

Dural Puncture with a 27-Gauge Whitacre Needle as Part of a Combined Spinal-Epidural Technique Does Not Improve Labor Epidural Catheter Function

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Background: This prospective, double-blind, randomized study was designed to examine whether the combined spinal-epidural technique without subarachnoid drug administration improved epidural catheter function when compared with the traditional epidural technique.

Methods: After institutional review board approval and informed consent, 251 healthy laboring parturients were randomly assigned to either group DP (combined spinal-epidural technique with 27-gauge Whitacre needle dural puncture but without subarachnoid drug administration) or group NoDP (traditional epidural technique). Patient-controlled epidural analgesia was initiated with 0.11% bupivacaine and 2 µg/ml fentanyl. Top-up doses in 5-ml increments of 0.25% bupivacaine were administered if needed. Previous power analysis revealed that a sample size of 108 patients/group was needed to show a clinically useful reduction of the catheter manipulation rate from 32% to 15%.

Results: In groups DP and NoDP, 107 and 123 evaluable patients, respectively, completed the study. Demographics and outcome variables measured, including epidural catheter manipulation and replacement rate, sacral sparing, unilateral block, number of top-up doses, average hourly epidural drug usage, highest sensory blockade level, and labor analgesia quality, were not different between groups. A subgroup of 18 patients without cerebral spinal fluid return during dural puncture had a higher catheter replacement rate than those of groups DP and NoDP, but it did not reach statistical significance.

Conclusions: Dural puncture with a 27-gauge Whitacre needle without subarachnoid drug administration during combined spinal-epidural labor analgesia did not improve epidural labor analgesia quality or reduce catheter manipulation or replacement rate when compared with a traditional epidural technique.

THE combined spinal-epidural (CSE) technique, which provides rapid onset of profound labor analgesia with high patient satisfaction and minimal or no motor blockade, has become popular for labor pain relief.¹⁻⁵ Some

have suggested that the CSE technique may provide better epidural catheter placement and subsequently better quality of labor analgesia when compared with the traditional epidural technique.¹⁻⁵ Several aspects of the CSE technique could contribute to improved functioning of the subsequent epidural catheter. These include verification of the subarachnoid space with the spinal needle before placement of the epidural catheter, the presence of a dural hole, or an effect of the subarachnoid medication administered. The effects of the subarachnoid drugs administered typically resolve in 1-2 h, after which the function of the epidural catheter and the effects of the epidurally administered drugs determine the quality of epidural analgesia. With the CSE technique, there is a clear and definitive endpoint of cerebral spinal fluid (CSF) return *via* the spinal needle, and this may lead to a more accurate midline placement of the epidural catheter.¹⁻⁴ In addition, the dural hole created during the CSE technique may increase subarachnoid transfer of epidurally administered drugs, thus improving the epidural analgesia.⁶⁻¹² However, the clinical significance of these proposed effects during CSE labor analgesia has not been demonstrated. We are not aware of any published, prospective, randomized clinical studies that support or refute these theories, but some have questioned the safety and reliability of and the need to use the CSE technique for labor analgesia.¹³⁻¹⁸

During labor analgesia, several authors have reported epidural catheter manipulation rates of up to 44% and failure rates of 12-13%.¹⁹⁻²⁴ Failure rates of 7.110.5% have been reported when catheters placed for labor analgesia were used to provide anesthesia for cesarean delivery.¹⁹⁻²⁴ With subarachnoid drug administration *via* the CSE technique, the subarachnoid analgesia must partially or fully resolve before the function of the epidural catheter and the quality of the epidural blockade can be fully assessed. This may delay the detection of a malfunctioning or malpositioned epidural catheter. Currently, it is not known whether epidural catheters placed *via* the CSE technique function better than catheters placed with a traditional epidural method. The goal of this double-blind, prospective, randomized study was to examine whether a dural puncture by a 27-gauge Whitacre spinal needle in a needle-through-needle CSE technique (without subarachnoid drug administration) improved epidural catheter function when compared with a traditional epidural catheter placement without dural puncture.

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Methods and Materials

After institutional review board approval (Wake Forest University, School of Medicine; Forsyth Medical Center, Winston-Salem, North Carolina) and informed consent, 251 healthy laboring parturients with uncomplicated pregnancies and with cervical dilation less than 6 cm were enrolled. Upon request for neuraxial labor analgesia, the subjects were randomly assigned according to a computerized random number generator to one of two groups: group DP (dural puncture with CSE technique) and group NoDP (no dural puncture with traditional epidural technique). In both groups, the neuraxial block was performed at L3-L4 or L4-L5 levels, with patients in the sitting position, using a 17-gauge, 8.9-cm Weiss epidural needle (Baxter Healthcare Corporation, Deerfield, IL) and loss of resistance to air technique for identification of the epidural space. Group DP received a dural puncture with a 27-gauge, 11.9-cm Whitacre spinal needle (Baxter Healthcare Corporation) inserted through the epidural needle as part of the needle-through-needle CSE technique, but no subarachnoid drug was administered. The spinal needle protruded 12.5 mm beyond the epidural needle tip when fully inserted. Dural puncture made by the spinal needle was confirmed with free flow of CSF returning spontaneously and by aspiration *via* the spinal needle. After confirmation of dural puncture, the spinal needle was removed, and a 19-gauge, closed-tip, multiport epidural catheter (Baxter Healthcare Corporation) was inserted 4–6 cm into the epidural space. In group NoDP, the epidural catheter was inserted the same as in group DP, except without insertion of the spinal needle or dural puncture.

After a negative aspiration of blood and CSF, the catheters were tested with a 2-ml, 2% plain lidocaine subarachnoid test dose. If the aspiration and the subarachnoid test dose were negative, 5 ml plain lidocaine, 2%, was given 5 min later as an intravenous test dose. After initial negative subarachnoid and intravenous test doses, an additional 3 ml plain lidocaine, 2%, was administered. All patients then received patient-controlled epidural analgesia (PCEA) with 0.11% bupivacaine and 2 μ g/ml fentanyl. The PCEA infusion setting was initiated at 10 ml/h, with a 5-ml demand dose, a 10-min lockout time, and an hourly limit of 30 ml. Additional top-up doses were administered as needed throughout labor with 0.25% bupivacaine in 5-ml increments to a total of 15 ml at the patient's request if PCEA was not adequate. If top-up doses did not provide adequate pain relief, the catheter was withdrawn in 1–2 cm increments, and additional top-up doses of 5 ml bupivacaine, 0.25%, were administered up to an additional 10 ml total. If pain relief was still inadequate, the catheter was replaced.

Variables during the procedure, such as initial paresthesia, intravenous or intrathecal insertion, and the presence or absence of CSF with dural puncture were re-

corded by the unblinded operator performing the procedure. A blinded observer, not knowing the subject group assignment, collected information on all other variables, including inadvertent intravenously placed or intrathecally placed catheters not recognized initially, inadequate analgesia, unilateral block, sacral sparing, manipulation or replacement of epidural catheter, requirement of additional top-up doses through the epidural catheter, pain scores, and sensory dermatomal levels. Verbal analog pain scores and sensory dermatomal levels to temperature were obtained before neuraxial procedure, at 0 and 15 min after the initial dosing of the epidural catheter was completed, and at the time of delivery. Demographics and labor outcomes were also recorded. In a subset of the first 88 patients, in whom the detailed hourly epidural drug usage was available and recorded, we analyzed and compared among groups the hourly epidural medication requirement and the total epidural medication consumption for labor analgesia.

For the purpose of this study, the following definitions were used:

Paresthesia was defined as a sharp or tingling sensation radiating down either lower extremity or the back during insertion of the epidural catheter or spinal needle.

Intravenous epidural catheter was defined as continuous blood return *via* the epidural catheter spontaneously or by aspiration, or by positive clinical intravenous symptoms produced by a 5-ml, 2% lidocaine intravenous test dose administered through the epidural catheter.

Intrathecal epidural catheter was defined as CSF return *via* epidural catheter spontaneously or by aspiration, or by clinical motor block produced by a 2-ml, 2% lidocaine subarachnoid test dose administered through the epidural catheter.

Top-up doses were 0.25% bupivacaine administered in 5-ml increments to treat pain during labor and delivery in addition to the local anesthetic solution administered *via* PCEA.

Inadequate analgesia was defined as any patient requiring additional manipulation of the epidural catheter or requesting top-up doses despite PCEA after initial dosing and testing of the epidural catheter.

Manipulation of epidural catheter was defined as any physical adjustment or manipulation of the catheter, such as pulling back the catheter or replacement required to achieve a better quality of analgesia to patient satisfaction.

Unilateral block was defined as sensory blockade with a difference of greater than three dermatomal levels between the left and right side of the patient anytime during labor after administering the initial doses through the epidural catheter.

Sacral sparing was defined as pain perceived by the patient at delivery despite adequate top-up dose admin-

Table 1. Demographic Data

| | Group DP (n = 107) | Group NoDP (n = 123) |
|--|-----------------------|-------------------------|
| Age, yr | 28 (6) | 29 (6) |
| Weight, kg | 87 (18) | 85 (18) |
| Height, cm | 165 (8) | 165 (7) |
| Gravida, n | 2.5 (1.4) | 2.7 (1.3) |
| Parity, n | 1.0 (0.97) | 1.2 (0.9) |
| Nulliparous parturients, % | 29 | 20 |
| Gestational age, weeks | 39.5 (1.3) | 39.3 (1.6) |
| Cervical dilation at time of epidural placement, cm | 3.6 (1.4) | 3.7 (1.1) |
| Spontaneous vaginal delivery, % | 77.6 | 82.1 |
| Instrument-assisted vaginal delivery, % | 9.3 | 7.3 |
| Cesarean delivery, % | 13.1 | 10.6 |
| Oxytocin use,* % | 78 | 72 |
| Butorphanol use during early labor before neuraxial analgesia, % | 38 | 37 |
| Verbal analog pain score before initiation of neuraxial analgesia (0–10) | 8.3 (1.6) | 8.6 (1.6) |
| Duration of labor epidural analgesia,† min | 292 (190) | 290 (256) |

Data are presented as mean (SD) unless otherwise stated. There are no significant differences between groups.

* Oxytocin was used for both induction and augmentation. † Duration of labor epidural analgesia is defined as the time from labor epidural placement until the time of delivery of fetus.

DP = dural puncture; NoDP = no dural puncture.

istration, or pain necessitating perineal local anesthetic administration for delivery. Top-up doses for second-stage delivery consisted of 5-ml increments of 0.25% bupivacaine up to 10 ml, then 5-ml increments of 2% lidocaine or 2-chloroprocaine if needed up to 10 ml.

Replacement of an epidural catheter was defined as an epidural catheter replaced anytime during labor after initial placement, including those replaced for intravenous or intrathecal catheter placement and inadequate analgesia requiring replacement despite administration of appropriate top-up doses.

Hypotension was defined as 20% decrease from baseline systolic blood pressure, or deteriorating fetal heart rate tracing in association with a decrease in maternal blood pressure. Hypotension was treated with left uterine tilt positioning, increased intravenous fluid hydration, facemask oxygenation, and intravenous ephedrine in incremental doses of 5–10 mg.

Statistical Analysis

For statistical analysis, Sigma Stat (SPSS Inc., Chicago, IL) was used. Previous power analysis revealed that an estimated minimal sample size of 108 patients/group was required to detect a reduction in the epidural catheter manipulation rate from 32% to 15% with a power of 0.80 and an α of 0.05. Our previous study found a 31.4% overall incidence of epidural manipulation rate at our institution.²³ We consider a reduction to 15% in epidural catheter manipulation rate to be clinically significant and important in reducing the work load of managing labor epidural analgesia at our institution, as well as improving patient care and satisfaction. Categorical data were assessed by Fisher exact test, chi-square test, or Mann-Whitney rank sum test as appropriate. Continuous data were analyzed with an unpaired *t* test or analysis of

variance as appropriate. Continuous data were expressed as mean \pm SD, and categorical data were expressed as median and mode. A *P* value less than 0.05 was considered to be statistically significant.

Results

A total of 251 patients were enrolled, with 127 patients in group DP and 124 patients in group NoDP. Twenty patients were excluded from group DP for data analysis: 2 because of an inadvertent dural puncture by the epidural needle and 18 because of no CSF return from spinal needle during the CSE technique. These 18 patients with no CSF return were separated into a subgroup (group DP-NoCSF) for separate data analysis. One patient was excluded from group NoDP because of inadvertent dural puncture by the epidural needle. Therefore, 107 and 123 evaluable patients remained in groups DP and NoDP, respectively.

Demographics were similar between groups DP and NoDP (table 1). The incidences of vaginal delivery were 88%, 86%, and 89% for both groups combined, group DP, and group NoDP, respectively. The characteristics and side effects of the two techniques were compared between groups (table 2). The intravenous catheter rate was 10% in group DP and 6% in group NoDP, without statistical difference between the two groups. Overall inadvertent dural puncture rate was 1.2% (3 of 251), without significant difference between groups. The incidence of no CSF return through the 27-gauge spinal needle in the CSE technique was 14.4% (18 of 125).

The outcome variables for epidural catheter function and the quality of labor analgesia were not significantly different between groups (table 3). The overall epidural catheter manipulation rate was 32% for both groups

Table 2. Characteristics and Side Effects of Labor Analgesic Techniques

| | Group DP (n = 107) | Group NoDP (n = 123) |
|--|-----------------------|-------------------------|
| Intravenously placed epidural catheter, % | 10.3 | 6 |
| Intrathecally placed epidural catheter, % | 0 | 0 |
| Paresthesia with spinal needle insertion, % | 9.3 | NA |
| Paresthesia with epidural catheter insertion, % | 36 | 41 |
| Inadvertent dural puncture, % | 1.6* | 0.8† |
| Highest thoracic dermatomal level of sensory blockade 15 min after initial epidural dosing, median | 10 | 8 |
| Highest thoracic dermatomal level of sensory blockade at delivery, median | 8 | 8 |
| Hypotension, % | 32 | 31 |
| Use of ephedrine, % | 34 | 34 |
| Intravenous ephedrine, mg‡ | 16.0 (8.6) | 16.1 (8.6) |

Data are presented as mean (SD) or percent unless otherwise stated. There are no significant differences between groups.

* Denominator used for calculating inadvertent dural puncture percentage was 127, which included 107 in group DP with cerebrospinal fluid return *via* spinal needle, 18 without cerebrospinal fluid return *via* spinal needle, and 2 inadvertent dural puncture by epidural needle. † Denominator used for calculating inadvertent dural puncture percentage was 124, which included 123 in group NoDP without inadvertent dural puncture and 1 with inadvertent dural puncture by epidural needle. ‡ Mean (SD) intravenous ephedrine dose (mg) among patients who had received intravenous ephedrine.

DP = dural puncture; NoDP = no dural puncture.

combined, 37% for group DP, and 28% for group NoDP, without difference between groups. The epidural catheter replacement rates were 8.7%, 9.3%, and 8% for both groups combined, group DP, and NoDP, respectively. The highest sensory dermatomal level blocked 20 min after initial epidural dosing was also similar between groups. With the PCEA regimen used in this study, approximately 60% of patients in each group still required at least one top-up dose to supplement the PCEA during the course of labor.

The subgroup of 18 patients (group DP-NoCSF) in whom there was no CSF return *via* the spinal needle when inserted during the CSE technique was compared with groups DP and NoDP. In this small subgroup, the overall epidural catheter replacement rate (including initial failure after placement and subsequent failure) was 22% *versus* 9% and 8% in groups DP and NoDP, respectively, and the intravenous catheter rates were 17%, 10%, and 6% in groups DP-NoCSF, DP, and NoDP, respectively (table 3). With the small sample size, these differences did not reach statistical significance.

Table 3. Epidural Analgesic Characteristics and Outcomes

| | Group DP (n = 107) | Group NoDP (n = 123) | Group DP-NoCSF (n = 18) |
|--|-----------------------|-------------------------|----------------------------|
| Epidural catheter required replacement, % | 9.3 | 8 | 22.2 |
| Epidural catheter required manipulation, % | 37.4 | 28 | 38.9 |
| Inadequate analgesia, % | 20.6 | 30 | 27.8 |
| Unilateral block, % | 25.2 | 23 | 27.8 |
| Sacral sparing, % | 29.9 | 25 | 27.8 |
| Percent of patients required top-up dose(s) | 58.9 | 61 | 44.4 |
| Number of top-up doses required per patient among those receiving top-up dose(s) | 1.8 (0.9) | 1.7 (1.0) | 2 (1.5) |
| Patient-controlled epidural analgesia—volume used, ml/h of 0.11% bupivacaine with 2 μ g/ml fentanyl* | 15.9 (6.5) | 16.2 (3.8) | 17.6 (7.3) |

Data are presented as percent or mean (SD) unless otherwise stated. There are no significant differences among groups.

* In the subgroups of 42 patients in group DP, 41 patients in group NoDP, and 5 patients in group DP-NoCSF.

DP = dural puncture; NoDP = no dural puncture.

In a subset of 88 patients (42 in group DP, 41 in group NoDP, and 5 in group DP-NoCSF), the detailed hourly usage of epidural drugs was recorded, analyzed, and compared among groups. The mean (SD) amounts of hourly epidural medication (0.11% bupivacaine with 2 μ g/ml fentanyl) or its equivalent required for labor analgesia were 15.9 (6.5), 16.2 (3.8), and 17.6 (7.3) ml/h for groups DP, NoDP, and DP-NoCSF, respectively, without significant difference among groups.

Discussion

The epidural catheter manipulation rates of 37% and 25% for groups DP and NoDP, respectively, were not statistically different. Our overall epidural catheter replacement rate of 8.7% was similar to that previously reported, and there were no significant differences between groups DP and NoDP.¹⁹⁻²² Eappen *et al.*²⁰ reported failure rates of 13.1% and 7.2% in a retrospective review of 4,240 charts of traditional epidural and CSE labor analgesia, respectively. However, CSE analgesia

was administered more frequently by an experienced provider and in rapidly laboring multiparous parturients, both of which were confounding factors possibly contributing to a lower failure rate in the CSE group in the retrospective study of Eappen *et al.* Norris²⁵ reported that epidural catheters inserted as part of the CSE technique were more likely to produce bilateral sensory changes, adequate analgesia, and less complete failure when compared with the traditional epidural technique. However, epidural catheter manipulation and replacement rate were not specifically recorded. It is also unclear whether the clinical improvement in epidural blockade and reduction in epidural drug requirement after a CSE technique was a result of the residual subarachnoid drug effects, a better-positioned epidural catheter placed by CSE technique, or the subarachnoid transfer of epidural drugs through the dural puncture made during the CSE technique.

When a labor epidural catheter is needed for cesarean delivery anesthesia, often urgently hours after initial placement, the subarachnoid drug effects from CSE typically would have been mostly resolved and the function of the epidural catheter would less likely be affected by the subarachnoid drugs administered hours previously. In this study, we did not administer any subarachnoid medication to evaluate the technical difference between the CSE and traditional epidural techniques. Our intention was strictly to separate the effects of dural puncture and the epidural catheter insertion in the CSE technique from the residual effects of the administered subarachnoid drugs that might have masked a patchy block or a poorly functioning epidural catheter in the previous reports. We know of no other published, prospective, randomized clinical study examining the effects of the dural puncture and the epidural catheter inserted with the CSE technique (without the subarachnoid drug) on the function of the labor epidural catheter and the quality of labor analgesia it provided. Our results showed no difference between CSE (without the effect of subarachnoid drug administered) and traditional epidural techniques on the function of the epidural catheter inserted and the quality of labor analgesia it provided. Therefore, the epidural catheter placed after a dural puncture made in the CSE technique may have a similar likelihood of providing successful labor epidural analgesia or cesarean epidural anesthesia hours later, when the effects of the subarachnoid drugs administered would have been mostly resolved.

In an *in vitro* study, Bernards *et al.*¹⁰ demonstrated and concluded that the significance in the subarachnoid flux of an epidurally administered drug through a previous dural puncture, by 18- to 25-gauge needles, was directly proportional to the size of the dural puncture and inversely proportional to the intact meningeal surface area exposed to the drug, the intrinsic diffusion capacity of the drug through an intact dura, and the

distance of the dural puncture from the site of epidural drug administration. Whether drug movement through the dural puncture is clinically relevant depends on whether the rate of drug movement through the dural puncture is significantly faster than the rate of drug diffusion through the intact dura.¹⁰ In an *in vitro* study, Swenson *et al.*¹² showed similar conclusions when morphine was administered epidurally shortly after a dural puncture. Bernards *et al.*¹⁰ also showed that the subarachnoid flux of lidocaine, but not morphine, was insignificant, especially when the dural puncture was created by a small-gauge spinal needle.

In a nonrandomized clinical study, Leighton *et al.*²⁶ showed that laboring parturients had a higher sensory blockade from epidural drug administration after receiving subarachnoid sufentanil by CSE technique (24- and 25-gauge spinal needles) when compared with the traditional epidural technique without dural puncture. However, the residual effect of the subarachnoid sufentanil affecting the blockade level in the CSE group could not be ruled out. Suzuki *et al.*⁶ demonstrated a more extensive caudad but not cephalad spread of epidural mepivacaine anesthesia in nonpregnant patients after a 26-gauge spinal needle dural puncture but without subarachnoid drug administration. Our results showed no difference in the cephalad spread, but we did not measure the caudal spread. However, Beaubien *et al.*⁹ found no difference in postoperative PCEA requirements or blocked sensory dermatomal levels in 40 patients when comparing traditional epidural *versus* CSE technique for knee surgery. Despite some evidence of an increase in sensory blockade levels from epidural drugs after a spinal needle dural puncture, we found no significant clinical difference in labor analgesia or the epidural catheter function when the dural puncture was made by a 27-gauge Whitacre spinal needle. The spinal needle we used was of smaller diameter than those used in the other studies discussed.^{6,10,26} Furthermore, we also administered the epidural medication shortly after the dural puncture as in the usual standard clinical practice of test dosing the epidural catheter and initiating the epidural infusion. The resting CSF pressure is typically higher than pressure in the epidural space; therefore, a net efflux of CSF to epidural space can be expected immediately after dural puncture. This net efflux, together with a small dural puncture, might have significantly limited the transfer of epidural drug into subarachnoid space through the dural puncture.

It is of interest that a subgroup of 18 patients did not have CSF return with the attempted dural puncture during CSE technique. In this small subgroup, the replacement and the intravenous catheter rate were higher but did not reach statistical significance when compared with group DP or group NoDP. It warrants further study to determine whether the difference exists with a larger sample size and power. The results from group DP-

NoCSF suggest that it may be prudent to correct the placement of the epidural needle in the event of a failure to obtain CSF during CSE, because a malpositioned needle may result in higher epidural catheter manipulation, replacement, or poor analgesia.

It should be noted that our study had a number of limitations. The study was conducted at an institution with a dedicated obstetric anesthesia service but also with a residency training program. With good availability of personnel, the staff encouraged our residents to have a low threshold of manipulating or replacing the epidural catheters when analgesia was less than optimal. This might be responsible for higher manipulation, replacement, or top-up rates compared with some institutions, even though our current results were comparable to our previous studies.^{19,23,24} Furthermore, the definition of failure or manipulation rates often varies among studies published from different institutions, making comparison difficult.

At our institution, the customary practice is to use 2 and 5 ml lidocaine, 2%, for subarachnoid and intravenous test doses, respectively. These doses are larger and more concentrated than what are used at many institutions, but our power analysis was based on data from previous studies performed at our institution using similar doses. Furthermore, the higher concentration would have exaggerated the effect, if any, on the dermatomal spread of epidural local anesthetic *via* the dural puncture. Our incidence of no CSF return after attempted dural punctures was also higher than some reported previously.^{6,10,26} This might be in part due to the facts that (1) we used a smaller 27-gauge Whitacre spinal needle and had residents in training performing the procedures, and (2) we did not manipulate the epidural or spinal needle at all, even when no CSF returned after an attempted dural puncture and accepted the loss of resistance as confirmation of the epidural space. Even though our incidence of inadvertent intravenously placed 19-gauge polyamide epidural catheters was similar to those previously reported,^{1,19,23,24} the use of a softer or larger-diameter catheter might result in a lower incidence of intravenous catheter, and a lower overall epidural replacement rate for both traditional epidural or CSE technique. Future studies can also incorporate a third group with subarachnoid drug to compare with those two studied here.

In conclusion, epidural catheters inserted after a dural puncture with a 27-gauge Whitacre spinal needle in a needle-through-needle CSE technique without administering subarachnoid drugs did not improve the function of labor epidural catheters, the manipulation and replacement rate, or the quality of epidural labor analgesia when compared with epidural catheters inserted *via* the traditional epidural technique. However, when no CSF returned from the spinal needle after an attempted dural

puncture with the CSE technique, the catheter inserted into the epidural space might be less functional, with a higher replacement rate, which warrants further investigation. We would also caution readers not to extrapolate the results of this study to dural punctures made by larger-diameter needles or with the use of highly hydrophilic epidural drugs such as morphine, which may significantly alter the rate of transdural transfer.

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