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REPORTS OF ORIGINAL INVESTIGATIONS

Stimulating thoracic epidural placement via a lumbar approach causes significant spinal cord damage in a porcine model

Le positionnement d'un cathéter péridural thoracique stimulant par voie lombaire provoque des lésions importantes à la moelle épinière sur un modèle porcin

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Abstract

Background *Continuous thoracic epidural analgesia is a valuable and common technique for analgesia but involves risk to the spinal cord. There is significant pediatric experience safely placing thoracic epidurals via a caudal approach. The use of a stimulating catheter offers the advantage of real-time confirmation of appropriate catheter placement. We hypothesize that the tip of a stimulating epidural catheter can be reliably advanced to the thoracic epidural space with lumbar insertion in a porcine model.*

Methods *This prospective experimental porcine study evaluated the feasibility of placing the tip of a stimulating epidural catheter to a predefined thoracic epidural location after percutaneous lumbar epidural access in six live pigs. After the lumbar epidural space was accessed, a stimulating epidural catheter was advanced until the targeted thoracic myotome was stimulated. The final position of the catheter in relation to the targeted location was determined by fluoroscopy. All animals were euthanized at the end of the experiment, necropsy and spinal cord histology were then performed to assess the extent of spinal cord damage.*

Results *In all animals the epidural catheter tip could be accurately advanced to the targeted thoracic myotome. Gross subdural bleeding occurred in three of the six animals and deep spinal damage was observed in two of the six animals. In one animal, the catheter was placed in the subarachnoid space.*

Conclusions *Accurate access to the thoracic epidural space is possible via a lumbar approach using a stimulating epidural catheter. Based on gross and histopathological examination, this technique resulted in frequent complications, including subdural hemorrhage, deep spinal cord damage, and subarachnoid catheter placement.*

Résumé

Contexte *L'analgésie péridurale thoracique continue est une technique analgésique précieuse et répandue, mais elle peut endommager la moelle épinière. Il existe de nombreuses données soutenant le positionnement*

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Author contributions The manuscript is the collaborative work of five authors. *Jonathan Gamble* and *Barbara Ambros* conceptualized the study and provided theoretical guidance in interpretation. *Jonathan Gamble*, *Barbara Ambros*, *Patrick Séguin*, *Perrine Benmansour*, and *Elemir Simko* acquired and analyzed the data. *Jonathan Gamble* wrote the initial draft and all five authors revised the manuscript.

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sécuritaire de péridurales thoraciques par approche caudale chez l'enfant. L'utilisation d'un cathéter stimulant offre l'avantage de confirmer en temps réel le bon positionnement du cathéter. Nous avons émis l'hypothèse que l'extrémité d'un cathéter péridural stimulant pouvait être avancée de façon fiable dans l'espace péridural thoracique par insertion lombaire chez un modèle porcin.

Méthode *Cette étude prospective expérimentale sur un modèle porcin a évalué la faisabilité de positionner l'extrémité d'un cathéter péridural stimulant à un emplacement péridural thoracique prédéterminé après avoir obtenu un accès péridural lombaire percutané chez six porcs vivants. Une fois l'accès à l'espace péridural lombaire obtenu, un cathéter péridural stimulant a été poussé jusqu'à ce que le myotome thoracique ciblé soit stimulé. La position finale du cathéter par rapport à l'emplacement cible a été déterminée par fluoroscopie. Tous les animaux ont été euthanasiés à la fin de l'expérience; ensuite, une autopsie et une histologie de la moelle épinière ont été réalisées afin d'évaluer l'étendue des lésions à la moelle épinière.*

Résultats *Chez tous les animaux, l'extrémité du cathéter péridural a pu être avancée avec précision jusqu'au myotome thoracique ciblé, alors que d'importants saignements sous-duraux sont survenus chez trois des six animaux, et des lésions profondes à la moelle épinière ont été observées chez deux des six animaux. Le cathéter a été placé dans l'espace sous-arachnoïdien chez un animal.*

Conclusion *Il est possible d'accéder précisément à l'espace péridural thoracique par une approche lombaire à l'aide d'un cathéter péridural stimulant. En se fondant sur l'examen grossier et histopathologique, cette technique a provoqué des complications fréquentes, notamment une hémorragie sous-durale, des lésions profondes à la moelle épinière et un placement du cathéter dans l'espace sous-arachnoïdien.*

Thoracic epidural analgesia is an effective analgesic modality following thoracic or upper abdominal surgery in patients of all ages.[1] Although technique failure is the most common risk, more worrisome complications of thoracic epidural analgesia include devastating spinal cord injury.[2,3] The increased risk of spinal cord injury with a lumbar epidural approach is secondary to the risk of spinal cord injury with caudal epidural placement.[4]

In the pediatric population, advancement of an epidural catheter to the thoracic space from a caudal entry has been shown to be an alternative to direct thoracic placement.[5–8] Tsui *et al.* have refined the technique using a stimulating epidural catheter, allowing real-time catheter location during advancement to the desired thoracic level.[9–16] This technique has become very popular among pediatric anesthesiologists because of its high rate of success.[17] The advantages of this technique are both the technical ease of access to the epidural space and the ability to locate the epidural catheter tip without fluoroscopy.

Other than the work by Blanco *et al.* there is a lack of documented literature of thoracic epidural catheter placement from the technically easier lumbar approach.[2,3,8] The purpose of this study was twofold: first, to determine the feasibility of advancing a stimulating epidural catheter to a predetermined thoracic level with a lumbar percutaneous entry point; and second, to determine if this technique risked damage to the spinal cord. A living anesthetized porcine model was used for this study.

Methods

This prospective observational study was approved by the University of Saskatchewan Animal Research Ethics Board, and the study protocol adhered to the Canadian Council on Animal Care guidelines for humane animal use.

Animals

A convenience sample of six healthy ten-week-old male pigs (Camborough) with an average weight of 30.1 kg was used. A porcine model was used because of its similarities with human spinal anatomy.[18,19] The porcine bony spine is very similar to that of humans except for an increased number of vertebrae, usually in the thoracic region. The major difference is that the porcine spinal cord extends to the sacral spine whereas the human spinal cord terminates high in the lumbar spine. All animals were group housed in a climate-controlled room with 12-hr light-dark cycles. Pigs had free access to standard food and water. They were fasted eight hours prior to the experimentation but were not denied water.

Anesthesia

The pigs were initially sedated with intramuscular ketamine (5 $mg \cdot kg^{-1}$) and midazolam (0.5 $mg \cdot kg^{-1}$). After sedation was achieved, intravenous access was established, and alfaxalone [mean 2.5 (SD 0.8) $mg \cdot kg^{-1}$] was administered intravenously to effect. Once anesthesia was induced, the pigs' tracheas were intubated with an appropriately sized cuffed endotracheal tube. Muscle relaxants were not used in order to facilitate nerve stimulation. Anesthesia was maintained with isoflurane (end-tidal concentration 1.1-1.8%) in 100% oxygen. A peripheral artery was percutaneously cannulated, and a multichannel physiological monitor (Datex-Ohmeda Cardiocap™/5 GE

Healthcare, Finland Oy, Helsinki, Finland) was used to monitor electrocardiography, arterial oxygenation, heart rate, blood pressure (systolic, mean, and diastolic), respiratory rate, tidal volume, minute volume, end-tidal CO_2, and expired isoflurane concentration.

Experimentation

After each animal was anesthetized and physiologic monitoring was established, the animal was positioned in the left lateral decubitus position without forced flexion. The fourth thoracic spinous process was clinically identified, and a 3.81-cm 16G needle was then introduced perpendicular to the skin at the interspace between the fourth and fifth thoracic spinous processes. The needle position was confirmed with fluoroscopy. If the study team members were not confident using radiographic diagnosis to identify the needle's anatomic location, confirmation was obtained from a veterinary radiologist. The needle location was used as the target myotome for the tip of the epidural catheter. A line joining the iliac crests was then drawn. The interspinous space immediately caudal to this line was the initial choice for percutaneous access to the epidual space.

An 18G insulated Tuohy needle (PAJUNK®, Dyna Medical Corp, ON, Canada) was advanced to the epidural space with a loss-of-resistance (LOR) to saline technique (all epidural placements were performed by a single member of the research team [J.G.]). Strict adherence to sterile techinque was not followed as the animals were euthanized at the conclusion of the experiment. If it was not possible to enter the epidural space at a chosen level, an attempt was made at the immediate cranial or caudal interspinous space. After the epidural space was located, a 20G styletted stimulating plexus catheter (PAJUNK Kit 521156-35C, Dyna Medical Corp, ON, Canada) was advanced through the needle into the epidural space. If it was not possible to advance the epidural catheter past the tip of the epidural needle, subtle needle advancement and rotation were performed to faciliate catheter advancement. If this was unsucessful, normal saline 10 mL was injected into the epidural space and catheter advancement was attempted. If it was still not possible to advance the catheter, the epidural space was accessed cranially or caudally at one level from that previously attempted, provided a previous attempt at the level had not been done. When catheter advancement was stalled in the epidural space, a saline injection was performed through the catheter during advancement . Once the catheter was placed in the epidural space approximately 10 cm from the epidural needle hub, it was connected to a peripheral nerve stimulator (PAJUNK, MultiStim SWITCH, Germany) with an initial output of 1 mA. The pulse width used in all experimentation was 0.2 msec. The current was increased (to a maximum of 5 mA) until muscle twitch was observed and then titrated to continue to achieve adequate stimulation while the catheter was advanced. Myotome twitch was observed in all animals with current between 1–5 mA. The catheter was advanced until the targeted thoracic myotome was stimulated. This was the clinical endpoint of the study. The final position of the catheter tip was located with fluroscopy. At the end of the experiment, the animals were euthanized with a lethal dose of pentobarbital. A veterinary pathologist performed a necropsy on the animals with attention to the spine and spinal cord to assess for gross spinal damage. Selected areas of the spinal cord were prepared for histology and examined under microscopy by a veterinary pathologist.

Statistics and data analysis

This study presents the summary results and qualitative findings of a convenience sample of six animals; no statistical assumptions or tests were applied.

Results

Epidural access

It was possible to access the lumbar epidural space in all animals. In most animals, it was difficult to advance the catheter past the distance to the tip of the Tuohy needle, and frequent re-siting was required. Although one catheter was placed in the subarachnoid space, there was no clinical indication of subarachnoid needle or catheter placement in any animal (see Table 1).

Clinical accuracy of epidural tip placement with electrical stimulation guidance

The final position of the stimulating catheter tip was within one vertebra (T3-5) of the target in all six pigs (see Table 1).

Complications of technique

The macroscopic and microscopic examination of the spinal cord revealed presence of pathological changes in

Table 1 Entry point of catheter, level of catheter tip, and location of catheter

Animal	Catheter Entrance	Catheter tip level	Location of catheter
1	T16 – L1	T4/5	Extradural
2	L2 – L3	T3	Extradural
3	L1 – L2	T4/5	Subarachnoid
4	T16 – L1	T5	Extradural
5	T16 – L1	T4/5	Extradural
6	L1 – L2	T5	Extradural

Table 2 Complications associated with catheter placement

Animal	Catheter Entrance	Subdural Hemorrhage	Hemorrhagic Cavitation in Spinal Cord
1	T16 – L1	None	None
2	L2 – L3	L4	L4 – L5
3	L1 – L2	Multifocal adjacent to catheter	T6 – L5
4	T16 – L1	None	None
5	T16 – L1	None	None
6	L1 – L2	T15 – 16; L1 – 2	None

Fig. 1 Lumbar section of pig #3's formalin-fixed spinal cord showing entry point and cranial continuation of the stimulating catheter in the subarachnoid space

Fig. 2 Thoracic (left side of panel) and lumbar portions (right side of panel) of the formalin-fixed spinal cords. Note the extent of the subdural hemorrhaging in pigs #2, 3, and 6. The catheter in pig #3 was placed in the subarachnoid space

50% of the experimental animals. In one animal (Pig #3), the epidural catheter was placed in the subarachnoid space and caused severe multifocal hemorrhagic cavitations of the spinal cord accompanied by multifocal subdural

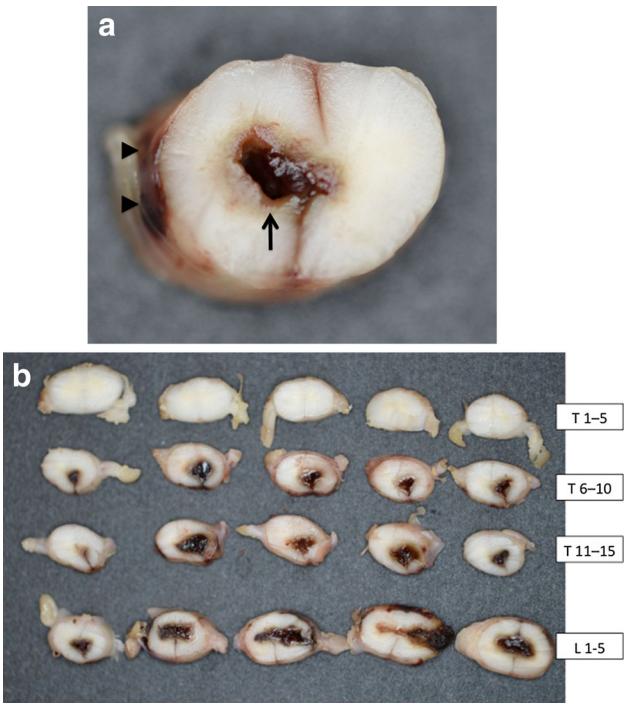

Fig. 3 (**a**) Cross section of L4 – 5 spinal cord showing hemorrhagic cavitation (arrow) and subdural hemorrhage (arrow heads) in pig #2. (**b**) Cross section from T1 to L5 showing severe hemorrhagic cavitation from L5 to T6 accompanied by variable degrees of subdural hemorrhaging in pig #3 most likely caused by subarachnoid placement and advancement of the catheter

hemorrhaging from L5 to T6. In another animal (Pig #2), hemorrhagic cavitation of the spinal cord and subdural hemorrhaging were restricted to the L4 to L5 region. Pig #6 had multifocal subdural hemorrhaging in the region from L2 to T15. The other three animals (Pigs #1, 4, and 5) did not have evidence of gross or histological lesions associated with the experimental procedure (see Table 2 and Figs 1, 2, and 3).

Discussion

This study shows that the tip of a stimulating epidural catheter can be placed accurately in the thoracic epidural space of a porcine model after percutaneous lumbar epidural entry. The study also shows that the technique is associated with a high rate of spinal cord injury, with both subdural hemorrhaging (3/6) and hemorrhagic cavitations (2/6) observed. Additionally, one catheter was placed in the subarachnoid space.

The primary objective of this study was to assess the feasibility and initial safety of the described technique with the final goal of human application; the strengths of our study reflect this goal. The live animal model selected shares a close anatomical similarity to the human spine, and

the technique used to place the epidural catheter is similar to that used in human clinical medicine.[20,21] The use of an animal model negated the risk of potential neurological or hemodynamic complications to humans posed by this experiment. Additionally, the use of anesthetized animals provides ideal conditions for success of the technique. The necroscopic and histological examinations of the spinal cord offer a robust assessment of spinal cord damage.

A potential criticism of this study is the differences in the spinal cord anatomy of pigs compared with that of humans, limiting the applicability of the results to humans. Other than the additional vertebra, the bony anatomy between species is very similar, but in swine, the spinal cord extends to the sacral spine.[19] This difference may have accounted for some of the observed spinal cord trauma, as the spinal cord is in proximity to the epidural needle in a lumbar epidural approach. Additionally, the animals weighed approximately 30 kg, differing from an average adult in both weight and spinal length. An additional criticism is the potential inability to extrapolate the results of most animal species to humans.[22,23] A further limitation relates to the use of anesthetized animals. The standard of care in adult human practice is to place thoracic epidurals in an awake patient in order to maximize safety. If the animals were awake during the procedure, it is possible that there would have been an early indication of contact with the spinal cord, limiting the observed damage. Given our results showing significant damage to the spinal cord, it appears prudent to err on the side of caution and not to subject humans to such an experiment. Previous research using a swine model for epidural placement has led to useful human experimentation, suggesting that our results may be applied to human medicine.[21]

Access to the epidural space was easily achieved in all animals on first attempt. Nevertheless, we experienced significant difficulty advancing the epidural catheter despite using numerous maneuvres to assist catheter advancement and having an experienced anesthesiologist (J.G.) perform the epidural placement. We observed that this difficulty occurred almost invariably at the point where the catheter was just at the needle tip. Advancement continued easily to the final location once it was started. There are several possibilities to explain these observations. The first is related to the type of catheter used. The stimulating catheter is styletted and much stiffer than the soft plastic catheter normally used with lumbar or thoracic epidural placement. It is possible that the stiff catheter punctured the dura and spinal cord and could not be advanced, or it "tented" the dural tissue leading to resistance to advancement. A second, and less likely, possibility is related to inherent differences between the tissue of pigs and that of humans. We surmise that significant technical difficulties would dissuade most clinicians from using this technique even without the observed spinal cord damage.

The gross necropsy and histological evidence of spinal cord damage is very concerning. It is possible that the damage was secondary to direct needle trauma; however, this seems unlikely as we did not observe cerebrospinal fluid (CSF) return through the 17G needle with aspiration. It seems more plausible that either the catheter penetrated the dura when passing the tip of the needle and directly damaged the spinal cord or a significant force was transmitted across intact dura to damage the spinal cord. Of these possibilities, the deep damage to the cord would indicate direct catheter trauma. This conclusion is further strengthened with the observation that one catheter was placed in the subarachnoid space. Further, this confirmed subarachnoid catheter placement did not show CSF return with aspiration. It is possible that CSF return was not observed because the tip of the catheter was in the spinal cord. Additionally, there are excellent safety data in human thoracic epidural placement where the spinal cord is at risk of direct needle trauma, which further supports our hypothesis that the observed spinal cord damage is secondary to the catheter and not the needle.[24,25] We cannot comment with confidence on the functional impact of the observed spinal cord damage as we did not keep the animals alive to perform neurological testing. Despite this methodological limitation, there is abundant literature to support similar injuries leading to significant functional impact.[26,27] Given the abovementioned differences in spinal cord length between pigs and humans, it is possible that the application of this technique to humans would not result in the observed rate of spinal cord damage, but it is likely that a high rate of unplanned subarachnoid catheter placement would occur. Additionally, if unrecognized subarachnoid catheter placement occurred (as occurred in our experiment), there would be a high likelihood of spinal cord damage and risk of subarachnoid overdose with advancement of the catheter and drug administration. The concern regarding subarachnoid catheter placement is further heightened as the current required to achieve appropriate myotome twitch in all animals was within the published range (1-5 mV) consistent with epidural catheter placement.[16] The high risk of spinal cord damage must preclude the application of this technique to clinical practice as patient safety is paramount.

The previously published literature on this topic is sparse. Blanco *et al*. attempted to advance a 19G soft plastic epidural catheter to the thoracic spine from a lumbar insertion in pediatric patients.[8] Their study showed varying results with most catheters coiling at the entry point of the needle. A catheter tip reaching the 12th thoracic vertebra was considered successful. Unfortunately, most patients undergoing thoracic or upper abdominal surgery require a higher block than could be reliably provided by this catheter position. Our study using a styletted catheter shows the possibility of accurately placing

an epidural catheter tip at a high thoracic level, but it is associated with frequent spinal cord damage.

Although our study shows that it is possible to reach the thoracic space from the lumbar percutaneous entry point, we also observed significant spinal cord damage in 50% of animals. Perhaps a different catheter design with a more flexible tip but rigid body, or a needle that directs the catheter at a more acute angle, or a combination of these may provide safer results. The concept of a thoracic epidural catheter that is easy to place from a lumbar insertion remains an attractive and plausible technique, but our study clearly indicates that further investigation is required before this technique can be applied to humans.

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Conflict of interest No author has any commercial or other affiliations that are or may be perceived to be a conflict of interest.

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