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Original Research

Cadaveric Porcine Spines as a Model for the Human Epidural Space

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Most patients who undergo epidural anesthesia are pregnant and thus a protected population, which has limited investigations of the human epidural space. Among the several species studied as models for the human spine, the porcine spine has been used as a model for spine instrumentation. Although the spread of colored dye within the porcine epidural space has been investigated, no model has demonstrated in situ spread by using radiopaque contrast dye. To this end, we here used 10 Yorkshire swine cadavers through an approved tissue sharing agreement. Epidural catheters were placed by using a landmark-based loss-of-resistance technique; placement was confirmed through radiography. The catheters were connected to epidural infusion pumps to ensure consistent dosing, 2-mL boluses of contrast dye were injected into the space, and radiographs were taken and recorded after each bolus. The total spread of the contrast dye was analyzed. We demonstrated consistent and reliable spread of fluid in the epidural space among the animals used, with low variability between animals of different weights. Our results support the use of the epidural space of cadaveric swine as a model for the human epidural space. Furthermore, the technique for epidural administration by using the landmark-based loss-of-resistance demonstrated in this model was validated, thus supporting future investigations of medication delivery into the epidural space.

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Epidural catheter placement for labor analgesia is extremely common, being used in approximately 60% of all deliveries in the United States.[8] The need for further investigations into the spread of epidural injectate in humans is important, given the variability in response to and efficacy of epidural administration for labor analgesia. Factors affecting the efficacy of epidural analgesia include the intensity of block (as reflected by the depth of analgesia) and extent of motor blockade, dermatomal spread of analgesia, and distribution of analgesia coverage. Patients often need adjustments to the epidural infusion rate, additional boluses, or other interventions to achieve sufficient labor analgesia. In addition, investigations into human labor epidurals are challenging due to the protected status of pregnant patients in investigational research.

The primary goal of this study was to assess the degree of variability in the spread of injectate in the cadaveric porcine epidural space. The porcine spine has previously served as a model for the human epidural space in studies using electrical stimulation to monitor epidural advancement and in research assessing the effects of fluid administration into the epidural space on intracranial pressure.[6,9] No studies have investigated the variability in size and volume of the epidural space in swine through real-time administration of fluid into the epidural space. Recent studies have used the porcine model to determine spread of dye in the porcine epidural space as a model for human spread for labor analgesia by administering dye in porcine cadavers and assessing dye distribution on necropsy.[9,10] Due to limitations with using colored dye and the destruction of tissue during necropsy, these studies were limited in their ability to demonstrate spread in real time and to quantify variability within the space. We hypothesized that the porcine epidural space would demonstrate low variability of spread among animals and that we would be able to quantify the degree of spread for future studies using the porcine spine as a model for the human epidural space. These investigations may allow for more effective labor analgesia for this at-risk population.

Materials and Methods

This study was conducted using swine carcasses through tissue-sharing agreements with protocols approved by the IACUC of Naval Medical Center Portsmouth, which is AAALAC-accredited and therefore adheres to the principles of the *Guide for the Care and Use of Laboratory Animals*. All animal research is conducted in compliance with federal animal welfare laws and regulations[1,7] relating to the use of animals. Female Yorkshire-cross swine (n = 12; age, 7 mo; weight, 70 to 90 kg) under a surgical plane of anesthesia were euthanized by sodium pentobarbital overdose (1 mL/10 lb IV; 390 mg pentobarbital sodium per 100 mL; Euthasol, Virbac Animal Health, Fort Worth, TX). Epidural procedures were performed within 2 h of euthanasia.

Euthanized animals were placed in ventrodorsal recumbency with the hindlimbs flexed craniad to facilitate access to the lumbosacral epidural space. Landmarks for injection were identified by palpating the highest points of both wings of the ilium and inserting the needle along midline, cranial to the palpable landmarks at the vertebral level of L5L6. A 17-gauge, 90-mm Touhy needle (Braun Medical, Bethlehem, PA) was used to access the space through a loss-of-resistance technique. After the space was accessed, 3 mL of saline was injected to maintain consistency across subjects, due to variation in the amount of saline injected during the loss of resistance technique.

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A 20-gauge Perifix catheter (Braun Medical) was inserted 5 cm into the epidural space and secured to the cadaver. An epidural infusion pump (CADD-Solis, Smiths Medical, St Paul, MN) was attached to the catheter and programmed to deliver five 2-mL boluses of iohexol (Omnipaque 240, GE Healthcare, Marlborough, MA) at a bolus flow rate of 250 mL/h, thus delivering each 2-mL bolus over approximately 30 s. Prior to infusion of contrast dye, correct placement of the catheter was confirmed through anatomic landmarks, appropriate loss of resistance, lack of cerebrospinal fluid, and appropriate vertebral level according to a lateral radiograph. To determine the spread of the contrast dye, additional lateral and ventrodorsal radiographs were obtained approximately 30 s after each programmed bolus (Figure 1) during the 5-min interval before the next programmed bolus. Spread was measured from the tip of the catheter cranially, in terms of the number of vertebral bodies traversed. During prestudy investigations, fluoroscopy revealed no evidence of epidural contrast spread after completion of the boluses, measured initially in real time and monitored for 60 min afterward (data not shown). Therefore, traditional plain-film radiographs were used due to their increased resolution and improved ability to compare images between subjects. All statistical analyses were performed using the Data Analysis toolkit within the Microsoft Excel environment. A P value of < 0.05 was used to define statistical significance representing an α of 0.95. Linear regression analysis was performed to determine suitability for a linear model of these data, and standard intercept and slope calculations were determined.

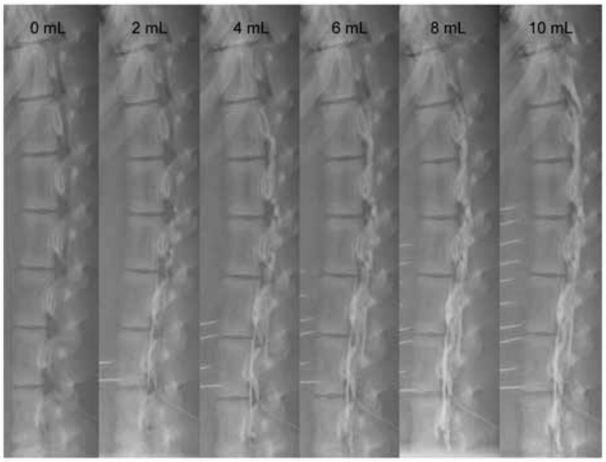

Figure 1. Epidural spread of contrast agent after serial 2-mL injections. Note the radiopaque catheter visible at the L5L6 level. The vertebral body level was identified relative to the sacrum (not shown).

Table 1. Mean epidural contrast spread in swine (n = 10)

Total volume of contrast medium (mL)	Epidural spread (no. of vertebrae traversed)	95% CI
2	3.1	2.92 – 3.37
4	4.7	4.19 – 5.20
6	5.7	5.12 – 6.29
8	6.9	6.22 – 7.58
10	7.9	7.12 – 8.69

Results

Overall, 10 pigs with a median weight of 78.6 kg (interquartile range, 71.0 to 81.2 kg) were used in evaluating the spread of contrast dye in the epidural space. One cadaver was excluded from the study due to inadvertent dural puncture, and another was excluded due to inability to access the epidural space.

Overall, we identified that the spread of contrast dye travels in a linear manner, estimated at 0.585 vertebrae transversed per 1 mL of contrast dye given as an epidural bolus. The spread of contrast dye in terms of the number of vertebral bodies traversed is shown in Figure 1 and conformed to the equation

$$\text{Dye spread}\ \left(\text{in vertebrae traversed}\right) = 0.585x + 2.16,$$

where x is the volume (in milliliters) of contrast dye injected ($R^2 = 0.99354$, $P < 0.001$; Table 1). There was overall low variability of longitudinal spread between animals as demonstrated by the relatively narrow confidence intervals and significant differences seen in epidural spread between each injection. This indicates a consistency of volume spread in the porcine epidural space. The y-intercept in this regression model represents the initial spread of the first 2-mL bolus. Although not quantified during the study, marked circumferential spread of the dye at the vertebral bodies and nerve roots was apparent radiographically.

Discussion

Previous studies have considered the influence of bolus compared with infusion rates for delivery of epidural medications.[5,11] Both the rate and pressure of administration affect the degree to which liquid spreads in the space.[3] We determined that, as evidenced by radiographic imaging, the spread of contrast dye in the epidural space was fairly consistent among adult Yorkshire swine cadavers. In humans, there is a concern regarding variability in the spread of epidural local anesthetics, but our current investigation demonstrated minimal variability, with consistent and predictable results regarding the spread of contrast agent delivered as set-volume boluses by a pump. Although we used pump-driven boluses, the same pump can perform continuous infusion, which is often used for labor anesthesia. Future studies should investigate epidural spread when the same volume of contrast agent is given as an infusion compared with boluses.

Our findings support future investigations regarding the spread of epidural medications that are administered by using a variety of epidural dosing schemes, such as programmed intermittent bolus delivery and continuous infusion, in the cadaveric Yorkshire swine model. These data allow for internal consistency when the spread of epidural contrast in cadavers is compared between different dosing regimens. The reproducibility of the spread of epidural infusions in cadaveric swine enables the testing of dosing schemes in a minimal risk environment while ensuring that any findings may reasonably be extrapolated to a human model.

Similarly, the determination of a linear spread of contrast is encouraging still in terms of the predictability and consistency of spread in the epidural space.[9] Limitations to the cadaveric model exists, such as the inability to assess the influence of blood circulation on the spread and persistence of contrast. This could potentially be influenced by both the space occupied by engorged veins and arteries, as well as the effect of redistribution of drug from the epidural space. Although vertebral body size and spinal canal dimensions, including length, are similar between swine and humans,[2,4] notable differences include 6 (rather than 5) lumbar vertebrae and deeper distance from the skin for catheter placement in swine. In the current study, we used female porcine cadavers only, but we do not anticipate any sex-associated variability within the epidural space. Using spines from swine of similar size, age, sex, and breed could potentially improve reproducibility of data in future studies. The porcine spine may represent the best nonhuman model for the epidural space in light of anatomic similarities and relative size. Continued use of either cadaveric or live porcine spines for epidural infusion investigations could dramatically expand our understanding of the spread of local anesthetic solutions used during human epidural infusions.

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