

Short title: Indwelling ear catheter technique in sows

Development and refinement of a technique for short-term intravascular ear catheter placement in mature sows

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Abstract

Intravenous drug administration in adult swine is difficult to perform due to inaccessible superficial veins and thick subcutaneous fat layers. However, successful intravenous drug administration is critical for many biomedical applications including pharmacokinetic studies as extravascular drug administration can influence the drug's absorption and elimination rate. The purpose of this study was to develop and refine an effective technique for indwelling ear vein catheter placement in the conscious mature sow. We developed a protocol using a topical anesthetic cream and minimal physical restraint to place indwelling catheters in the auricular vein of six multiparous sows. This method was quick (3 minutes 20 seconds \pm 8 seconds (mean \pm SE per catheter)), effective (11/12 catheters successfully placed) and reliable, allowing a large drug volume (20-22ml) to be administered successfully during the trial without relying on prolonged restraint or general anesthesia of the sow.

Keywords: Catheterization, Ear vein, Sow, Refinement

Intravenous access is important in veterinary medicine to administer drugs for treatment of clinical disease. However, intravenous drug administration is difficult to perform on swine due to inaccessible superficial veins and thick subcutaneous fat layers¹. For all swine ages and weights, the two most common methods for intravenous administration include: 1. Temporary catheterization² or 2. Jugular vein injection using a "blind stick" approach (defined as drug administered without vein visualization^{3,4}). Blind-stick injection is unreliable as it is difficult to ensure that drug is not administered extravascularly. Thus, access to the vein using an indwelling catheter is the most appropriate method for intravenous drug administration.

To the authors' knowledge three procedures for auricular vein catheterization for swine have been reported in the literature^{5, 6, 7}. Phillips and colleagues⁵ successfully placed ear vein catheters for blood collection while sows were anesthetized. General anesthesia use can contribute to increased variation when conducting pharmacokinetic studies because anesthetic agent systemic effects on clearance, absorption time and volume of distribution for the drug of interest are most often unknown. Porter and colleagues⁶ placed catheters in restrained sows with no local or general anesthesia used. Single catheter placement took on average 30 minutes requiring prolonged sow restraint. Rushen and colleagues⁷ did not provide detail on the catheter placement process itself. Due to a gap in the literature, our research team developed and refined an effective method for indwelling ear vein catheter placement and access as a means to confidently administer drugs intravenously in adult swine without relying on prolonged restraint or general anesthesia. Although catheterization of other veins including the jugular vein^{8,9}, subcutaneous abdominal vein¹⁰, and uterine vein¹¹ has been successfully conducted in swine, catheterization of these veins requires anesthesia or prolonged restraint of the patient. This technique is novel as catheters are placed in the auricular vein of mature swine without the use of prolonged restraint, or general anesthesia. In addition, this technique utilizes a local anesthetic to minimize pain sensitivity to catheter placement, thus developing a reliable method for intravenous access for drug administration while keeping the sow's welfare and comfort a priority.

This laboratory technique was carried out on healthy female sows (*Sus scrofa domestica*; age: 1-3 years, weight: 202-222 kg). Health status was determined by physical examination of each sow. Physical examination included lung and heart auscultation, rectal temperature and reproductive tract ultrasonography. The animals were cared for in accordance with the Animal

Welfare Act and the Guide for the Care and Use of Laboratory Animals, 8th edition. This work was performed in an Association for Assessment and Accreditation of Laboratory Animal Care (AALAC) accredited facility at the Iowa State University College of Veterinary Medicine. Sows were housed individually in pens (3.7 m length x 1.4 m width x 1.2 m height) with a rubber mat (3.5 meter length x 1.3 m width). Lights were on a 12:12 light dark cycle (light hours [0600 and 1800]) and room temperature ranged between 12.5°C to 20.5°C. No other additional bedding material (straw, hay etc.) was provided but sows were provided with cotton rope for environmental enrichment. Animals had free access to drinking water and were hand-fed a custom mixed diet composed of corn, soybean meal and soy hulls. They were allowed a 14-day acclimatization period before the beginning of the study. Experimental procedures were approved by the Institutional Animal Care and Use Committee at Iowa State University (United States).

Sows were concurrently enrolled in a pharmacokinetic study in which they received either an oral or intravenous meloxicam (Loxicam, Norbrook Inc. Lenexa, USA) dose and had blood collected up to 48 hours post drug administration. Twelve blood samples were collected over the 48 hour trial period with a total of 108 ml of blood collected from the jugular vein. Two sows were used to refine the catheterization technique prior to study commencement, and the remaining 6 sows were catheterized twice, once in each ear during the trial.

One hour prior to catheterization, a topical anesthetic cream (15g; EMLA cream; Hi-Tech Pharmacal Co Inc, Amityville, USA) was applied to each sows' ear pinna covering the entire length of the ear from base to tip (Figure 1). After 1 hour, excess cream was wiped off using a paper towel. Once sows were manually restrained with a pig snare, the ear was cleaned with 70%

isopropyl alcohol and 0.75% iodine scrub. An indwelling catheter (22 gauge, 2.54 cm long; manufacturing code: SMIT-9986, Smiths Medical, Dublin, USA) was inserted into the distal portion of the largest and most prominent auricular vein (per visual assessment) until blood was present in the catheter hub. Once placed, the stylet was removed and transparent tape (Dermiclear Tape, Johnson & Johnson, New Brunswick, USA) was placed over the catheter to temporarily secure it. The catheter was capped with a threaded injection cap (Hospira Inc, Lake Forest, USA) and the skin surrounding the catheter was dried with gauze to absorb any blood that may prevent proper tape adherence to the skin.

The catheter hub was glued to the ear skin using surgical glue (3M Vetbond Tissue Adhesive, 3M Animal Care Products, St. Paul, USA) applied underneath the transparent tape for further security. Two transparent dressings (Tegaderm, 3M Animal Care Products, St. Paul, USA) were placed over the entire catheter hub and injection port. Special care was taken to orient the dressing where the distal edges could be folded over the ear for further security (Figure 2). A 30.5 cm butterfly catheter (SurFlo Plastics & Engineering Inc, Warren, USA) was inserted through the transparent dressing perforating the injection cap and flushed with 6 ml heparinized saline (Hospira Inc, Lake Forest, USA; 50 IU Heparin/ml saline) to ensure patency.

Three hours after drug administration, transparent dressing, tape and the catheter were removed from the ear vein. Gauze was taped over the catheter site providing pressure to prevent bleeding. Gauze was removed 1 hour later and the ear was checked for bleeding. If excess surgical glue was difficult to remove, hydrogen peroxide was applied to the ear to assist in removal. Ears were cleaned with isopropyl alcohol and evaluated for inflammation or hematoma formation.

Prior to the study commencement, 2 sows were used to refine catheter placement and access technique. Catheters were placed as described above with the exception that sows were not physically restrained. For these efforts, sows were controlled by providing feed in a small pan to limit excessive movement. Success rate for catheter placement was low (25%) resulting in multiple hematoma formation and failed patency. Therefore manual restraint with a snare was required.

The original goal for this project was to develop a technique for indwelling catheter placement without the use of physical restraint. However, during our pilot study using only 2 sows, catheter placement without restraint was difficult to perform and had a low success rate. Based on these difficulties, the 6 sows on-trial were restrained using a pig snare for catheter placement and drug administration. Although restraint may have caused temporary stress, success rate improved dramatically (92%), hematoma formation was rare and overall handling and interaction time per sow decreased. Placement time was also less compared to previous published techniques using physical restraint⁹. Although the use of a sedative to restrain the sow may have caused less temporary stress compared to the snare, the sedative drug's unknown systemic effects on clearance, absorption time and volume of distribution made its use problematic.

Intravenous catheters were successfully placed in both ears of 6 on-trial restrained sows for a total of 12 successful ear vein catheter placements. Catheters were placed in ears within 3 min 20 sec \pm 8 sec (mean \pm SE per catheter) from the time sow restraint began. Catheter patency was evaluated with a sterile saline flush and all catheters with one exception remained patent for drug administration. Each sow was administered 20-22 ml meloxicam over 90 seconds. Total drug volume was successfully administered to each sow while restrained using a pig snare.

No permanent physical alterations were noted with this technique. The most prominent change to the ear was temporary pinna discoloration at cream application site and mild epithelial bruising around catheter placement site. Full recovery of ear occurred one week after placement.

The catheter that failed to maintain patency was removed by a neighboring sow through pen bars. After this incident, sows were moved before the trial start into housing that minimized sow to sow contact until after the drug was administered via the catheter. Although catheters could hypothetically be removed by physical force (rubbing, scratching), no such behavior was noted during the trial. No sows appeared to react to catheter presence and no sows attempted to remove their own catheter.

We found the described catheter placement technique to be an effective and quick way to administer drug intravenously. This technique provides secure intravenous access and can be utilized for studies or treatments requiring intravenous drug administration. Blood was not collected from the auricular vein catheter and further evaluation of the efficacy of this type of catheter for blood collection is needed. The application of this method contributes to the ‘refinement’ of experimental procedures, according to the principle of ‘3Rs’, by reducing unnecessary sow stress and pain associated with prolonged restraint and catheter placement.

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Figure 1. Topical anesthetic cream (15g; EMLA cream; 2.5% lidocaine and 2.5% prilocaine) was applied to each sows' ear pinna covering the entire length of the ear from base to tip.

Figure 2. Final layer of transparent dressing is placed over the catheter hub and injection port and prevented displacement of the catheter from the vein.

