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Subdural Injection of Morphine for Analgesia Following Cesarean Section: A Report of Three Cases

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The subdural area is a potential space between the dura and the arachnoid membranes. It exists in the spinal meninges just as it does in the cranial meninges. In the past 17 yr a number of clinical reports have described the unintentional catheterization of this potential space[1–3] and the delayed subdural migration of an epidural catheter.[4,5]

Recently Miller *et al.* reported a case of confirmed subdural administration of morphine.[6] In that case, a young woman having a cesarean section under presumed epidural anesthesia was given 1.0 mg preservative-free morphine *via* the lumbar catheter. The patient had good postoperative analgesia, which lasted for 22 h with no side effects. The authors speculated that subdural injection of morphine may result in higher cerebrospinal fluid levels of drug than does epidural injection. In another recently published case, Brown *et al.* reported an intended epidural placement for long-term management of a patient with cancer pain, but a postoperative epidurogram showed the catheter to be subdural.[7] It was left in place and used for pain management. Although the patient had required as much as 1,000 mg oral morphine daily, a dose of morphine usually administered intrathecally was chosen because of the potential for the catheter to migrate into the subarachnoid space. The patient achieved good pain control with an initial dose of 0.75 mg morphine. In both of these cases, the authors noted a markedly reduced dose requirement compared to that usually required by the epidural route, suggesting the potential for respiratory depression in the event of unintentional subdural morphine administration with usual epidural doses.

We report three cases of radiographically confirmed subdural catheters that were used for cesarean section anesthesia. All three patients were given subdural morphine for post–cesarean section analgesia. The dose of morphine chosen, more typical of an epidural dose than of a subarachnoid dose, was considerably greater than those reported previously.

CASE REPORTS

Case 1. A 30-yr-old woman (gravida 1, para 0), 151 kg in weight and 157 cm in height, was admitted to labor and delivery for evaluation. Ultrasound examination revealed an intrauterine pregnancy at an estimated gestational age of 38 weeks with breech presentation. Version was not attempted because fetal parts could not be palpated. Past medical history and laboratory evaluations were unremarkable. Physical examination was remarkable only for obesity. The patient gave consent for an elective primary Cesarean section under epidural anesthesia.

The patient received 1,000 ml lactated Ringer's solution. With the patient in the sitting position, an 18-G Tuohy needle was advanced in

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the midline through the L3–L4 interspace using a loss-of-resistance technique with normal saline. An end-hole polyamide epidural catheter was threaded 3 cm beyond the tip of the needle and taped in place. No blood or cerebrospinal fluid could be aspirated from the catheter. A test dose consisting of 3 ml 2% lidocaine with 15 μg epinephrine was given. Because of a slight increase in heart rate, the test dose was repeated, but no evidence of intravascular or subarachnoid injection was noted.

Two doses of 5 ml lidocaine 2% with epinephrine 1:200,000 were then injected through the catheter. Approximately 5–10 min after the injection, evidence of developing bilateral block in the midthoracic area was noted. Fifteen minutes after injection the patient demonstrated a sensory block in the upper extremities that reached the C2 level before surgery was begun. Baseline blood pressure was 140/70 mmHg and the pulse 90 beats/min, but these decreased to lows of 85/50 mmHg and 85 beats/min, respectively, approximately 10–15 min after injection of the local anesthetic. Hypotension was treated with intravenous ephedrine and fluids. The patient was unable to move her arms or fingers but was comfortable and remained calm.

A 3,060-g infant with Apgar scores of 8 at 1 min and 9 at 5 min was delivered approximately 45 min after injection of local anesthetic. Ten minutes after the delivery, 2 mg preservative-free morphine was injected through the catheter. Because of prolonged surgical time an additional 7 ml lidocaine 2% with epinephrine was injected in divided doses approximately 60 min after the initial injection. Over the course of the procedure the patient was given a total of 65 mg ephedrine and 4,900 ml lactated Ringer's solution (including initial fluid prehydration).

The patient was admitted to the postanesthesia care unit (PACU) with a bilateral T4 sensory level 105 min after the initial injection. The block regressed normally, and after being discharged from the PACU, the patient consented to a radiologic study to determine catheter location. In the radiology suite, 4 ml iopamidol (Isovue-300) was injected through the catheter and showed the catheter entering at the L3–L4 interspace and the contrast media located in the subdural space. The patient had good postoperative pain relief, with no apparent side effects. The lowest respiratory rate was 16 breaths/min, with no unusual sedation noted. Supplemental postoperative analgesic was required 36 h after the administration of preservative-free morphine and consisted of oral oxycodone.

Case 2. A 19-yr-old woman (gravida 4, para 2) at 41 weeks gestational age and 100 kg in weight and 160 cm in height was admitted to labor and delivery because of a nonreactive nonstress test and severe oligohydramnios. Past medical history was remarkable for preeclampsia with her first pregnancy, two prior cesarean sections, and cocaine abuse. Physical examination was unremarkable except for moderate obesity and a cervix that was unfavorable for induction of labor. Laboratory results were unremarkable. After attempted induction failed, consent was obtained for cesarean delivery under epidural anesthesia.

The patient received 1,000 ml lactated Ringer's solution administered through two 16-G intravenous catheters. With the patient in the left lateral decubitus position an 18-G Tuohy needle was advanced through the L2–L3 interspace using a loss-of-resistance technique with normal saline. An end-hole polyamide epidural catheter was threaded 4 cm beyond the tip of the needle and taped in place. No blood or cerebrospinal fluid could be aspirated from the catheter. A test dose consisting of 3 ml 2% lidocaine with 15 μg epinephrine produced no evidence of intravascular or subarachnoid injection. Ten milliliters lidocaine 2% without epinephrine and 50 μg fentanyl were then injected through the catheter in divided doses. Approximately 5–10 min after the injection, onset of bilateral block in the midthoracic area was evident. Fifteen minutes after injection, the patient demonstrated a sensory block at T2 on the right and at T4 on the left.

The patient was comfortable during the procedure and remained hemodynamically stable, with no need for vasopressors or unusual amounts of fluid. A 3,411-g infant with Apgar scores of 8 at 1 min and 9 at 5 min was delivered 32 min after injection of local anesthetic. Immediately after the delivery, 3 mg preservative-free morphine was given through the catheter.

The patient was admitted to PACU 85 min after local anesthetic injection with the block level still at T2 on the right and T4 on the left. Ninety-five minutes later, the block had regressed, and the patient complained of pain, which she reported as 7 on a verbal scale of 0–10 in severity. This was treated with fentanyl 50 μg through the catheter and morphine 2 mg intravenously. After her recovery room stay the patient agreed to a radiologic determination of catheter location. In the radiology suite, 4 ml iopamidol (Isovue-M 200) was injected through the catheter. Radiographically, the catheter was shown to enter at the

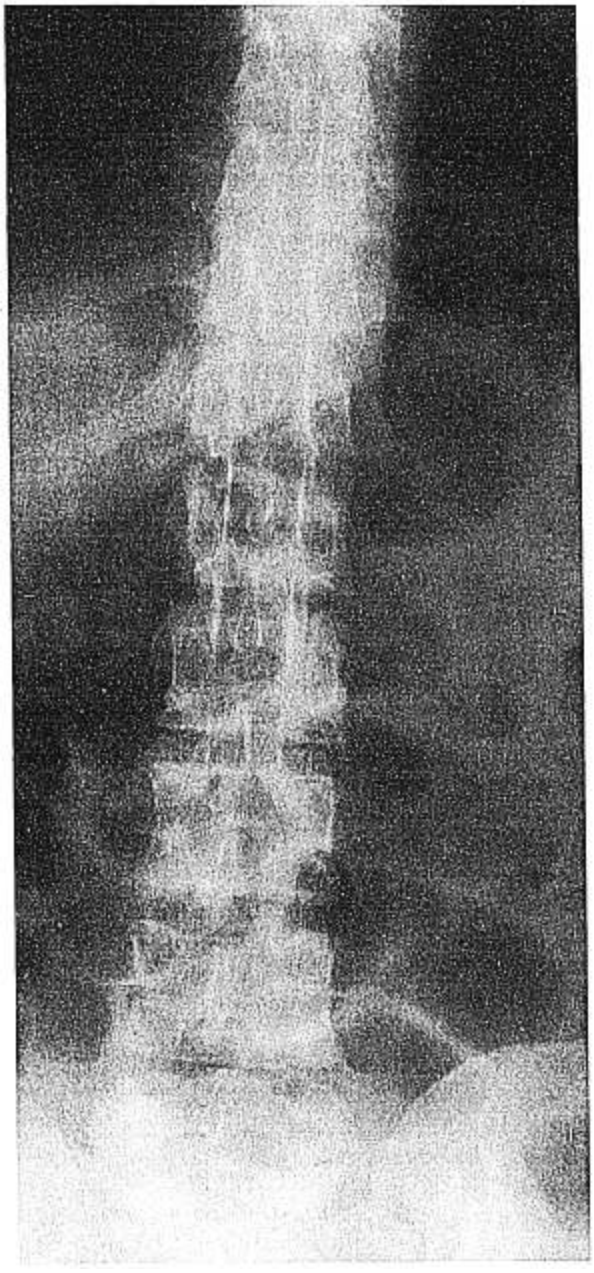

FIG. 1. Anteroposterior view of spinal column showing typical "railroad track" appearance of contrast material extending from T9 to L3 following the injection of 4 ml solution. The catheter is visible at the L1–L2 interspace.

L1–L2 interspace, and the contrast media was located in the subdural space (figs. 1 and 2). The postoperative course was unremarkable except that the patient was treated for pruritus with diphenhydramine and naloxone with moderate success. The lowest respiratory rate was 16 breaths/min, with no excessive sedation noted. Supplemental postoperative analgesic was required 25 h after the administration of preservative-free morphine and consisted of oral oxycodone.

Case 3. A 32-yr-old woman (gravida 6, para 3) at 39 weeks gestational age and 106 kg in weight and 167 cm in height was admitted to labor and delivery for elective cesarean section and bilateral tubal ligation. Past medical history was remarkable for a prior cesarean section due to fetal distress and for cocaine abuse, although the patient was currently in a rehabilitation program. Physical examination was unremarkable except for obesity. Laboratory results were normal. She consented to have the procedure done under epidural anesthesia.

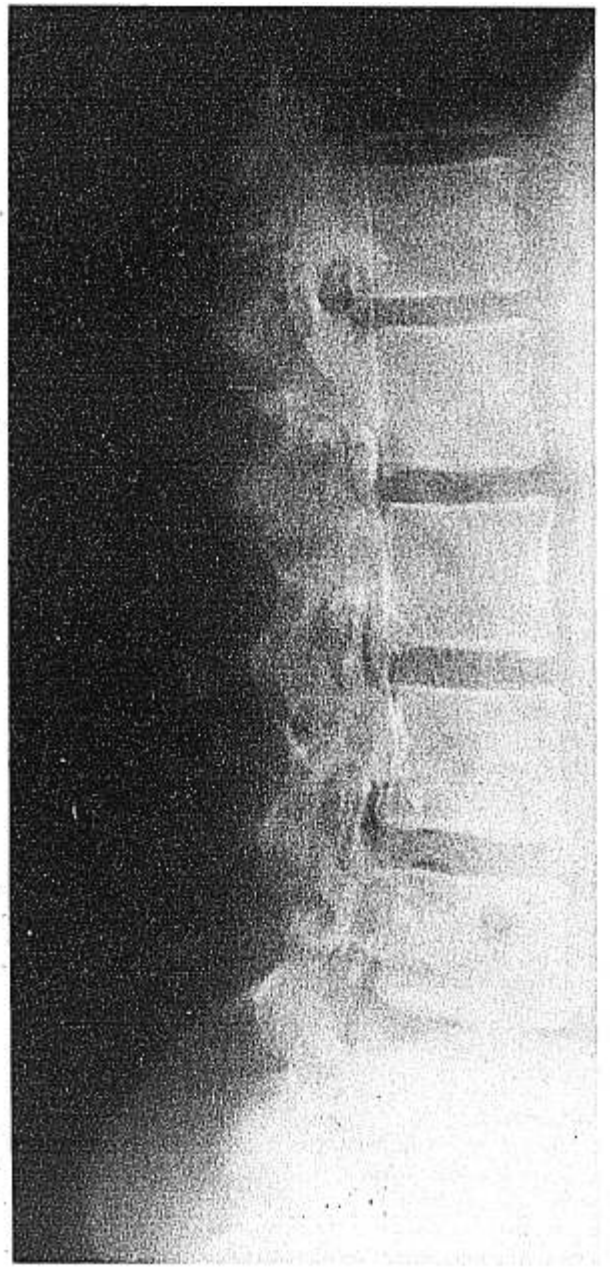

FIG. 2. Lateral view of spinal column with contrast visible in the subdural space.

Before epidural placement, the patient received 1,000 ml lactated Ringer's solution administered through a 16-G intravenous catheter. With the patient in the sitting position, an 18-G Tuohy needle was advanced through the L2–L3 interspace using a loss-of-resistance technique with normal saline. An end-hole polyamide epidural catheter was placed 3.5 cm into the epidural space and taped in place. No blood or cerebrospinal fluid could be aspirated from the needle or catheter. A test dose consisting of 3 ml 2% lidocaine with 15 μg epinephrine produced no evidence of intravascular or subarachnoid injection. Ten milliliters lidocaine 2% with epinephrine 5 μg/ml was injected in two 5-ml increments. Approximately 5–10 min after the injection, evidence of developing bilateral block in the midthoracic area was noted. Baseline blood pressure was 118/70 mmHg and the pulse 90 beats/min, but these decreased to lows of 78/35 mmHg and 55 beats/min, respectively, approximately 10 min after injection of the local anesthetic. Hypotension and bradycardia were treated with intravenous ephedrine (35 mg total), atropine 0.4 mg, and fluids.

Fifteen minutes after injection, the patient demonstrated a sensory block extending to the T3 dermatome bilaterally. Before surgery was begun, 50 μg fentanyl and an additional 6 ml of the anesthetic solution was injected in two 3-ml doses. A 2,943-g infant with Apgar scores of 9 at 1 min and 9 at 5 min was delivered 20 min after skin incision. Because of prolonged surgical time (88 min), an additional 12 ml lidocaine 2% with epinephrine was injected in 3-ml increments during the procedure. At the end of the surgical procedure, 3 mg (3 ml) preservative-free morphine was injected through the catheter. During the course of the operation, the patient was given a total of 55 mg ephedrine and 3,000 ml lactated Ringer's solution (including the initial fluid prehydration).

The patient was admitted to the PACU 145 min after the initial epidural injection with a bilateral T3 sensory level. The block regressed normally, and the patient consented to a radiographic study to confirm the catheter location. In the radiology suite, 7 ml iopamidol (Isovue-M 300) was injected through the catheter. Radiographic determination indicated that the contrast media was located in the subdural space with focal extravasation noted around the nerve roots at T12–L1. The patient had good postoperative pain relief. The only side effect that the patient experienced was nausea while in the PACU; this was treated with metoclopramide. The lowest respiratory rate was 16 breaths/min, with no unusual sedation noted. Supplemental postoperative analgesic was required 25 h after the administration of preservative-free morphine and consisted of oral oxycodone.

DISCUSSION

Although Dawkins accurately described the characteristics of subdural block and referred to it as "massive extradural," he probably did not appreciate the anatomic basis of the complication.[8] Sechzer[9] and later Cohen and Kallos[10] postulated that some failed spinal blocks may be due to the unintentional injection of local anesthetic solution into the subdural space. The first case of unintentional subdural catheterization as a complication of epidural anesthesia was reported in 1975.[1] The authors confirmed the position of the catheter radiographically and suggested that the phenomenon of "massive extradural" anesthesia may be explained on this basis.

The incidence of inadvertent injection of contrast into the subdural space during myelography has been estimated to be as high as 10%.[11] Subdural injection as a complication of epidural anesthesia had been estimated

to occur with a frequency of 0.82%.[12] The time to onset of block is more similar to that seen with epidural anesthesia than with spinal anesthesia, and for this reason a typical test dose to rule out subarachnoid block is unlikely to identify a subdural injection.[3,4] The extent of block produced from a given volume of local anesthetic is, however, usually much greater with subdural injection. It is not uncommon to see spread of block to the cervical level with 6–10 ml local anesthetic solution.[2,3] Because the spinal subdural space does not end at the foramen magnum, as does the epidural space, it is possible for local anesthetic to spread into the head and produce anesthesia involving the cranial nerves.[2] When a small volume of water-soluble contrast media is injected into the lumbar subdural space, it rapidly spreads over a relatively large number of segments, often in a cephalad direction (fig. 1).[1,2] Subdural blocks can be patchy or asymmetric[2] and the degree of motor block produced may be variable.[1,3]

Although it has been stated that testing for subdural catheter placement is impractical,[4] a subdural test dose can be given with a minimum of additional time requirement. It is our practice to initiate epidural blocks for cesarean section with an epinephrine-containing test dose (*e.g.*, 3 ml 2% lidocaine with 15 μg epinephrine) to rule out intravascular or subarachnoid injection. After approximately 3–5 min, 10 ml of anesthetic solution (*e.g.*, lidocaine 2%) is injected in divided doses. We then wait approximately 10 min to establish evidence of bilateral block before continuing to inject additional local anesthetic. Typically, after 10 min it is possible to demonstrate onset of block in the upper lumbar dermatomes. We follow this procedure to allow the catheter to be repositioned (*e.g.*, pulling it back 1 cm) or replaced without having to abandon the epidural technique because of local anesthetic drug requirements that exceed maximum dose recommendations. In these three cases, this practice allowed us to identify developing subdural anesthesia. In all three cases, the onset of block, when first detected, was found to be much higher than expected (mid- to upper thoracic levels), thereby alerting us to an atypical block.

In two previously reported cases of subdural opioid administration, the authors reported good pain control with 1.0 mg morphine[6] and with 0.75 mg morphine.[7] From these reports readers might conclude that 1.0 mg or less of morphine is the appropriate dose for subdural analgesia and that larger doses may be excessive.

Recently, Bernards and Hill, using an *in vitro* permeability model, demonstrated that the arachnoid mater is the principal permeability barrier for drugs diffusing between the epidural space and the spinal cord.[13] They observed that the arachnoid mater accounted for 85% of the resistance to diffusion across the spinal meninges whereas the dura accounted for only 4–5% of the resistance. The probable explanation for this finding is that the arachnoid mater is composed of overlapping tiers of flattened cells connected to one another by frequent tight junctions and occluding junctions, whereas the dura mater is composed of loose bundles of collagen and elastin.[14,15] The arachnoid, therefore, represents a specialized cellular permeability barrier, and the dura mater functions more like a molecular sieve.[16] The clinical implications of these data are that drugs, such as opioids, which have their site of action in the spinal cord, should reach the cord at the same rate and in the same concentration whether they are placed in the epidural or the subdural space.

These *in vitro* data suggest that the subdural dose of an opioid should be similar to the epidural dose requirement; however, it seems prudent to reduce the normal (epidural) dose for subdural administration. A given volume of fluid injected into the subdural space spreads to higher segments than does the same volume injected into the epidural space. For this reason, a given dose of opioid in a large volume of solution or injected in association with a relatively large volume of local anesthetic may spread to the cervical or cranial level and result in higher concentrations of opioid in the brainstem than would be the case with epidural injection.

Although at the time we did not know with certainty that these catheters were subdural, it was clinically suspected. We chose a larger-than-usual subarachnoid dose of morphine because we were confident that the catheters were not subarachnoid and because it was unlikely that the catheters would migrate into the subarachnoid space in the short interval between local anesthetic and opioid administration. However, because the local anesthetic requirement was less than the usual epidural requirement, we chose a morphine dose that was somewhat less than our usual post–cesarean section epidural dose (4–5 mg). It is our practice to remove epidural catheters before a patient is discharged from the obstetric recovery room, and consequently these catheters were not used for repeated opioid injections. All patients were monitored according to our standard spinal morphine protocol, which includes recording respiratory rates and sedation scores at 1-h intervals for 24 h after morphine administration. Our first patient had excellent postoperative analgesia with no side effects. The second patient required early supplementation with 50 μg epidural fentanyl and 2 mg intravenous morphine, but thereafter she had 25 h of excellent postoperative analgesia. The side effects that we observed in the second and third patients were similar to those seen with typical doses of epidural or subarachnoid morphine.

In conclusion, we describe three cases in which subdural catheters were used for providing anesthesia for cesarean section and for postoperative opioid analgesia. Although *in vitro* studies have shown the arachnoid to be the major diffusion barrier for morphine movement through the meninges, optimum subdural dose requirements may be different from epidural doses. The lack of adverse effects

in our three patients, in whom we used 2–3 mg morphine, does not confirm that this represents the appropriate subdural dose. We recommend that the anesthesiologist exercise caution when faced with uncertainty regarding the location of the catheter.

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Dapsone-induced Methemoglobinemia and Pulse Oximetry

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Dapsone, a sulfonamide derivative, has been used in the treatment of malaria, leprosy, and dermatitis herpetiformis, and most recently in the prophylactic treatment of *Pneumocystis carinii* pneumonia in patients infected with the human immunodeficiency virus (HIV).[1–3] Side effects associated with the use of dapsone include the development of methemoglobinemia.[1,2] This report relates an incident of methemoglobinemia secondary to dapsone presenting as an intraoperative decrease in the pulse oximeter hemoglobin oxygen saturation (Sp_{O_2}). In this patient, the methemoglobinemia was treated with methylene blue administered intravenously, with a subsequent increase in the Sp_{O_2} and decrease in the methemoglobin (MetHb) level.

Case Report

A 60-yr-old woman with a history of transient ischemic attacks and carotid stenosis presented for a right carotid endarterectomy. Her past medical history included a left carotid endarterectomy in 1985, coronary artery disease with an old myocardial infarction, dermatitis herpetiformis, and cigarette smoking. She denied a history of shortness of breath or chest pain and described tolerance of moderate levels of exercise. Preoperative medications included oral metoprolol 25 mg three times per day and furosemide 40 mg, dapsone 100 mg, and aspirin 325 mg every day. Laboratory studies included a hemoglobin concentration of 11 g/dl; electrocardiogram revealed an old anterolateral myocardial infarction; chest x-ray demonstrated no active disease; and echocardiogram showed normal left ventricular function with mild ventricular dilatation.

The morning of surgery, the patient received oral diazepam 5 mg, metoclopramide 10 mg, and ranitidine 150 mg. Upon arrival in the operating room, the patient was calm and responsive to verbal commands. After placement of routine monitors, including a pulse oximeter probe (Nellcor DS-100A) placed on the right index finger, and with the patient breathing room air, the pulse oximeter (Nellcor N-100) displayed an Sp_{O_2} of 90%. The patient denied the presence of dyspnea. Oxygen 4 l/min by nasal cannulae increased the Sp_{O_2} to 93%. A catheter was inserted into a radial artery, and a blood gas determination revealed a Pa_{O_2} of 184 mmHg. After denitrogenation with 100% ox-

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