

Intravenous Regional Limb Perfusion in the Horse

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Introduction

In equine practice, patients with wounds to the distal extremities are commonly encountered and many times these wounds are extensively contaminated and/or infected. Wounds involving synovial structures and those with significant vascular compromise can be especially challenging due to the limited blood supply of the infected tissues. In these cases, systemic administration of antimicrobials alone often yields local concentrations well below those needed to eliminate the bacterial population from the tissues involved. Intravenous regional limb perfusion (IVRLP) alone yields higher tissue antimicrobial concentrations than systemic administration and often results in a more favorable outcome.¹

Basic Technique

A superficial vein proximal to the area to be perfused should be identified for needle or IV catheter placement. The palmar/plantar digital veins can be utilized although the use of more proximal veins such as the cephalic or the saphenous vein has been shown to be effective in perfusing the tissues of the distal limb.^{2,3} A tourniquet is applied to the limb proximal to the proposed perfusate administration site and area to be perfused. A second tourniquet can be applied distal to the area to be perfused depending on the location (e.g. carpus or tarsus.) The administration site is aseptically prepared, and a 20-22 gauge IV catheter is placed or a 22-25 gauge winged infusion needle set is inserted into the vein from proximal to distal. The perfusate volume is then administered at a slow, constant rate over 1-5 minutes either by hand or using a syringe pump. If the perfusate is administered using a needle set, a small pressure bandage should be applied over the venipuncture site following removal of the needle to prevent leakage and hematoma formation. The tourniquet is left in place for a period of time (20-30 minutes), allowing the antibiotic to distribute into the tissues isolated by the tourniquet. After the required time has passed, the tourniquet is removed allowing reperfusion of the limb. If an IV catheter was utilized, it can be "hep-locked" and maintained under a bandage for future IVRLPs or removed. In most cases, IVRLP can be performed effectively in the standing, sedated patient however fractious patients may require general anesthesia. IVRLPs can be performed as frequently as deemed necessary by the practitioner, but are generally performed once daily for 1-7 days.

Variations in IVRLP technique are common, both in experimental studies and in clinical practice. Inconsistencies in technique make direct comparison of results difficult and some conflicting evidence relating to efficacy or superiority of a particular technique exists. Variables include tourniquet location, duration, number and pressure, antibiotic class and dosage, and perfusate volume. The following text discusses some of these variables and provides scientific evidence relative to the efficacy of various techniques frequently used in equine IVRLP.

General Anesthesia vs. Sedation

Movement of the horse during IVRLP is thought to affect tourniquet integrity and IVRLP efficacy. Appropriate general anesthesia does eliminate movement and is more comfortable and safer for veterinary personnel, but it is expensive and harbors its own challenges and potential complications. When general anesthesia is required to appropriately address the injury (laceration, septic synovial structure etc.), IVRLP under general anesthesia is certainly indicated; however, inducing general anesthesia specifically for IVRLP is not warranted in most cases. Adequate tissue antimicrobial concentrations can be achieved via IVRLP in standing, sedated horses.¹⁻³ Peri-neural local anesthesia does decrease movement and is recommended.^{4,5} Anesthesia of the median, ulnar and musculocutaneous nerves or tibial and deep peroneal nerves prior to tourniquet application and perfusion can provide appropriate local analgesia for standing, sedated cephalic or saphenous IVRLP, respectively.

Tourniquet Type and Pressure

For IVRLP to be effective, at least one tourniquet must be applied to the limb, at a location proximal to the target area and the site of antibiotic perfusate administration. Tourniquet type has been directly compared and both pneumatic and wide-rubber (Esmarch bandages) tourniquets have been shown to be effective. Narrow-rubber tourniquets are ineffective and not recommended.⁶ The optimal sub-tourniquet pressure for IVRLP in horses has not been established but pneumatic tourniquet pressures between 300 and 420 mm Hg have been used clinically and in experimental studies. The sub-tourniquet pressure achieved with a wide-rubber tourniquet is not routinely measured but has been shown to be adequate when the tourniquet is applied as tightly as possible.⁷ Interestingly, a recent equine IVRLP meta-analysis⁴ concluded that wide-rubber tourniquets were more effective than pneumatic tourniquets when pneumatic tourniquet sub-tourniquet pressure was set at ≥ 400 mm Hg.

Tourniquet Duration

A desired tourniquet application time of 30 minutes is practical and clinically effective and is used by many researchers and practitioners. When IVRLP is performed under appropriate general anesthesia, no movement occurs; however, in standing, sedated horses, the amount of movement is often unpredictable. It is thought that the tourniquet is the greatest source of discomfort for the horse, and it is this discomfort that induces movement. Horses tend to move more toward the end of the tourniquet time, as the sedation starts to wear off. Therefore, a shorter tourniquet time, provided effective concentrations are achieved, may be optimal. Recent research has evaluated different tourniquet durations.^{8,9} In one cephalic IVRLP study, no difference in synovial fluid amikacin concentration was seen in the radiocarpal joint (RCJ) or metacarpophalangeal joint at 20 and 30 minutes of tourniquet time.⁷ In another study, no difference was found between 10 and 30 minutes.⁸ The results of these studies^{7,8} indicate a shorter tourniquet time may be effective, but a longer time of 30 minutes is not detrimental and should be desired clinically.

Tourniquet Number

The addition of a second tourniquet distal to the area to be perfused has been described.¹⁰ Studies^{3,11} have observed inadequate RCJ synovial fluid amikacin concentrations following cephalic IVRLP using a single proximal tourniquet and a 1 g amikacin perfusate, but therapeutic concentrations were noted with the addition of a second tourniquet placed distal to the carpus.¹¹ In contrast, another study¹² reported adequate concentrations in the RCJ with a single tourniquet; however, a larger volume perfusate with 2 g amikacin was used. Inadequate amikacin concentrations in the synovial fluid of the tarsocrural joint have also been noted using a single gaskin tourniquet and up to 2 g amikacin perfusate.¹³ These results indicate IVRLP using two tourniquets, one above and one below, is likely necessary for treatment of sepsis or injury to the carpal or tarsal area.

Perfusate Volume

The optimal volume of perfusate has not been accurately determined and volumes ranging from 10 to 250 mLs are reported. Several recent experimental studies have been conducted comparing perfusate volume.^{3,14-16} Several studies^{3,14} report no difference in amikacin concentrations achieved regardless of volume (10-120 mL) while others report a higher volume to be superior (60-100 mL).^{15,16} Variations in IVRLP technique such as antimicrobial dose and joint(s) sampled make comparisons between these experimental studies difficult.

Antimicrobial Selection

Ideally, selection of the antimicrobial(s) to be used in IVRLP should be based on culture and sensitivity results; however, this is usually not clinically practical. Aminoglycoside antimicrobials are most commonly used for IVRLP in clinical practice and experimental studies. Currently, amikacin is considered to be more effective than gentamicin against both gram-positive and gram-negative pathogens common in equine orthopedic sepsis. Many other antimicrobials have been studied and administered clinically via IVRLP. Pharmacokinetic and pharmacodynamic properties of available antimicrobials and the clinical scenario should be considered when formulating an IVRLP treatment protocol.

The optimal dose of a specific antimicrobial administered as an IVRLP has not been clearly established. Administration of one-fifth to one-third of the recommended systemic dose is commonly cited but most practitioners use a pre-set dosage for adult horses regardless of body weight. For amikacin in adults, a 1 g perfusate is typically adequate for cephalic IVRLP, but a 2 g perfusate is recommended for saphenous IVRLP.¹⁷ One study comparing 2 g to 3 g amikacin cephalic IVRLP reported 3 g as excessive and not recommended.¹⁸ Foals with septic arthritis are also generally systemically ill, requiring systemic antimicrobial therapy administered concurrently with IVRLP. Thus, peak and trough systemic antimicrobial concentrations are just as important as local concentrations. In one study using amikacin in healthy neonatal foals¹⁹, 1/3rd of the systemic dose (8.3 mg/kg) given as a cephalic or saphenous IVRLP and 2/3rd (16.7 mg/kg) of the dose given IV resulted in therapeutic and safe plasma and synovial fluid amikacin concentrations for pathogens considered to have intermediate susceptibility.

Individual Horse Variation

Most equine IVRLP studies report a large range of antibiotic concentrations achieved in tissues and synovial fluid. Equine practitioners should keep in mind that individual horses may achieve vastly different local antimicrobial concentrations following IVRLP. Experimental studies are generally performed on healthy horses with normal limbs. The presence of disease or injury in the limb can alter physiologic parameters that could influence the antimicrobial concentration achieved by IVRLP.

Author Preference

Clinically, the author prefers cephalic/saphenous IVRLP using a single wide-rubber tourniquet applied in the proximal antebrachium/gaskin for distal limb injury or disease. For carpal/tarsal injury or disease, a second wide-rubber tourniquet is applied in the mid-cannon region. A winged infusion set is preferred over an indwelling IV catheter in most cases. Amikacin is most often utilized for therapy unless culture results are available and indicate a different antimicrobial. For adults, 1 g of amikacin in a total perfusate volume of 60 mLs is used for cephalic IVRLP while 2 g is used for saphenous IVRLP. Foals are administered 1/3 of the calculated systemic dose in a 30 mLs perfusate volume in addition to the 2/3 systemic dose. A 30-minute duration in tourniquet time is desired but 20 minutes is considered acceptable. General anesthesia is used in adults only if required to address the injury or in extremely fractious horses but is always used in foals. Regional peri-neural anesthesia is almost always administered for standing IVRLP prior to tourniquet application and perfusion. Cephalic/saphenous IVRLP is often performed for several (7+) consecutive days without complication.

References

- 1) Rubio-Martínez LM, Cruz AM. Antimicrobial regional limb perfusion in horses. *J Am Vet Med Assoc.* 2006;22:706-12.
- 2) Kelmer G, Bell GC, Martin-Jimenez T, et al. Evaluation of regional limb perfusion with amikacin using the saphenous, cephalic, and palmar digital veins in standing horses. *J Vet Pharmacol Ther.* 2013;36:236-40.
- 3) Moser DK, Schoonover MJ, Holbrook TA, et al. Effect of regional intravenous limb perfusate volume on synovial fluid concentration of amikacin and local venous blood pressure in the horse. *Vet Surg.* 2016;45:851-858.
- 4) Redding LE, Elzer EJ, Ortvad KF. Effects of regional limb perfusion technique on concentrations of antibiotic achieved at the target site: A meta-analysis. *PLoS One.* 2022;17:e0265971.
- 5) Mahne AT, Rioja E, Marais HJ, et al. Clinical and pharmacokinetic effects of regional or general anaesthesia on intravenous regional limb perfusion with amikacin in horses. *Equine Vet J.* 2014;46:375-9.
- 6) Levine DG, Epstein KL, Ahern BJ, et al. Efficacy of three tourniquet types for intravenous antimicrobial regional limb perfusion in standing horses. *Vet Surg.* 2010;39:1021-4.

- 7) Plunkett AH, Schoonover MJ, Young JM, et al. Subtourniquet pressures generated by application of wide-rubber tourniquets in standing, sedated horses. *Vet Surg.* 2019;48:417-423.
- 8) Aristizabal FA, Nieto JE, Guedes AG, et al: Comparison of two tourniquet application times for regional intravenous limb perfusions with amikacin in sedated or anesthetized horses. *Vet J* 2016;208:50-54.
- 9) Kilcoyne I, Dechant JE, Nieto JE: Evaluation of 10-minute versus 30-minute tourniquet time for intravenous regional limb perfusion with amikacin sulfate in standing sedated horses. *Vet Rec* 2016;178:585.
- 10) Whitehair KJ, Blevins WE, Fessler JF, et al: Regional perfusion of the equine carpus for antibiotic delivery. *Vet Surg* 1992;21:279-285.
- 11) Schoonover MJ, Moser DK, Young JM, et al. Effects of tourniquet number and exsanguination on amikacin concentrations in the radiocarpal and distal interphalangeal joints after low volume intravenous regional limb perfusion in horses. *Vet Surg.* 2017;46:675-682.
- 12) Bergstrom TC, Kilcoyne I, Magdesian KG, et al. Increasing tourniquet number has no effect on amikacin concentration within the radiocarpal joint in horses undergoing intravenous regional limb perfusion. *Am J Vet Res.* 2022;83:364-370.
- 13) Jurek KA, Schoonover MJ, Williams MR, et al. Effect of perfusate volume on amikacin concentrations after saphenous intravenous regional limb perfusion in standing, sedated horses. *Vet Surg.* 2022;51:665-673.
- 14) Hyde RM, Lynch TM, Clark CK, et al: The influence of perfusate volume on antimicrobial concentration in synovial fluid following intravenous regional limb perfusion in the standing horse. *Can Vet J* 2013; 54:363-367.
- 15) Oreff GL, Dahan R, Tatz AJ, et al: The effect of perfusate volume on amikacin concentration in the metacarpophalangeal joint following cephalic regional limb perfusion in standing horses. *Vet Surg* 2016;45:625-630.
- 16) Godfrey JL, Hardy J, Cohen ND: Effects of regional limb perfusion volume on concentrations of amikacin sulfate in synovial and interstitial fluid samples from anesthetized horses. *Am J Vet Res* 2016; 77:582-588.
- 17) Jurek KA, Williams MR, Schoonover MJ, et al. Unpublished data
- 18) Harvey A, Kilcoyne I, Byrne BA, et al. Effect of dose on intra-articular amikacin sulfate concentrations following intravenous regional limb perfusion in horses. *Vet Surg.* 2016;45:1077-1082.
- 19) Wallace PD, Schoonover MJ, Williams MR, et al. Unpublished data