, New Hampshire

A number of reports have shown that epidural or intrathecal administration of morphine provides pain relief. Since February, 1981, the authors have used an implantable pump and epidural catheter for continuous epidural morphine infusion in patients with chronic pain. This system has functioned well, without respiratory or infectious complications. Functional characteristics of the system, technique of implantation, and preliminary results in two patients treated by this method are presented.

KEY WORDS • analgesia • epidural infusion • morphine • pain • spinal cord

STANDARD treatment of chronic pain remains inadequate in many patients. Laboratory demonstration of spinal cord opiate receptors and inhibition of nociceptive neurons by morphine has led to the investigation of intraspinal morphine administration for intractable pain. Both intrathecal and epidural narcotics have been shown to produce prolonged pain relief in various settings, including cases of chronic cancer pain.

Despite such encouraging reports, the hazards of respiratory depression following intraspinal morphine injections and the risk of infection with percutaneous catheters have delayed implementation of this therapy. In addition, injections at frequent intervals, or percutaneous indwelling catheters interfere with the mobility and independence of the patient. Consequently, a completely implantable delivery system has been developed to provide a continuous epidural infusion of morphine. This system circumvents some of the problems encountered with intraspinal morphine analgesia. The functional characteristics and reliability of this system, operative technique, and preliminary results in two cases are presented.

Materials and Methods

Drug Delivery System

The drug delivery system consists of the Infusaid implantable pump with a constant flow rate connected to a Silastic epidural catheter. Before use in patients was considered, the system was tested for up to 9 months of continuous function in the Dorset ram. No respiratory depression occurred with doses of up to 12 mg/day in these trials, and factory-designated flow rates were found to be reliable (unpublished data).

The Infusaid Model 100 pump is shown in Fig. 1. Its empty weight is 187 gm and it has a reservoir capacity of 47 ml. A cross section of the pump (Fig. 2) demonstrates its functional characteristics. Inside the discoid titanium shell, a drug reservoir is formed by a metal bellows. Vapor pressure, generated by a two-phase fluorocarbon in the charging fluid chamber, compresses the bellows, forcing the morphine solution in the drug chamber through an outlet flow...
restrictor and into the epidural catheter. After implantation, the drug chamber can be refilled percutaneously via the inlet septum. At a given temperature and barometric pressure, each pump has a preset constant flow rate of 2 to 3 ml/day. The dose administered is varied by changing the concentration of the infusate.

Use of this system in patients was approved by the committee for the protection of human subjects at this institution. Informed consent was obtained prior to intraspinal narcotic therapy. The patients' pain was not responsive to conventional therapy, and they chose this treatment in preference to neurostimulation or ablative therapy. Before a system is implanted, each patient must show a therapeutic response to epidural narcotic injection. A 50% reduction from baseline in visual pain analogue scale scores (VPASS), which is maintained for more than 8 hours following a single injection of morphine sulfate (0.06 to 0.08 mg/kg), has been chosen as a minimum therapeutic response. Patients manifesting significant depression (Zung self-rating depression score of more than 0.6524) are excluded.

Postoperatively, the patients are evaluated for 3 to 5 days in the hospital. Before discharge, the patient, family members, visiting nurse, and local physician are given information regarding the system and its possible side effects. The pump is refilled either at an outpatient visit to our institution or by the visiting nurse every 14 days. Patients are instructed to monitor their analgesic response and their intake of oral analgesics.

Operative Technique

Under regional epidural anesthesia, the patient is positioned lying on his side. The operative field is prepared with iodophor soap and solution, and sterile drapes are placed. Catheter position is chosen by dermatomal levels involved in the patient's pain syndrome. A 5-cm vertical midline incision is made over the spinous processes several segments below the level of permanent catheter placement. A modified No. 9 Tuohy needle is placed in the epidural space. The Silastic catheter (1.65 mm in outer diameter) over a cardiovascular guide wire is then passed under fluoroscopic control to the appropriate level in the epidural space. An epidurogram is performed by injection of 3 to 5 ml of water-soluble myelographic contrast material through the catheter for confirmation of placement. Following placement, the epidural catheter is secured to the paraspinal fascia with a nonabsorbable suture ligature.

A subcutaneous pocket is made on the anterior abdominal wall. The filled Infusaid pump is warmed to 37°C and placed into this pocket. The Silastic catheter is tunneled subcutaneously and connected to the pump outlet catheter with a straight metal connector. Connections are secured by nonabsorbable ligatures. The incisions are closed and a sterile dressing is applied.

The following two case reports illustrate the operative technique and preliminary results.

Case Reports

Case 1

This 60-year-old man underwent abdominal perineal resection for adenocarcinoma of the rectum in November, 1973. He did well until February, 1980, when pain developed in his back, buttock, and left leg. In July, 1980, a mass in the left buttock was biopsied and diagnosed as adenocarcinoma. The patient received radiotherapy but continued to have constant pain despite an intake of 400 to 500 mg of codeine a day. He was evaluated for continuous epidural morphine infusion and showed a good response (18 to 20 hours of pain relief with a 4.5-mg injection).

On February 6, 1981, the patient underwent operation for implantation of the continuous epidural morphine infusion system. The catheter was positioned at T12–L1, and the initial dose of morphine delivered to the epidural space was 1 mg/day. The patient obtained marked pain relief following implantation, and discontinued all oral narcotics. Clonidine, 2 mg twice a day, was begun to minimize withdrawal.
Epidural morphine infusion system

symptoms. He was discharged home on February 9, 1981. During the following 5 months, epidural morphine dosage was increased to 30 mg/day to achieve continued analgesia. Rapidly progressing adenocarcinoma, with widespread metastatic disease, did not respond to chemotherapy and the patient died on July 31, 1981. Postmortem examination revealed adenocarcinoma involving the lungs, nodes, liver, small bowel, lumbar spine, and pelvis. Cultures of the epidural catheter, pump, and cerebrospinal fluid (CSF) were negative, and there was no evidence of epidural inflammation at the catheter site.

Case 2

This 83-year-old woman was doing well following a left hemicolectomy for carcinoma of the colon until February, 1981. At that time, she began having constant aching pain in her back, left buttock, and leg. She refused diagnostic testing and was treated with oral narcotics. Oral medication did not result in significant analgesia but did cause lethargy and confusion. Because of continued pain and her intolerance to oral narcotics, the patient was evaluated for epidural morphine infusion. On May 1, 1981, a percutaneous epidural catheter was placed at T-10, with an exit site in the right flank. She responded dramatically to epidural morphine, with 24 to 48 hours of analgesia following a 2-mg injection. Her lethargy and confusion resolved. She continued to have marked pain relief with 2-mg morphine injections every 1 to 2 days, and the decision was made to implant the system for continuous infusion.

On May 28, 1981, the patient underwent implantation without incident. She was pain-free postoperatively, and demanded to be discharged on May 30. She was receiving 2 mg of epidural morphine per day via the implanted system. Mild buttock discomfort was noted the day before the pump was refilled and her dosage was increased to 4 mg of morphine per day. She has continued to be pain-free on this dose, about twice a month. This is done as an outpatient procedure and can be performed at the patient’s home by a specially instructed visiting nurse. Lower flow rates could prolong the intervals between refilling. It has also been suggested that a continuous infusion of narcotics is less likely to cause respiratory depression than bolus injections, and epidural infusion may be safer than intrathecal administration, although this remains unproved. The identification of opiates that produce analgesia but not respiratory depression may substantially decrease the risk of intraspinal narcotic analgesia. In addition, a totally implantable system for intraspinal narcotic administration decreases the risk of infection.

The cases presented here illustrate a number of these points. Neither patient experienced respiratory depression, sedation, pruritus, nausea, or urinary retention, despite infusion rates of up to 30 mg of morphine per day. Our preliminary investigations in sheep demonstrated a low, stable, cisternal narcotic level with continuous lumbar narcotic infusion. A state of equilibrium between CSF and plasma narcotic levels developed with continuous epidural infusion (unpublished data). This equilibrium state makes a sudden rise in the CSF narcotic concentration unlikely. An additional six patients are now being treated with the same system and no untoward side effects have been noted.

Both patients described here were able to lead independent lives at home without frequent narcotic injections or the special care required for externalized catheters. Neither patient had an infectious complication, despite the presence of a colostomy in both.

We wish to stress the efficacy of this procedure for analgesia remains unproven. Although dramatic pain relief without other analgesics was reported, long-term quantitative evaluation of these patients and others presently undergoing treatment will be needed to substantiate our preliminary findings. A number of other studies have suggested the efficacy of intraspinal narcotic analgesia; however, many questions remain unanswered. The problem of tolerance may limit the therapeutic response. In Case 1, narcotic dosage had to be increased from 1 mg/day to 30 mg/day to maintain adequate analgesia over a period of 6 months. Conversely, the second patient has maintained adequate analgesia with 4 mg/day for a period of 5 months and demonstrates no increase in tolerance to the drug. Why the response is so different in these patients is speculative. It may be significant that the first patient had been taking large doses of oral narcotics preoperatively, while the second patient could not tolerate oral narcotics.

Other indwelling systems for intraspinal narcotic analgesia with encouraging results have been described recently. Although it is too early to determine the efficacy of these methods, the feasibility is established. Continued investigation of intraspinal narcotic analgesia should determine if such therapy will gain a place in the treatment of chronic pain.

References


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ADDRESS REPRINT REQUESTS TO: ROBERT E. HARBAUGH, M.D., SECTION OF NEUROSURGERY, DARTMOUTH-HITCHCOCK MEDICAL CENTER, HANOVER, NEW HAMPSHIRE 03755.