Best practices for use of regional limb perfusion in a field setting

Regional limb perfusion is an effective method of local antimicrobial delivery to the distal extremities of the horse. This technique is easy to perform and can augment the treatment of infectious orthopaedic injuries and wounds. Understanding the benefits and limitations of the procedure, recognising appropriate case selection and optimising the approach to regional limb perfusion will enable the field practitioner to incorporate this technique into their clinical approach and skillset, and implement it effectively.

https://doi.org/10.12968/ukve.2024.8.4.164

Jesse Tyma DVM DACVS-LA; Surgeon at Rhinebeck Equine, Rhinebeck, New York, USA.
Email: jftyma.dvm@gmail.com

Key words: infection | orthopaedic | injury | field medicine | equine

Submitted: 6 November 2023; accepted for publication following double-blind peer review: 10 March 2024

Critical evaluations of regional limb perfusion and reports on its use in horses have expanded over the past 40 years. The increased interest in regional limb perfusion for treatment of equine orthopaedic infection began with a series of papers published in the early 1990s evaluating experimental intraosseous regional limb perfusion of the carpus in horses (Whitehair et al, 1992a; 1992b), and a small case series evaluating the treatment of implant-associated osteomyelitis (Whitehair et al, 1992c). Since then, dozens of studies have been performed evaluating the efficacy of the technique with a breadth of variables and mostly using normal, healthy horses (Levine et al, 2010; Hyde et al, 2013; Kelmer et al, 2013; Aristizabal et al, 2016; Godfrey et al, 2016; Harvey et al, 2016; Moser et al, 2016; Oreff et al, 2016; Sole et al, 2016). Thus, information on the effect of local and systemic disease and prospective evaluation in naturally occurring cases is limited. While defined endpoints of successful treatment differ between studies, resolution of clinical infection, return to clinical soundness and ultimately, return to previous level of activity remain the goals in treatment of any orthopaedic infection.

An understanding of the findings and limitations of these studies can help practitioners to optimise their use of regional limb perfusion in clinical cases (Watts, 2011), as many of the conclusions remain largely speculative and often contradictory between studies. A review of the literature around regional limb perfusion was last compiled in 2021 (Biasutti et al, 2021) and provides a foundation of evidence-based best practices for performing this procedure, and thus, can guide recommendations for its use in a field setting. Although the volume of data evaluated may seem daunting, this review concisely identifies nine essential aspects of regional limb perfusion for the practitioner to consider: administration route, antimicrobial selection, antimicrobial dose, perfusate volume, application and type of tourniquet, use of sedation versus anaesthesia, the benefits of local analgesia, frequency of treatment and critically evaluating whether the technique improves clinical outcome (Biasutti et al, 2021).

Technique

The principle of regional limb perfusion entails applying a tourniquet to the distal extremity and delivering antimicrobials locally to achieve a focally high concentration (Kilcoyne and Nieto, 2021). The mechanism of action is not well understood, but it is thought that regional limb perfusion creates both a concentration gradient that drives antimicrobials into the local tissues (Moser et al, 2016) and a pressure gradient from increased hydrostatic pressure in the local vasculature (Langer et al, 1996). Regional limb perfusion results in high peak tissue concentrations of antimicrobials soon after tourniquet release, and the tissues may serve as an ongoing reservoir of antimicrobials (Finsterbusch and Weinburg, 1972). Proposed benefits of regional limb perfusion include high antimicrobial concentrations in the affected region despite using lower amounts of antimicrobials, ultimately decreasing the potential for systemic complications, and lower cost of drugs, which may be prohibitively expensive at a systemic dose (Kelmer et al, 2012).

Administration route

While regional limb perfusion can be performed via an intravenous or intraosseous approach, the intravenous approach is far more practical in a field setting, often more efficacious and safer, with fewer complications (Butt et al, 2001; Scheuch et al, 2002; Parker et al, 2010). Therefore, the remainder of this discussion will focus on practices specific to the intravenous route. While any vessel that can be isolated can be used for regional limb perfusion, the cephalic, saphenous and digital vessels are most commonly used in the horse. Investigations were initially focused on the use of the digital vein, but have expanded to include evaluation of the technique at the saphenous and cephalic vessels. These studies show that similar, therapeutic antimicrobial concentrations can be achieved through the saphenous, cephalic and digital vessels (Kelmer et al, 2013). This is clinically useful for horses with injuries proximal to the digit or that preclude access to the digital vessels, injuries treated with distal limb bandages and/or casts, and/or when injuries result in significant distal limb oedema that prevents identification of vessels (Kelmer et al, 2012; Moser et al, 2016). The cephalic and saphenous vessel diameter is also larger, so presumptively technically easier to access (Kelmer et al, 2012; Oreff et al, 2016).

Antimicrobial selection

Generally, an antimicrobial should always be chosen in light of culture and sensitivity of a presumptive or potential site of infection, but these results are rarely available at the time of treatment initiation. Empirical antimicrobial selection should be based on an understanding of the mechanism of action of the antimicrobial and levels reached in tissues following regional limb perfusion in combination with knowledge about the most common isolates from orthopaedic infections and their respective mean inhibitory concentrations. *Staphylococcus* spp. and *Enterobacteriaceae* spp. are the most common isolates in traumatic wounds and orthopaedic infections (Schneider et al, 1992), with other commonly encountered isolates including *Streptococcus* spp., *Enterococcus* spp., *Pseudomonas* spp., *Proteus* spp., *Actinobacillus* spp. and anaerobes in puncture wounds (Harvey et al, 2016).

As a result of the ability to attain high peak concentrations (C_{max}), concentration-dependent antimicrobials are thought to be best suited for regional limb perfusion, with maximal efficacy at C_{max}/mean inhibitory concentrations >10 (McKellar et al, 2004). Aminoglycosides are readily available, have an appropriate spectrum of activity for many of the aforementioned organisms (Snyder et al, 1987; Moore et al, 1992), and are freely distributed through the aqueous interstitial fluid compartment (Brumbaugh, 2005). Amikacin is often preferred because it has a broader spectrum of activity and less resistance to common orthopaedic pathogens (Moore et al, 1992; Moser et al, 2016). Time-dependent antimicrobials are less suited for regional limb perfusion. To be effective, the drug concentration must remain higher than the mean inhibitory concentration for at least 50% of the dosing interval for bactericidal drugs, and near 100% of the time for drugs that are bacteriostatic (McKellar et al, 2004). Because of the rapid reduction of drug concentration following tourniquet release experimentally (Oreff et al, 2016; Kelmer et al, 2017), the use of time-dependent antimicrobials is considered less practical. However, in cases in which Gram-positive bacteria, and in particular, beta-haemolytic *streptococci*, have been isolated (Moore et al, 1992; Robinson et al, 2016), the third-generation cephalosporin ceftiofur may be an appropriate choice. Other antimicrobials have been studied, but are uncommonly used in a clinical setting (Whitehair et al, 1992a; Palmer and Hogan, 1999; Kettner et al, 2003; Rubio-Martinez et al, 2006). Enrofloxacin should be avoided because it is irritating to local tissues (Parra-Sanchez et al, 2006). Antimicrobial combinations in regional limb perfusion have been studied, but limited synergistic effects have been observed, the benefits remain unclear and antimicrobial efficacy may even be reduced (Zantingh et al, 2014).

Antimicrobial dose

Dose selection for regional limb perfusion can be challenging, as doses are reported with high variation and conflicting findings on efficacy. Reported single amikacin doses range from 250 mg (Parra-Sanchez et al, 2006) to 3 g (Harvey et al, 2016), and single gentamicin doses range from 500 mg (Hyde et al, 2013) to 6.6 mg/kg (Richardson and Ahern, 2012), the full systemic dose based on the weight of the patient. The most common recommended dose (albeit arbitrary) for regional limb perfusion based on weight is one-third of the systemic dose; amikacin (5 mg/kg; Beccar-Varela et al, 2011) and gentamicin (2.2 mg/kg; Mattson et al, 2004) have both been investigated at this dose. Other antimicrobials have incomplete data guiding dosage recommendations. Ultimately, reported dose selection is highly varied, and clinicians are advised to use available study data to guide appropriate dosing choice. Further practical advice is provided later in this article.

Perfusate volume

Before the injection, the antimicrobial is diluted with a sterile, physiological fluid (most commonly 0.9% saline) to provide a larger volume for injection. As with the dose of the antimicrobial, the volume of perfusate can be based on weight calculation or a fixed volume extrapolated from experimental studies. Historically, the most frequently studied volume based on weight was 0.1 ml/kg (Mattson et al, 2004; 2005), which is 50 ml when extrapolated to a 500 kg horse. The perfusate volumes studied vary widely, from 4 ml (Depenbrock et al, 2017) to 250 ml (Cimetti et al, 2004). Advantages of a lower perfusate volume include less force required to administer the solution, shorter administration time (thus more likely to be at a steady rate), decreased risk of perivascular leakage, quicker diffusion because of steeper concentration gradient and less discomfort associated with vessel distention (Hyde et al, 2013; Moser et al, 2016; Oreff et al, 2016; Schoonover et al, 2017). A higher perfusate volume is beneficial in cases of a large affected tissue mass, because it increases intravascular pressure and thus drives the drug into the tissues (Kelmer et al, 2012; Godfrey et al, 2016). Ultimately, studies on perfusate volume yielded the following, limited conclusions: volume alone is not a predictor of tissue concentrations (Hyde et al, 2013), effective isolation of the regional vasculature dictates the success of regional limb perfusion (Godfrey et al, 2016) and there is no clear recommendation for perfusate volume. Thus, clinician discretion will guide this decision.

Tourniquet

An effective tourniquet is vital for a successful regional limb perfusion. Tourniquet failure or leakage has been recognised by the identification of antimicrobials in the systemic circulation and/or little to no antimicrobials in local tissues or synovial fluid in multiple studies (Errico et al, 2008; Levine et al, 2010; Rubio-Martínez et al, 2012; Godfrey et al, 2016). Experimentally, tourniquet failure has been identified in the following:

- With rubber tourniquets (Whitehair et al, 1992a; Mattson et al, 2004; Parra-Sanchez et al, 2006; Levine et al, 2010)
- With pneumatic tourniquets (Beccar-Varela et al, 2011)
- At the level of the metacarpus (Murphey et al, 1999; Mattson et al, 2004)
- At the level of the antebrachium (Parra-Sanchez et al, 2006; Beccar-Varela et al, 2011)
- In horses under general anaesthesia (Whitehair et al, 1992c; Murphey et al, 1999; Beccar-Varela et al, 2011)
- In horses under standing sedation (Mattson et al, 2004; Parra-Sanchez et al, 2006; Levine et al, 2010).

Although a pneumatic tourniquet is ideal in its ability to standardise tourniquet pressure, it is not pragmatic in a field setting (Kilcoyne and Nieto, 2021). It has been found that a wide tourniquet (>10 cm), such as an Esmarch tourniquet, is essential. Experimentally, narrow tourniquets failed reliably (Levine et al, 2010), and wider tourniquets have been found to occlude blood flow at lower pressures (Graham et al, 1993).

A horse's leg is not a perfect circle, and depressions adjacent to tendons may predispose to leakage. It is possible that placing rolls of gauze or sponges over any concave regions beneath the tourniquet may provide more even pressure. In the metacarpal/metatarsal region, they can be placed medially and laterally between the deep digital flexor tendon and the suspensory ligament. In the antebrachial region, they can be placed over the cephalic vein. In the crus region, they can be placed medial and lateral in the depression cranial to the calcanean tendon. Use of more than one tourniquet to better isolate the affected region (with tourniquets placed both proximal and distal to the targeted region) has been described, and may be used for injuries at the level of the carpus or tarsus, but the study results are inconclusive as to the benefits of this technique (Schoonover et al, 2017). Similarly, although exsanguination of a limb before regional limb perfusion has been described with a purported advantage of reduced leakage around the tourniquet (Grice et al, 1986), resultant local antimicrobial concentrations are variable and this added step can complicate the otherwise simple regional limb perfusion technique (Sole et al, 2016; Schoonover et al, 2017), making it less practical in a field setting.

Recommended tourniquet application times range from 10–45 minutes (Kilcoyne et al, 2016; Depenbrock et al, 2017), but, based on the data available, a duration of 15–20 minutes appears adequate to achieve maximal antimicrobial concentrations for most applications (Aristizabal et al, 2016; Harvey et al, 2016). Additionally, horses move more during longer tourniquet maintenance times (Kilcoyne et al, 2016), likely contributing to tourniquet failure. Practically speaking, limiting tourniquet time to just enough to achieve adequate tissue antimicrobial concentrations while also minimising motion and required sedation is clinically ideal (Biasutti et al, 2021).

Sedation and anaesthesia

When considering the effects of standing sedation vs general anaesthesia on regional limb perfusion, it is clear that standing sedation is most practical in an ambulatory setting given the resources, logistics, time required of general anaesthesia and the risks to the patient. Although initial investigations of regional limb perfusion were performed with horses under general anaesthesia, local antimicrobial concentrations have been shown to be comparable in regional limb perfusion with standing sedation vs general anaesthesia (Mahne et al, 2014; Aristizabal et al, 2016). When performing this technique under standing sedation, it is imperative to use adequate sedation to limit motion, which has repeatedly been shown to reduce the efficacy of the technique (Levine et al, 2010; Colbath et al, 2016). Movement associated with discomfort of the venipuncture and/or tourniquet can be further limited with the use of local anesthesia, either with a perineural block or as part of the intravenous perfusate (Mahne et al, 2014; Colbath et al, 2016). Given the relative ease of either performing a local perineural nerve block before regional limb perfusion or adding local anaesthetic to the perfusate and the potential benefit of limiting motion and thus promoting a more effective tourniquet, these principles can readily be applied to enhance regional limb perfusion techniques in the field setting.

Frequency of treatment

The recommended frequency of regional limb perfusion treatment is variable based on various factors, but several studies support the benefits of daily use (Kelmer et al, 2012; Harvey et al, 2016; Kelmer et al, 2017). For repeated application, an indwelling catheter may be beneficial, but this is not pragmatic or safe outside of a hospital setting. Similarly, field clinicians may be limited in their ability to perform daily regional limb perfusion, and the patient's tolerance, wound care needs, response to treatment and clinical improvement should be considered when making treatment frequency decisions.

Critical evaluation

The literature exploring whether or not regional limb perfusion improves case outcomes contains mixed reports. Regional limb perfusion was initially introduced as a viable, adjunct treatment for distal limb infection (Whitehair et al, 1992c). One study found that the use of regional limb perfusion as an adjunct treatment for synovial sepsis yielded similar results to treatment without it, although the study design makes it challenging to interpret the specific effect of regional limb perfusion on the cases (Rubio-Martínez et al, 2012). Other studies show mixed effects of regional limb perfusion in cases of synovial sepsis (Whitehair et al, 1992c; Botha et al, 1996); in many retrospective studies, case selection bias may skew results and interpretation of the efficacy of regional limb perfusion. Investigations of non-synovial wound treatment are similarly confounding (Biasutti et al, 2021).

Limitations

Ultimately, it is important to address the limitations and potential drawbacks of the use of regional limb perfusion. Clinically, it is impossible to ensure that therapeutic concentrations of drug are achieved in the local intended tissue, thus calling into question the efficacy of antimicrobial administration through regional limb perfusion in cases of distal limb infection, and further drawing concern for development of bacterial resistance (Biasutti et al, 2021). However, the benefits are still thought to outweigh the downsides and unknowns when used in a suitable clinical scenario.

Practical application

The appropriate use of regional limb perfusion in a field setting cannot be overstated; while it is a valuable tool, it is not a substitute for standard of care for wound management otherwise. The mainstays of treatment for orthopaedic infection remain debridement and lavage to remove bacteria, inflammatory mediators and any foreign material, accompanied by appropriate systemic antimicrobial therapy. Regional limb perfusion should be advertised as an adjunctive therapy to attain high concentrations of local antimicrobials in conjunction with an appropriate local and systemic treatment plan.

Cases that are most appropriate for adjunctive treatment with regional limb perfusion in a field care setting include distal limb wounds without synovial contamination, cellulitis limited to the distal limb, penetrating injuries to the hoof without synovial contamination and surgical site infections of the distal limb. Cases of known or suspected synovial sepsis should always be offered hospital and surgical referral. While a spectrum of care exists in practice and not all cases undergo referral centre care, more severe cases limited to field management may also benefit from regional limb perfusion as an adjunct to the primary therapeutic principles. For example, in a case of known synovial sepsis, synovial lavage with high volume sterile fluids, intra-synovial antimicrobials and broad-spectrum systemic antimicrobials should be prioritised with regional limb perfusion to further high local antimicrobial concentrations. The author feels strongly that cases of prolonged synovial sepsis that either went initially undiagnosed, untreated or did not respond to treatment should not be treated with regional limb perfusion without otherwise aggressive care.

As discussed in the above literature review, there is a lacking consensus on 'best practices' of technique. The author uses the technique as follows. The wound itself is addressed based on the specific injury in conjunction with the use of regional limb perfusion. This should be performed under standing sedation adequate to tolerate tourniquet placement, safe distal limb venipuncture and to maintain a still posture for 15–20 minutes. In the author's experience, a combination of intravenous detomidine (3–5 mg) and butorphanol (3–5 mg) is ideal. For penetrating injuries to the hoof, heel bulb lacerations and/or traumatic pastern wounds, use of the lateral digital vein with tourniquet placement at the level of the distal metacarpus/tarsus is recommended. The procedure at this level is better tolerated by performing a perineural abaxial nerve block prior to tourniquet placement.

For those injuries proximal to the pastern and at, or distal to, the carpus or tarsus, use of the cephalic or saphenous veins, respectively, with tourniquet placement at the distal antebrachium or crus, respectively, is recommended. The author prefers a 12 cm Esmarch bandage applied tightly across the intended level, ensuring that the full width of the bandage is used as the tourniquet is pulled taut and secured in place. The intended vessel should be able to be palpated as a raised, turgid but compressible structure. If palpable or visual identification of the vessel is challenging, the location and course of the vessel can be confirmed sonographically with a linear transducer. The hair can be clipped if the coat is long, and the site aseptically prepared before needle puncture.

KEY POINTS

- Regional limb perfusion is a simple and effective method of local antimicrobial delivery to the distal extremities of the horse
- Regional limb perfusion is an adjunctive treatment technique to be used in conjunction with appropriate systemic and local therapies
- Regional limb perfusion is safe to perform in a field setting under standing sedation

The author prefers a 21–23 gauge butterfly catheter and secures the extension set to the limb by taping it to the tourniquet; the cap should be removed before puncture to allow for blood flow. Ahead of needle puncture, the antibiotic and perfusate solution are prepared; the author prefers to keep them in separate syringes in case the vessel fails or the needle becomes dislodged, thus ensuring that the full volume of antibiotic is administered before the perfusate.

For distal limb injuries and regional limb perfusion of the lateral digital vein, the author commonly uses 1 g of amikacin and 20–30 ml sterile saline as a perfusate. For more proximal injuries and regional limb perfusion of the cephalic or saphenous vein, the author commonly uses 1–2 g amikacin and either 50–60 ml sterile saline, or 20–30 ml sterile saline and 20–30 ml mepivacaine as a perfusate. Additionally, a small bandage of white gauze sponges and white tape are prepared to place over the vessel following the procedure.

The needle is placed into the intended vessel with a swift, longitudinal, proximal to distal puncture with the entirety of the needle positioned inside the vessel for security; proper placement is confirmed with rapid blood flow through the catheter line. The antibiotic (4–8 ml volume) should be administered slowly (over approximately 30 seconds), pausing positive pressure every few ml to confirm rapid flow back of blood, and following completion of antibiotic, the perfusate should follow in a similar manner, with the entire antibiotic and perfusate volume injected over 2–3 minutes. Over time, the intensity of the blood flow back will lessen. The venipuncture site should be monitored to ensure that there is no extravasation; if extravasation occurs and there is no longer blood flowback, the author will terminate the perfusion before administering the full perfusate in an attempt to maintain vessel integrity for future regional limb perfusion administration. The small bandage is placed snugly over the perfusate site before removing the needle, and the horse is maintained in the same position for an additional 10–15 minutes before removing the tourniquet. The venipuncture bandage is removed and the author places a small volume (approximately 1 cm ribbon) of diclofenac ointment over the venipuncture site. If bandaging is being used for the wound under treatment, this can either be performed before or after the regional limb perfusion, depending on the site of the wound and needed vessel access. Repeat regional limb perfusion is often based on clinical progression and convenience based on frequency of visiting the patient in a field setting; ideally the author prefers three daily treatments, then chooses additional therapy based on case progression.

Conclusions

Regional limb perfusion is a simple technique that can augment local antimicrobial therapy in cases of infectious or traumatic injury to the equine distal limb. When used with the knowledge of the benefits and limitations of the technique, it broadens the field practitioner's clinical toolbox for managing orthopaedic infection in an ambulatory setting. EQ

Conflicts of interest

The author declares that there are no conflicts of interest.

References

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. https://doi.org/10.1016/j.tvjl.2015.10.017

Beccar-Varela AM, Epstein KL, White CL. Effect of experimentally induced synovitis on amikacin concentrations after intravenous regional limb perfusion. Vet Surg. 2011;40(7):891–897. https://doi.org/10.1111/j.1532-950X.2011.00875.x

Biasutti SA, Cox E, Jefcott LB, Dart AJ. A review of regional limb perfusion for distal limb infections in the horse. Equine Vet Educ. 2021;33(5):263–277. https://doi.org/10.11111/eve.13243

Botha FJ, van der Bijl P, Seifart HI, Parkin DP. Fluctuation of the volume of distribution of amikacin and its effect on once-daily dosage and clearance in a seriously ill patient. Intensive Care Med. 1996;22(5):443–446. https://doi.org/10.1007/BF01712162

Brumbaugh GW. Use of antimicrobials in wound management. Vet Clin North Am Equine Pract. 2005;21(1):63–75. https://doi.org/10.1016/j.cveq.2004.11.012

Butt TD, Bailey JV, Dowling PM, Fretz PB. Comparison of 2 techniques for regional antibiotic delivery to the equine forelimb: intraosseous perfusion vs. intravenous perfusion. Can Vet J. 2001;42(8):617–622

Cimetti LJ, Merriam JG, D'Oench SN. How to perform intravenous regional limb perfusion using amikacin and DMSO. Presented at the 50th American Association of Equine Practitioners National Convention, Colorado, 4–8 December 2004

Colbath AC, Wittenburg LA, Gold JR, McIlwraith CW, Moorman VJ. The effects of mepivacaine hydrochloride on antimicrobial activity and mechanical nociceptive threshold during amikacin sulfate regional limb perfusion in the horse. Vet Surg. 2016;45(6):798–803. https://doi.org/10.1111/vsu.12515

Depenbrock SM, Simpson KM, Niehaus AJ, Lakritz J, Papich MG. Pharmacokinetics of ampicillin-sulbactam in serum and synovial fluid samples following regional intravenous perfusion in the distal portion of a hind limb of adult cattle. Am J Vet Res. 2017;78(12):1372–1379. https://doi.org/10.2460/ajvr.78.12.1372

Errico JA, Trumble TN, Bueno AC, Davis JL, Brown MP. Comparison of two indirect techniques for local delivery of a high dose of an antimicrobial in the distal portion of forelimbs of horses. Am J Vet Res. 2008;69(3):334–342. https://doi.org/10.2460/ajvr.69.3.334

Finsterbusch A, Weinberg H. Venous perfusion of the limb with antibiotics for osteomyelitis and other chronic infections. J Bone Joint Surg Am. 1972;54(6):1227–1234

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(6):582–588. https://doi.org/10.2460/ajvr.77.6.582

Graham B, Breault MJ, McEwen JA, McGraw RW. Occlusion of arterial flow in the extremities at subsystolic pressures through the use of wide tourniquet cuffs. Clin Orthop Relat Res. 1993;(286):257–261

Grice SC, Morell RC, Balestrieri FJ, Stump DA, Howard G. Intravenous regional anesthesia: evaluation and prevention of leakage under the tourniquet. Anesthesiology. 1986;65(3):316–320

Harvey A, Kilcoyne I, Byrne BA, Nieto J. Effect of dose on intra-articular amikacin sulfate concentrations following intravenous regional limb perfusion in horses. Vet Surg. 2016;45(8):1077–1082. https://doi.org/10.1111/vsu.12564

Hyde RM, Lynch TM, Clark CK, Slone DE, Hughes FE. 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(4):363–367

Kelmer G, Tatz A, Bdolah-Abram T. Indwelling cephalic or saphenous vein catheter use for regional limb perfusion in 44 horses with synovial injury involving the distal aspect of the limb. Vet Surg. 2012;41(8):938–943. https://doi.org/10.1111/j.1532-950X.2012.01006.x

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(3):236–240. https://doi.org/10.1111/j.1365-2885.2012.01414.x

Kelmer G, Tatz AJ, Kdoshim E, Britzi M, Segev G. Evaluation of the pharmacokinetics of imipenem following regional limb perfusion using the saphenous and the cephalic veins in standing horses. Res Vet Sci. 2017;114:64–68. https://doi.org/10.1016/j.rvsc.2017.02.020

Kettner NU, Parker JE, Watrous BJ. Intraosseous regional perfusion for treatment of septic physitis in a two-week-old foal. J Am Vet Med Assoc. 2003;222(3):346–350. https://doi.org/10.2460/javma.2003.222.346

Kilcoyne I, Nieto JE. Orthopedic infections - clinical applications of intravenous regional limb perfusion in the field. Vet Clin North Am Equine Pract. 2021;37(2):275–291. https://doi.org/10.1016/j.cveq.2021.04.003

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(23):585. https://doi.org/10.1136/vr.103609

Langer K, Seidler C, Partsch H. Ultrastructural study of the dermal microvasculature in patients undergoing retrograde intravenous pressure infusions. Dermatology. 1996;192(2):103–109. https://doi.org/10.1159/000246331

Levine DG, Epstein KL, Ahern BJ, Richardson DW. Efficacy of three tourniquet types for intravenous antimicrobial regional limb perfusion in standing horses. Vet Surg. 2010;39(8):1021–1024. https://doi.org/10.1111/j.1532-950X.2010.00732.x

Mahne AT, Rioja E, Marais HJ, Villarino NF, Rubio-Martinez LM. Clinical and pharmacokinetic effects of regional or general anaesthesia on intravenous regional limb perfusion with amikacin in horses. Equine Vet J. 2014;46(3):375–379. https://doi.org/10.1111/evj.12125

Mattson S, Bouré L, Pearce S, Hurtig M, Burger J, Black W. Intraosseous gentamicin perfusion of the distal metacarpus in standing horses. Vet Surg. 2004;33(2):180–186. https://doi.org/10.1111/j.1532-950x.2004.04026.x

Mattson SE, Pearce SG, Bouré LP, Dobson H, Hurtig MB, Black WD. Comparison of intraosseous and intravenous infusion of technetium Tc 99m pertechnate in the distal portion of forelimbs in standing horses by use of scintigraphic imaging. Am J Vet Res. 2005;66(7):1267–1272. https://doi.org/10.2460/ajvr.2005.66.1267

McKellar QA, Sanchez Bruni SF, Jones DG. Pharmacokinetic/pharmacodynamic relationships of antimicrobial drugs used in veterinary medicine. J Vet Pharmacol Ther. 2004;27(6):503–514. https://doi.org/10.1111/j.1365-2885.2004.00603.x

Moore RM, Schneider RK, Kowalski J, Bramlage LR, Mecklenburg LM, Kohn CW. Antimicrobial susceptibility of bacterial isolates from 233 horses with musculoskeletal infection during 1979–1989. Equine Vet J. 1992;24(6):450–456. https://doi.org/10.1111/j.2042-3306.1992.tb02875.x

Moser DK, Schoonover MJ, Holbrook TC, Payton ME. 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(7):851–858. https://doi.org/10.1111/vsu.12521

Murphey ED, Santschi EM, Papich MG. Regional intravenous perfusion of the distal limb of horses with amikacin sulfate. J Vet Pharmacol Ther. 1999;22(1):68–71. https://doi.org/10.1046/j.1365-2885.1999.00180.x

Oreff GL, Dahan R, Tatz AJ, Raz T, Britzi M, Kelmer G. The effect of perfusate volume on amikacin concentration in the metacarpophalangeal joint following cephalic regional limb perfusion in standing horses. Vet Surg. 2016;45(5):625–630. https://doi.org/10.1111/vsu.12490

Palmer SE, Hogan PM. How to perform regional limb perfusion in the standing horse. Presented at the 45th Annual Convention of the American Association of Equine Practioners, Alberquerque, 8 December 1999

Parker RA, Bladon BM, McGovern K, Smith KC. Osteomyelitis and osteonecrosis after intraosseous perfusion with gentamicin. Vet Surg. 2010;39(5):644–648. https://doi.org/10.1111/j.1532-950X.2010.00685.x

Parra-Sanchez A, Lugo J, Boothe DM et al. Pharmacokinetics and pharmacodynamics of enrofloxacin and a low dose of amikacin administered via regional intravenous limb perfusion in standing horses. Am J Vet Res. 2006;67(10):1687–1695. https://doi.org/10.2460/ajvr.67.10.1687

Richardson DW, Ahern BJ. Synovial and osseous infections. In: Auer JA, Stick JA (eds). Equine surgery. 4th edn. St Louis: WB Saunders; 2012:1189–1201

Robinson CS, Timofte D, Singer ER, Rimmington L, Rubio-Martínez LM. Prevalence and antimicrobial susceptibility of bacterial isolates from horses with synovial sepsis: a cross-sectional study of 95 cases. Vet J. 2016;216:117–121. https://doi.org/10.1016/j.tvjl.2016.07.004

Rubio-Martínez LM, López-Sanromán J, Cruz AM, Tendillo F, Rioja E, San Román F. Evaluation of safety and pharmacokinetics of vancomycin after intraosseous regional limb perfusion and comparison of results with those obtained after intravenous regional limb perfusion in horses. Am J Vet Res. 2006;67(10):1701–1707. https://doi.org/10.2460/ajvr.67.10.1701

Rubio-Martínez LM, Elmas CR, Black B, Monteith G. Clinical use of antimicrobial regional limb perfusion in horses: 174 cases (1999–2009). J Am Vet Med Assoc. 2012;241(12):1650–1658. https://doi.org/10.2460/javma.241.12.1650

Scheuch BC, Van Hoogmoed LM, Wilson WD et al. Comparison of intraosseous or intravenous infusion for delivery of amikacin sulfate to the tibiotarsal joint of horses. Am J Vet Res. 2002;63(3):374–380. https://doi.org/10.2460/ajvr.2002.63.374

Schneider RK, Bramlage LR, Moore RM, Mecklenburg LM, Kohn CW, Gabel AA. A retrospective study of 192 horses affected with septic arthritis/tenosynovitis. Equine Vet J. 1992;24(6):436–442. https://doi.org/10.1111/j.2042-3306.1992.tb02873.x

Schoonover MJ, Moser DK, Young JM, Payton ME, Holbrook TC. 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(5):675–682. https://doi.org/10.1111/vsu.12662

Snyder JR, Pascoe JR, Hirsh DC. Antimicrobial susceptibility of microorganisms isolated from equine orthopedic patients. Vet Surg. 1987;16(3):197–201. https://doi.org/10.1111/j.1532-950x.1987.tb00938.x

Sole A, Nieto JE, Aristizabal FA, Snyder JR. Effect of emptying the vasculature before performing regional limb perfusion with amikacin in horses. Equine Vet J. 2016;48(6):737–740. https://doi.org/10.1111/evj.12501

Watts AE. How to select cases and perform field technique for regional limb perfusion. Presented at the 57th American Association of Equine Practitioners National Convention, Texas, 18–22 November 2011

Whitehair KJ, Blevins WE, Fessler JF, Van Sickle DC, White MR, Bill RP. Regional perfusion of the equine carpus for antibiotic delivery. *Vet Surg*. 1992a;21(4):279–285. https://doi.org/10.1111/j.1532-950x.1992.tb00064.x

Whitehair KJ, Bowersock TL, Blevins WE, Fessler JF, White MR, Van Sickle DC. Regional limb perfusion for antibiotic treatment of experimentally induced septic arthritis. Vet Surg. 1992b;21(5):367–373. https://doi.org/10.1111/j.1532-950x.1992.tb01713.x

Whitehair KJ, Bowersock TL, Blevins WE, Fessler JF, White MR, Van Sickle DC. Regional limb perfusion for antibiotic treatment of experimentally induced septic arthritis. Vet Surg. 1992c;21(5):367–373. https://doi.org/10.1111/j.1532-950x.1992.tb01713.x

Zantingh AJ, Schwark WS, Fubini SL, Watts AE. Accumulation of amikacin in synovial fluid after regional limb perfusion of amikacin sulfate alone and in combination with ticarcillin/clavulanate in horses. Vet Surg. 2014;43(3):282–288. https://doi.org/10.1111/j.1532-950X.2014.12119.x