Straight to the Source - Indications and Use of Regional Limb Perfusions
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Introduction

Regional limb perfusions (RLPs) are increasingly being performed and are an effective means of delivering a high concentration of solution directly to a selected region while decreasing the risks of side effects associated with standard systemic dosing. Depending on the needs of the patient, antimicrobials, analgesics, local anesthetics, and a variety of other solutions can be delivered via RLP. The technique for either intravenous (IV) or intra-arterial (IA) perfusion is relatively easy and can be performed on the farm as well as in a hospital setting. Patient selection, choice of medication, and familiarity with the procedure can improve treatment success. This program aims to offer a broader understanding of the indications and uses of RLPs, as well as an explanation of techniques and best practices.

History

Regional limb perfusions were originally developed for administration of anesthetic medications to provide regional anesthesia for surgical procedure in humans, now commonly referred to as Bier blocks[1]. They have since been adapted for animals, and the use and variety of drugs used for RLPs has expanded. Local delivery of antimicrobials is likely the most common indication for RLP; however, local anesthetics and analgesics can additionally be utilized for multimodal effects. More recently, IA perfusions have been performed for the administration of orthobiologics[2].

The Basics

Intravenous RLPs require application of a tourniquet to create a pressure gradient between the intra- and extravascular space to promote diffusion of the perfusate into the tissues[1]. The primary requirement is that there is an accessible regional vessel and a tourniquet, or two, can be applied to isolate the area of interest. While the cephalic or saphenous veins are most commonly used, any regional vessel may be used provided it can be accessed for venipuncture. In cases with extensive soft tissue compromise or vascular damage, use of RLPs may be limited. Ultrasound guidance can assist catheterization of peripheral vessels, particularly for arterial perfusion[3,4,5]. While tourniquets are necessary for IV RLPs, tourniquet application is generally contraindicated when performing IA RLPs due to increased risk of thrombosis and dermal compromise[4].

Case Selection & Preparation

In a clinical setting, case selection for RLPs is important to minimize risks to the individual performing the procedure and to maximize the effectiveness for the patient. RLPs were initially performed under anesthesia due to the uncertain ability of horses to tolerate tourniquet application[6]; however, the majority of horses tolerate the procedure well with standing sedation and this has since become standard practice[7]. However, inadequate sedation, inexperienced horse handlers, or noncompliant patients are a reality and can decrease the effectiveness of the procedure by allowing for excess patient motion and perfusate leakage proximal to the tourniquet. While most adult horses need only be well sedated for RLPs, foals should be anesthetized, and young or difficult horses may only be able to be treated with a single RLP while anesthetized for an initial wound debridement or arthroscopic lavage. Aside from anesthetizing the patient, methods for decreasing movement during tourniquet application include perineural analgesia or addition of a local anesthetic to the perfusate volume[8].

Supplies should be gathered prior to sedation of the patient. Either a wide rubber tourniquet (Esmarch bandage) or pneumatic tourniquet can be used[9]. A small gauge needle (25g butterfly catheter is preferred by the author) is recommended to reduce vascular trauma, particularly when repeated

perfusions are planned. Following perfusion, a pressure bandage should be applied over the venipuncture site to prevent perivascular leakage while the tourniquet is in place. Following removal of the tourniquet and pressure bandage, application of a topical anti-inflammatory (1% diclofenac sodium) and a support bandage can be used to decrease subcutaneous thickening and maintain vessel integrity[10].

Medications:

Antimicrobials

Use of RLPs with antimicrobials is common for the management of cellulitis, synovial sepsis, wounds, and osteomyelitis. While the specific technique varies with regard to the medication type, perfusate volume, and perfusion time, the goal is to achieve high concentrations of antimicrobial in the target tissue, increasing treatment efficacy and limiting systemic side effects. The concentration of antimicrobial in the target tissue should ideally be 8-10 times higher than the MIC to be efficacious, which is a concentration that is difficult to safely achieve with systemic administration[11]. With RLPs, these concentrations can be readily achieved in synovial fluid with administration of approximately one third of the systemic antimicrobial dose in a total perfusate volume ranging from 10-120ml[12].

Choice of antimicrobial is ideally based on culture and sensitivity. Unfortunately, however, RLPs are often used for high-risk musculoskeletal infections (i.e. synovial sepsis, infected orthopedic implants) while culture results are still pending or have negative results; empirical treatment with amikacin is frequently selected for its efficacy against common equine orthopedic pathogens and concentration-dependent properties allowing for a 24 hour treatment interval[1]. However, a variety of other antimicrobials have also been used for IV RLPs in clinical cases[13].

Analgesics & Local Anesthetics

Regional limb perfusions with local anesthetics were developed in humans and have long been performed in cattle for procedures of the distal limb. The addition of mepivacaine to the perfusate volume in horses can be helpful to decrease mechanical nociception and does not appear to impact the concentration of amikacin reaching the target tissue[14]. Anecdotally, the addition of local anesthetics to the perfusate can help with tolerance of the procedure and can provide additional analgesia when performing a standing laceration repair. The author has used 2% mepivacaine at a volume of 10ml for distal limb perfusions and 20-25ml for perfusion in the proximal limb with good success in difficult horses or to facilitate laceration debridement and repair. One should be mindful of the total volume of local anesthetic administered, as excessive amounts can result in toxicity. Dosing should not exceed 10 mg/kg or 250ml of 2% lidocaine hydrochloride for a 500kg horse at a time[15].

Opioids have also been evaluated for use in RLPs. The analgesic effects of both butorphanol and morphine could be useful in horses with painful musculoskeletal conditions as an adjuncts to nonsteroidal anti-inflammatory drugs. Butorphanol has been administered via RLP and noted to achieve measurable levels in synovial fluid[16]. Further, morphine, when combined with gentamicin for RLP, did not cause adverse effects or affect the concentrations of gentamicin in the target tissue[17]. Ability of these opioids to alter mechanical nociceptive thresholds following RLP remains unclear.

Bisphosphonates

Intravenous RLP of bisphosphonates has been clinically performed to decrease the cost and theoretically decrease systemic side effects, though the clinical evidence for this route of administration remains thin. Reported indications include the treatment of pain associated with navicular syndrome or dorsal metacarpal disease in racehorses[18,19]. However, in a recent study, use of tiludronate did not improve

lameness scores over medication of the coffin joint and therapeutic shoeing in horses with navicular syndrome[20]. Further, a study investigating the safety of RLP with tiludronate with respect to overall health of synovial fluid and cartilage suggested that perfusion with 50mg of tiludronate may adversely affect articular cartilage[21]. Further investigation into the use, route of administration, and indications for bisphosphonates is needed.

Regenerative Therapies

Intralesional injection of mesenchymal stem cells or orthobiologics for musculoskeletal injuries limits the anatomical regions that can be treated with these therapies. Injuries within the hoof capsule are being more frequently diagnosed with the increasing availability of advanced imaging. Both IV and IA RLPs have been described as alternative methods of administration of mesenchymal stem cells[4,22]. Persistence in the target tissues and more homogenous distribution of MSCs following IA RLP favors this route of administration over IV RLP, though it is technically more difficult[4]. Use of ultrasound guidance for IA injection can be readily performed in standing horses[23].

Contrast

Regional perfusion of intravascular contrast can allow for identification of local vascular anomalies. Clinically, venograms are utilized to investigate vascular integrity and can be correlated with severity of disease with laminitis[24]. Contrast can additionally be used to document venous thrombosis or vascular compromise secondary to traumatic injuries, which can have prognostic value. More recently, RLP with gadolinium contrast has been used to enhance visibility of lesions on MRI and understand the vascularity of these lesions[25].

Procedure:

IV Regional Limb Perfusion

A capable horse handler should first be identified. This is imperative as the safety of the veterinarian performing the procedure and the overall effectiveness of the procedure is reliant on this person. The handler should be able and comfortable applying and holding a twitch and ensuring that the horse bears weight on the affected limb throughout the procedure to minimize leakage around the tourniquet. Once a handler is secured, identify a location for performing the procedure. This should be a well-lit and open area with stable footing. A vessel should be selected for perfusion, and in most cases this will be the cephalic or saphenous vein. The venipuncture site should be proximal to the target area. Clipping of the hair over the venipuncture site is clinician dependent, but can be performed to better visualize the vessel if needed. The horse should then be sedated. In general, a combination of an alpha-2 agonist and an opioid (detomidine hydrochloride and butorphanol tartrate is preferred by the author) works well. The addition of acepromazine can be beneficial if clinically appropriate. Peripheral nerve blocks can be performed at this time, followed by preparation of the venipuncture site.

The horse should then be adequately restrained, and the tourniquet is applied. In the distal limb, applying a roll of brown gauze on either side of the flexor tendons and wrapping the tourniquet around this will aid in vascular occlusion. In the proximal limb, use of a roll of brown gauze or several gauze 4x4s squares folded in half and placed underneath the tourniquet and directly overlying the vessel is helpful. Once the tourniquet is in place, venipuncture is performed, and the limb is perfused over 1-3 minutes, checking frequently to ensure the catheter remains in place in the vessel. Following administration of the perfusate, firm pressure using 4x4 gauze is applied over the venipuncture site as the catheter is removed and secured in place with a pressure wrap to minimize perivascular leakage while the tourniquet is in place.

IA Regional Perfusion

For IA RLP in the standing horse, injection of the median artery in the thoracic limb[3] and cranial tibial artery in the pelvic limb[5] has been described. Preparation of the patient and technique is similar as for IV RLP; however, no tourniquet is applied, and injection is ultrasound-guided. Perineural anesthesia (median and ulnar nerve blocks in the thoracic limb and peroneal nerve block in the pelvic limb) can be performed; however, the author typically performs only local blocking at the proposed site of IA injection. Following injection of the perfusate, a pressure bandage is applied.

Complications

Primary complications with RLPs are related to treatment failure or secondary vascular trauma. Improper application of the tourniquet can inhibit ability to identify the vessel of interest, decrease the stimulated pressure gradient, and allow diffusion of the perfusate proximal to the tourniquet, thereby decreasing the concentration of perfusate in the desired tissue. Patient movement can also cause perfusate leakage and contribute to treatment failure. Prolonged application of the tourniquet can result in vessel and nerve injury. Repeated perfusions can cause local inflammation including subcutaneous thickening, local phlebitis, or thrombosis. Use of indwelling catheters can be utilized in cases where prolonged treatment is necessary; however, complications are reported to be as high as 27%[26] compared to 12%[13] with butterfly catheters. Thus, rotating use of regional vessels, smooth venipuncture technique, application of support bandages, and application of pressure is recommended for long-term RLPs.

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