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Transdermal spinal catheter placement in piglets: Description and validation of the technique

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HIGHLIGHTS

- A new technique for transdermal spinal catheter insertion in piglets was determined to be feasible and easy to perform.
- The technique did not evoke any complications associated with sudden intracranial hypertension due to the device insertion.
- Contrast imaging examination showed a uniform spread of the contrast medium until the more rostral parts of the Central Nervous System in the anatomical study (Phase I).

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ABSTRACT

Background: The swine species represents a perfect model for translational medicine due to its physiological and anatomical resemblance to humans. The development of techniques for spinal catheter insertion in swine is significantly useful but, at the moment, the only technique described requires laminectomy as a surgical approach.
New method: The proposed techniques represent a transdermal approach for catheter placement in piglets. The study was divided into Phase I (anatomical study on 8 cadavers) and Phase II (in vivo application of the technique in 20 anaesthetised 30-day old piglets). A spinal needle was introduced between the L2 and L3 spinous processes with a ventro-cranial orientation until cerebro-spinal fluid leakage. It was then replaced with a Tuohy needle, used to introduce the catheter into the intrathecal space. Before inserting the catheter, the approximate length from the insertion point to the external projection of the Cisterna Magna was measured using the gradation markings on the device.
Results: The technique described allowed spinal catheter placement in all piglets. In Phase I, the correct placement was confirmed using fluoroscopy while, in Phase II, cerebrospinal fluid leakage from the needle was relied on. No clinical alterations were detected either during the procedure or during the following days.
Comparison with existing method: This technique is easy and requires less skilled operators when compared to the other existing method which involves a surgical approach. Moreover, being less invasive, it potentially leads to fewer complications.
Conclusions: In conclusion, the technique can be performed safely in piglets, and provides an easier and less invasive approach for spinal catheter insertion.

1. Introduction

The swine species represents a perfect model for studying different techniques in translational medicine due to its physiological and anatomical resemblance to humans (Tumbleson and Schook, 1996; Swanson et al., 2004; Karali et al., 2011; Testa et al., 2011). Developing a specific technique for spinal catheter insertion in pigs

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could represent a significant advance in both veterinary clinical anaesthesia and analgesia, and in translational medicine, for example for gene therapy (Fairbanks, 2003; Bottros and Christo, 2014).

The administration of analgesic compounds using an intrathecal catheter represents a worthwhile technique for continuous pain relief (Fairbanks, 2003). The systemic administration of analgesic drugs could lead to systemic side effects, such as sedation, respiratory depression (Gutstein and Akil, 2011), bradycardia, nausea, vomiting and constipation (Lamont et al., 2007). It has been proven that regional analgesic techniques are superior in terms of postoperative analgesia when compared to intravenous opioid administration, reducing the above-mentioned adverse effects in the case of both thoracic (Behera et al., 2008) and abdominal surgery (Kainzwaldner et al., 2013).

The delivery of viral vectors directly into the intrathecal space rather than systemic administration (thus avoiding the immune response) has recently become a pivotal tool for gene therapy in the neurosciences. For example, the administration of adeno associated virus (AAV) vectors targeting central nervous system (CNS) cells is useful in gene therapy for the treatment of paediatric neurological diseases, such as lysosomal storage disorders (Spampanato et al., 2011; Bevan et al., 2011), spinal muscular atrophy, the Rett Syndrome, and amyotrophic lateral sclerosis (Federici et al., 2012).

The systemic administration of these vectors produces an extensive transgene expression throughout the brain as well as in multiple organs (Bevan et al., 2011). However, intrathecal administration improves the direct effect on the target cells using lower vector doses than the one used for parenteral injections, reduces peripheral expression and can minimise the risk of a systemic immune response (Bevan et al., 2011; Dayton et al., 2012). Intrathecal injection techniques using a single puncture of the spinal space have already been described in laboratory animals (Bevan et al., 2011), including pigs (Romagnoli et al., 2014); however, studies concerning the placement of a spinal catheter are limited to only a few animal models (Fairbanks, 2003; Poon et al., 2011).

To the best of the authors' knowledge, there is only one study describing the insertion of a spinal catheter in pigs using a surgical approach: laminectomy (Federici et al., 2012). However, there are no studies describing a less invasive insertion technique, such as refinement strategy, for animal experimentation.

The aim of this study was to evaluate and validate the technique for spinal catheter placement in piglets using a transdermal approach.

2. Materials and methods

The experiments were conducted in accordance with the provisions of European Economic Community (EEC) Council Directive 86/609 adopted by the Italian Government (DL 27/01/1992 No. 116).

The study was divided into two phases: Phase I (anatomical study on 8 piglet cadavers) and Phase II (in vivo application of the technique in 20 anaesthetised 30-day old piglets).

2.1. Phase I

The cadaver was placed in lateral recumbency with the hind limbs flexed forward in order to widen the intervertebral spaces. The operator palpated the last rib with the non-dominant hand and detected the spinous processes of the L2 and L3 lumbar vertebrae with the index finger and the corresponding intervertebral space, which is wider than the other spaces.

A 22 G 0.7 × 75 mm spinal needle was introduced between the L2 and L3 spinous processes with a ventro-cranial orientation forming an angle of 75° with the spinal cord as close as possible to L3 (Fig. 1a). The needle was inserted through the skin and the subcutaneous tissue, and then through the interspinous ligament over the epidural space up to the intrathecal space. Resistance was felt as the needle penetrated the ligament, and a loss of resistance as the needle penetrated the epidural space.

The needle was then removed and substituted with a 20 G 0.9 × 50 mm Tuohy needle (Perifix ONE; B. Braun, Melsungen AG, Germany) following the previously created path. The depth of needle insertion was decided on the basis of the resistance felt by the operator and was subsequently confirmed under fluoroscopy; it was recorded using the gradation markings on the needle. It was then removed after the introduction of a 24 G catheter (Fig. 1b) (Perifix ONE; B. Braun, Melsungen AG, Germany). The injection of radiopaque contrast medium (Optiray Mallinckrodt Italia S.p.A.) through the catheter, and its intrathecal spread, confirmed the correct placement of the device under fluoroscopy (Fig. 2).

2.2. Phase II

The piglets enrolled in this part of the study were transferred to our facility from a local breeding farm (Società Agricola Pasotti S.S., Imola, Italy) on the day of weaning (28 days post birth). They were control animals involved in research authorised by the Italian Ministry of Health.

On the day of the procedure, anaesthesia was induced with sevoflurane (SevoFlo; Abbott Laboratories, Chicago, IL, USA) in oxygen (1 l/min) delivered via a mask attached to a circle system and a small animal anaesthetic machine. He pigs were tracheally intubated, and anaesthesia was maintained with sevoflurane in oxygen (10 ml/kg/min). The heart rate (HR), respiratory rate (RR) and end tidal carbon dioxide ($EtCO_2$) were monitored during the procedure. Venous access was achieved from an auricular vein, and fluid therapy (Ringer Lactate) was administered at the rate of 10 ml/kg/h.

For the catheter insertion, the piglet was positioned in lateral recumbency. The area was clipped and surgically prepared using chlorexidine and alcohol as suggested by Campoy and Read (2013); a standard sterile surgical approach was used. The procedure was performed as described above. The correct placement of the Tuohy needle was confirmed by cerebrospinal fluid (CSF) leakage.

Before inserting the catheter, its length was measured from the insertion point to the external projection of the Cisterna Magna using the gradation markings along the catheter as a reference, and the device itself was filled with 0.2 ml of phosphate buffered saline (PBS). This step was crucial in order to avoid kneeling of the device into the intrathecal space and air injection. The catheter was inserted and advanced until the operator felt resistance, most probably due to the arrival of the tip at the cranial margin of the Cisterna Magna.

At the end of the procedure, the catheter was removed and sevoflurane administration was stopped. All the piglets were strictly monitored until complete recovery from anaesthesia and for the following 6 h in order to detect any complications caused by the procedure. The animals were housed in multiple stalls with heat lamps as requested by the mandatory standards of animal welfare laws and were monitored at least 5 times per day for the following week.

3. Results

The technique described allowed spinal catheter placement in all piglets. The catheter slid in easily, proving the size of the device to be adequate for such small animals.

During phase I, the authors confirmed the L2 and L3 intervertebral space to be the most reliable for the introduction of the needle since it is the widest and most palpable, and lateral recumbency