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Epidural distribution of dye administered via an epidural catheter in a porcine model

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Abstract

Background: Local anaesthetics are commonly delivered to the epidural space by either intermittent bolus or continuous infusion. While these methods have been investigated in terms of analgesia and total dose administered, they have not been compared in terms of their effect on the spread of injectate within the epidural space. This animal study compared the spread of dye delivered to the epidural space in a porcine model by either bolus or infusion.

Methods: After ethical approval, epidural catheters were placed at three vertebral levels in seven anaesthetized pigs. Aqueous dye (1 ml) was injected into the catheter as a bolus, or as an infusion over 30 min. Animals were euthanized at the end of the study and necropsy performed immediately to quantify the extent of dye spread.

Results: In seven animals, 20 catheters were successfully placed in the epidural space. The mean (SD) extent of dye spread was 8.9 (2.6) cm in the infusion group compared with 15.2 (2.7) cm in the bolus group ($P<0.001$). Segmental spread was significantly greater in the bolus group compared with the infusion group ($P<0.01$).

Conclusions: In the porcine epidural model, spread of one ml of epidural dye solution is more extensive after a single bolus compared with short term infusion.

Key words: analgesia, epidural; anesthesia, epidural; epidural space; injections, epidural

Editor's key points

- The effects of delivery of local anaesthetics through epidural catheters by bolus or infusion techniques on epidural spread, were compared in an anaesthetized pig model.
- Bolus injection of dye led to greater rostrocaudal extent of circumferential spread compared with infusion of the same volume.
- These findings are consistent with greater efficacy and lower dose requirements for bolus epidural injections of local anaesthetics.

Epidural anaesthesia and analgesia, first described in 1921, are commonly used techniques in the management of pain.[1] Despite a long history of safety and efficacy, spread of injected local anaesthetics is difficult to predict,[2] and is influenced by several factors[3] including dose[4] and volume[5–7] of the injectate. The extent of epidural local anaesthetic spread has been shown to correlate to the level of sensory blockade obtained.[8] However, inadequate analgesia remains an important problem.[9 10] Local anaesthetic agents can be delivered to the epidural space by either an intermittent bolus, or as an infusion.[11] These methods have been investigated in terms of effect on analgesia and total

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dose administered,[11] but have not been compared in terms of neuraxial spread. This information could guide clinicians as to the most effective method of delivery in terms of spread and allow for dose reduction of local anaesthetics.

Porcine spinal anatomy has been reported as comparable with that of humans,[12 13] and porcine models have been used in studies of the epidural space,[14] catheter placement,[15] and epidural anaesthesia.[16 17] The primary objective of this study was to determine if the delivery of dye to the epidural space, by either bolus or infusion, significantly influences spread. We hypothesized that delivery of a fixed volume of dye via a single bolus would result in greater spread compared with an infusion.

Methods

This study was approved by the Animal Research Ethics Board of the University of British Columbia on April 4, 2014, and registered with the Office of Research Services of the University of British Columbia (A12-0230). The study protocol adhered to the Canadian Council on Animal Care guidelines for humane animal use. These guidelines are comparable to the regulations set out in the Animal (Scientific Procedures) Act 1986 and the guidance provided by the National Centre for the Replacement, Refinement and Reduction of Animals in Research. Design, analysis and reporting of this study conforms with ARRIVE Guidelines.

Anaesthesia

A convenience sample of seven healthy Yorkshire cross breed female pigs (Abbotsford, British Columbia, Canada) was used. Animals were fasted overnight but received water ad libitum. After sedation with 20 mg kg^{-1} i.m. ketamine, inhalation anaesthesia was induced with 4–5% isoflurane in oxygen. After tracheal intubation and establishment of i.v. access, total i.v. anaesthesia was established with an infusion of 0.4–0.7 mg kg^{-1} midazolam and 50–150 mcg kg^{-1} min^{-1} of propofol. Subsequently, inhalation anaesthesia was discontinued, physiologic monitors (ECG, oxygen saturation, bp) were established and the animals were placed prone. Ventilation and anaesthetic gases were delivered using a Drager (Luebeck, Germany) AV 2824 anaesthetic machine. Physiological monitoring was displayed by an HP (Palo Alto, CA USA) 78354A X monitor. Capnography was provided using a Datex-Ohmeda (Madison, Wisconsin, USA) Capnomac Ultima capnograph.

Experimentation

The spinous processes were identified and marked at each level. A total of three epidural catheters were placed in each pig at lumbar (L3–4), low thoracic (T10–11) and mid-thoracic levels (T5–6). This allowed the necessary data to be collected, whilst minimizing the number of pigs required.

Epidural catheters were placed using a paramedian approach to the epidural space. For lumbar and low-thoracic levels, a 17G, 90 mm Touhy needle (Braun Medical Inc, Bethlehem, PA, USA) was used. For deeper, mid-thoracic levels, an 18G, 150 mm Touhy needle was used. The epidural space was identified using a loss-of-resistance to air technique with a glass syringe, with two-three ml of air injected at each level. At each level, a Perifix® (Braun Medical Inc) epidural catheter was advanced through the epidural needle so that two cm of catheter protruded into the epidural space. This distance was chosen to ensure that each port of the catheter would be in the epidural space whilst minimizing the risk of the catheter coiling or encroaching upon the other catheters. Epidural needles were left *in situ* to provide protection for the epidural catheters during dissection and were fastened to the skin with adhesive tape. All epidural placements were performed by a single member (IM) of the research team. If it was not possible to enter the epidural space at a chosen level, an attempt was made at the immediate cranial or caudal intervertebral space. Epidural pressure readings were obtained from each epidural catheter using an electronic transducer (Transpac® IV, ICU Medical, Inc. San Clemente, CA, USA).

Each catheter was either attached to a syringe driver or syringe to administer blue or green dye via infusion or bolus, respectively. The blue dye was a water-based solution of propylene glycol and triphenylmethane dye, and the green dye used was a similar solution with tartrazine. Both infusions and boluses were administered using a 10 ml syringe delivering one ml of dye. Green or blue dye was alternated between each protocol. We used one ml of dye in keeping with previous studies[7 12] in order to allow discrete spread of dye to be studied without spread at one level encroaching onto spread at another level; in addition, we surmised that as the cross-sectional area of the porcine spinal cord and vertebral canal is approximately one third that of the human spinal cord, this volume would be comparable with a top up dose in humans of X ml 3 ml.[12] The infusion was delivered over 30 min with a Next Advance (Averill Park NY, USA) SP-300 infusion pump, and the bolus was injected manually as a fast push over ~one s. Injection pressures were measured using a three-way stopcock and electronic transducer attached between the syringe and catheter.

Each pig received either two boluses and one infusion protocol, or two infusions and one bolus protocol in alternate fashion. For example, infusion protocol via both lumbar and mid-thoracic catheters, and a bolus protocol via the low-thoracic catheter. Physiological data recorded included arterial pressure, heart rate, pulse oximetry, end-tidal carbon dioxide, minute ventilation, tidal volume and peak airway pressure. Epidural pressure measurements were repeated immediately after dye delivery. All animals were euthanized at the end of the experiment using an i.v. bolus of pentobarbital sodium (Bimeda-MTC, Cambridge, Ontario, Canada) 120 mg kg^{-1}. Death was confirmed by the absence of cardiac electrical activity on continuous surface electrocardiography. An anatomist (CK) assisted by one investigator (IM) performed necropsy, with attention to the spine and spinal cord to assess dye spread and confirm level of epidural needles. Necropsy was completed within one h of the end of the dye injection to minimize tissue changes associated with death.[7] The longitudinal extent of circumferential dye spread was measured both in centimeters and in number of spinal nerve levels dyed bilaterally. Pattern or patchiness of spread was documented in descriptive terms. Spine length was measured in centimeters for each animal.

Statistics

Data were entered into a spreadsheet program (Microsoft Excel, Microsoft Corporation, Seattle, WA, USA) and analysed by an independent statistician using Statistical Package for the Social Sciences (SPSS, Version 20.0, IBM Corporation, Armonk, NY, USA). Tests for normal distribution were performed using the Shapiro-Wilk test of normality for small sample sizes. Normally distributed data are presented as mean (SD); non-normally distributed data are presented as median (interquartile range). Categorical data were compared using a χ^2test analysis. Comparisons of ordinal data were performed using the Mann-Whitney *U*-test. The level of significance was set at $P<0.05$.