Reference Point

Antimicrobial regional limb perfusion in horses

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Commonly, equine practitioners confront challenging orthopedic infections that are often complicated by a resistant bacterial strain. Although other aspects of treatment, such as surgical debridement of necrotic debris, control of inflammation, and appropriate rehabilitation, are important for a successful outcome, improved outcomes are possible when the bacterial population is eliminated. Ideally, this can be accomplished when high doses of appropriate antimicrobials reach the infected areas.

Regional limb perfusion provides high antimicrobial concentrations in the region of interest and greatly contributes to the elimination of the infection. It involves the administration of a drug solution into the vasculature of a selected portion of the limb that has been isolated from the systemic circulation by the controlled application of a tourniquet. After the tourniquet is applied, the antimicrobial solution is injected into the isolated portion of the vascular system. Vascular isolation is essential to perform RLP successfully. Infusion of the perfusate creates high concentration and pressure gradients between the intravascular and extravascular compartments. This maximizes diffusion from the intravascular compartment into the surrounding tissues (synovial fluid, soft tissues, and bone), including poorly vascularized tissues where bacteria are protected from systemically circulating antimicrobials. After the tourniquet is released, the perfused tissues serve as a depot for the drug, which continues diffusing.

Wide penetration of drugs into infected areas has been revealed by venography studies. Ultrastructural studies of dermal microvasculature reveal that during RLP, dilation of venous capillaries, postcapillaries, and lymphatic vessels occurs, causing relaxation of the contacts between endothelial cells and pericytes. Small gaps develop in the vascular wall that allow greater diffusion without cellular injury. Thus, in addition to the high concentration gradients that result from RLP, there is a mechanical effect that facilitates perfusion of the antimicrobial into the target area. Arterioles, conversely, do not contribute to the diffusion process.

History

After RLP was first described in 1908 as a method to induce regional anesthesia for certain surgical procedures, it was subsequently used for administration of substances such as antimicrobials and cytostatic drugs to humans and other animals. In 1990, Dietz and Kehnscherper described antimicrobial regional perfusion in horses. Presently, RLP with antimicrobials is considered an effective adjunctive therapy for the treatment of horses with orthopedic infections of the limbs.

Techniques

The antimicrobial solution is administered via either IVRLP or IORLP. For IVRLP, a superficial vein is commonly catheterized, whereas the solution is injected directly into the medullary cavity of a bone for IORLP. The intra-arterial route has been used for perfusion of the distal portion of the limb with miconazole in a mare with chronic pythiosis, but drug-induced toxic effects on the endothelium are much more frequent and severe in arteries than in veins, so the arterial route is discouraged in clinical practice.

The tourniquet must be secured proximal to the infected site so that it occludes the arterial and venous systems and prevents blood from refilling the vasculature and perfusate from leaking. Depending on the location of the septic focus, 2 tourniquets can be applied, 1 above and 1 below the septic focus, and the solution is administered between them. With any administration route, application of an Esmarch bandage can be used to exsanguinate the region to be perfused. The bandage is applied proximad, starting at the level of the distal tourniquet, if 2 tourniquets are used, or from the hoof capsule, if 1 tourniquet is used. The bandage is uniformly stretched as it is wrapped up the limb, overlapping half the width of the bandage. Regional perfusion can also be successfully performed without exsanguination of the region, however, the total volume of the perfusate should be reduced because the combined volume of the blood and perfusate could decrease the effectiveness of the tourniquet.

When the IV route is to be used, catheterization of a superficial vein prior to exsanguination of the limb is recommended because after exsanguination, the veins collapse and catheterization can be difficult. Eighteen- or 20-gauge, 1-inch (adult horses) or 22-gauge (foals)
butterfly needles or IV over-the-needle catheters can be used. Smaller diameters (26 gauge) cause less damage to the endothelium, which is desired if repeated perfusions are to be performed. Repeated attempts to catheterize the vein should be avoided because the vessel wall is disrupted, extravasation of the perfusate occurs, and perfusate accumulates in the subcutaneous space.

Placement of the injection system for IORLP can be performed prior to or after exsanguination. Human intramedullary needles are easy to place in small animals and foals, whereas bones of adult horses require drilling to permit insertion of the needle or cannulated screw. The distal end of the bone can be reached. This can be greatly reduced by sealing the interface with cyanoacrylate ester glue or by use of cannulated screws. During IVRLP and IORLP, the perfusate is infused under pressure. However, IVRLP maximal infusion pressure values are usually < 15 lb/inch², whereas IORLP infusion pressure values of 450 lb/inch² have been reached. This high pressure is believed to be associated with pain because substantially lower values have been reported to cause lameness in a horse. We have performed IORLP on anesthetized horses and usually observe an increase in arterial blood pressure and heart rate while injecting the solutions into the medullary cavity of the bone; the increase is more noticeable as the injected volume increases. Nonetheless, after IORLP, the horses are not usually lame, perhaps because the defect left open in the bone allows the intramedullary pressure to equilibrate.

The solution can be administered as a bolus, typically by hand, or as a slow, controlled CRI, usually at 2 mL/min. For IVRLP, either manual infusion or a conventional infusion pump can be used to accomplish the objective easily and safely. During IORLP, high intramedullary pressures offer more resistance to injection, so small-volume syringes (2 to 5 mL) are appropriate for manual infusion, whereas a slow, controlled CRI requires high pressure pumps such as angiographic injectors.

The distribution of the perfusate has been investigated. Perusions with radiopaque dye and India ink have been used to confirm that with either IVRLP or IORLP, the perfusate is distributed via the venous system. Indeed, when the tourniquet is applied around the diaphysis of the bone, the perfusate may enter the medullary cavity and then reach the systemic circulation through the proximal diaphyseal and epiphyseal vessels. In a radiographic study of both techniques, the density of contrast material in the tarsal venous system was greater after IV perfusion. However, perfusion with 99m-tecnnetium pertechnetate results in the same radionuclide activity in the distal portion of the limb in horses after IVRLP or IORLP. Because the perfusate is distributed through the venous system, authors of initial clinical studies recommended that the antimicrobial should be infused from a point distal to the infection site, and for infections involving the hoof, a superficial, more proximal vein should be catheterized with the catheter directed distally toward the foot. However, in a more recent study, RLP with radiopaque dye injected into the lateral digital vein at the level of the proximal sesamoid bone resulted in complete perfusion of the digit within seconds. Antimicrobial concentrations in structures distal to the infusion site are satisfactory, and higher antimicrobial concentrations in synovial fluid in the distal interphalangeal joint, compared with the metacarpophalangeal joint, have been obtained after IVRLP.

Regional perfusion maintains high antimicrobial concentrations for a limited period, exceeding 24 hours in some instances. Daily venipuncture with a small-gauge needle does not seem to be associated with serious adverse effects, although IV catheters can also be left in place for several days. When repeated IORLP is required, the hole drilled into the medullary cavity can also be used daily or a cannulated screw can be left in place. Experimental studies in pigs and goats reveal that intraosseous catheters maintain their functionality for periods up to 6 months, without substantial adverse effects.

No major complications have been related to RLP in horses. The most commonly reported adverse effect after IORLP is mild, nonpainful soft-tissue inflammation over the intraosseous infusion site, which resolves over a period of time without anti-inflammatory or antimicrobial treatment. No studies have thoroughly evaluated changes in bony tissues at the infusion portal site or in the medullary cavity of horses. Bone marrow fibrosis, increased bone density, and periosteal and cancellous new bone formation have been associated with chronic implantation of cannulated screws in goats. However, these changes may not be clinically important because repeated infusion through a permanent intraosseous device in pigs did not cause changes in pharmacokinetic values (eg, drug flow, drug distribution) during a 6-month study. In foals, RLP to treat septic conditions of the hocks has been associated with secondary septic foci. Therefore, some authors do not recommend RLP in neonates on a routine basis but only in foals with septic processes unresponsive to conventional treatment and after administration of systemic antimicrobials.

**Antimicrobial Selection**

The antimicrobial to be perfused must be water soluble and should be dissolved in a balanced isotonic solution (0.9% NaCl or Ringer’s lactated solution). Culture and susceptibility tests should guide antimicrobial selection, ideally before initiation of treatment. Initial antimicrobial selection can also be performed according to the pathogens most commonly associated with the infection. In studies on susceptibility of equine isolates, amikacin has the greatest efficacy against pathogens in horses with orthopedic problems, including gram-positive and gram-negative organisms. Gentamicin has decreased because of emergence of resistant strains. Third-generation cephalosporins such as cefotaxim also have high activity, and although experimentally administered by RLP to cattle, their regional use in horses has not been reported. In iatrogenic infections caused by multiresistant bacteria, such as methicillin-resistant *Staphylococcus aureus*, administration of highly effective narrow-spectrum

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**References**

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drugs has been necessary, but their clinical use in regional perfusion has not been described.

Pharmacokinetic and pharmacodynamic properties of the antimicrobial dictate the appropriate systemic dosage regimen and should guide the regional use of the drug. Time-dependent antimicrobials, such as penicillins, cephalosporins, carbapenems, and macrolides, require maintenance of concentration greater than the MIC for antibacterial activity, and increases in the peak concentration do not augment the killing rate. Conversely, maximal efficacy of concentration-dependent antimicrobials such as aminoglycosides is determined by high peak concentration because these drugs exert prolonged postadministration effects.

These characteristics allow aminoglycosides to be administered once daily, whereas β-lactams require maintenance of a minimum concentration during a high proportion of the treatment interval for adequate antibacterial activity. In clinical practice, RLP is usually performed once daily or once every 2 to 3 days. According to this schedule, concentration-dependent antimicrobials are more suitable for attaining proper antibacterial activity. However, the use of time-dependent antimicrobials for RLP can be justified because this technique is likely to result in therapeutic concentrations of the antimicrobial in infected ischemic tissues for a longer period than is possible with systemic administration. In addition, after the tourniquet is released, the high antimicrobial concentrations in the surrounding tissues serve as a depot because the drug diffuses from them. Concentrations of aminoglycosides remain greater than the desired concentration of protein for periods ≥ 24 hours in healthy horses. The concentration of vancomycin, a time-dependent glycopeptide, remains greater than the desired concentration for approximately 20 hours in synovial fluid and have been successfully used in adult horses. Higher aminoglycoside doses (500 mg to 1 g) are commonly used clinically. In our practice, we routinely administer 500 mg. For young foals, lower doses (50 mg) are recommended, although doses as high as 500 mg have also been used. β-Lactams have been less used, but RLP with sodium or regional pharmacokinetics of time-dependent antimicrobials administered by RLP would be useful to help avoid possible misuse of these antimicrobials in clinical situations. Clinically affected animals in which time-dependent antimicrobials have been administered have successfully responded to treatment.

Other pharmacodynamic characteristics of each drug can be important. For instance, because of the strong affinity of ceftiofur (a time-dependent antimicrobial) for proteins and because of its active metabolites, if high regional concentrations could be safely achieved initially, these concentrations would remain greater than therapeutic concentrations longer, thus prolonging the administration interval and making RLP more practical than systemic administration, as described in cows.

Several studies have investigated clinical effects, safety, distribution, pharmacokinetics, and efficacy of the most frequently used antimicrobials for orthopedic infections in horses. Antimicrobials with toxic effects on vascular tissues (eg, enrofloxacin) should not be used, and excessive doses of antimicrobials commonly administered via RLP can also damage vessels. This must be applied not only to IVRLP but also to IORLP because the medullary cavity contains large numbers of venous sinusoids surrounded by bone marrow cells and the intraosseous route provides ready access to the systemic circulation.

The optimal antimicrobial dose for RLP is not known. Antimicrobial doses used in clinical cases have been reported (Table 1). Although low doses (100 to 300 mg) of amikacin and gentamicin may result in extremely high concentrations in synovial fluid and have been successfully used in adult horses, higher aminoglycoside doses (500 mg to 1 g) are commonly used clinically. In our practice, we routinely administer 500 mg. For young foals, lower doses (50 mg) are recommended, although doses as high as 500 mg have also been used. β-Lactams have been less used, but RLP with sodium or regional pharmacokinetics of time-dependent antimicrobials administered by RLP would be useful to help avoid possible misuse of these antimicrobials in clinical situations. Clinically affected animals in which time-dependent antimicrobials have been administered have successfully responded to treatment.

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| Table 1—Reported use of RLP for treatment of horses with orthopedic infections. |
| Site or type of infection | No. of horses | Age | No. of RLPs/horse | Antimicrobial (dose range/RLP) | Reference No. |
| Distal portion of the limb | 24 | 30 d–24 y | 1–9 | Gentamicin (100–300 mg) | 12, 13, 15 |
| Fetlock joint and proximal sesamoid bones | 20 | 3 m–18 y | 1–4 | Gentamicin (100 mg–1 g) | 13, 15, 27 |
| Proximal portion of the limb | 5 | 10 d–3 mo | 1–3 | Gentamicin (100 mg–1 g) | 12, 13, 18 |
| Miscellaneous (septic arthritis, osteomyelitis) | 22 | Unspecified | 1–4 | Amikacin (1–2 g) | 15, 27 |

Distal portion of the limb includes septic processes in hoof, coronary band, podal laminae, phalanx, interphalangeal joints and navicular bursa. Proximal portion of the limb includes septic processes in digital flexor tendon sheath, metacarpal bones, metatarsal bones, carpus, and tarsus. Fetlock joint refers to metacarpophalangeal or metatarsophalangeal joints.

*Combined in some cases.

K+ Pen = Potassium penicillin.
potassium penicillin (10 X 10⁶ units), timentin (1 g), and sodium ampicillin (9 g) has resulted in satisfactory clinical outcomes. Use of the same dose for different animals results in high individual variability of antimicrobial concentrations. Therefore, dose adjustment to the volume or weight of the limb could be the most accurate method. Presently, this seems impractical, and some authors recommend administration of one third of the daily systemic dose as the general dose for RLP. This would mean approximately 1 g of gentamicin or amikacin for RLP in a 450- to 500-kg (990- to 1,100-lb) horse, which has been frequently used.

Occasionally 2 antimicrobials (a β-lactam and an aminoglycoside) have been combined in the same RLP. Some drugs have synergistic effects when administered together; however, other combinations can have antagonistic effects. This is true of aminoglycosides, which can be inactivated in vitro by some β-lactams. Although 1 report indicated that combined administration resulted in a successful outcome, it is generally recommended that RLP be performed with a single antimicrobial. A combination of antimicrobials with DMSO in the same perfusion also has been described, and clinical outcome was satisfactory.

When antimicrobials with known systemic toxic effects (eg, aminoglycosides) are used, concurrent systemic administration of the antimicrobial should be delayed or plasma drug concentrations monitored to avoid exceeding the toxicity threshold because after releasing the tourniquet, plasma concentrations may increase substantially. This is particularly important in systemically compromised or severely dehydrated horses.

**Volume of Perfusate Solution**

The optimal volume of perfusate is not accurately known. As a general rule, the higher the volume used, the higher the intravascular pressure achieved and the higher drug diffusion rate to surrounding tissues. Conversely, the higher the intravascular pressure, the higher the risk of perfusate leakage under the tourniquet into the systemic circulation. Antimicrobial perfusion of the distal portion of the limb in adult horses has been commonly performed with a perfusate volume of 60 mL, whereas lower (20 to 40 mL) and, recently, much higher (250 mL) volumes have also been used with satisfactory results. For perfusion of other anatomic locations, such as the carpus or tarsus, similar volumes have been used. In foals, smaller volumes (10 to 35 mL) are recommended.

After carpal perfusion with 60 mL, even distribution of contrast medium and India ink through the pericarpal tissues, synovial membranes, and carpal bones is evident and contrast medium is evident inside the carpal joint. Similarly, after perfusion of the distal portion of the limb with 40 mL of radiopaque dye, a radiographic study revealed complete distribution of the contrast medium through the digital tissues. Complete digital perfusion has been observed via digital venography after injecting 50 to 60 mL of contrast material. In a recent study, the perfusate volume (0.1 mL/Kg) was determined according to horse weight, which could be more proportional to the limb vasculature volume than a general unique volume. In another study that compared 30- and 60-mL volumes for tarsal perfusion, higher antimicrobial concentrations in synovial fluid were reached with the higher volume. In that study, lower intravascular pressure was achieved with the lower volume and this could have been the cause for a lower diffusion rate. However, the infusion site for each volume was different, and different anatomic venous accesses at each location and different distances between the infusion sites and the sampling location also likely contributed to the observed difference.

Clinically, we routinely use 40 to 60 mL for antimicrobial RLP in adult horses and find moderate vascular distention and resistance, especially in regions that have not been exsanguinated.

**Tourniquets**

Vascular isolation of the anatomic region to be perfused is achieved by the application of a tourniquet that compresses blood vessels as it is applied around the limb at a point proximal to the area to be perfused. The tourniquet’s ability to prevent perfusate leakage into the systemic circulation is the measure of its effectiveness. The MVP is the term for the highest pressure that can be achieved in the venous compartment during injection of a solution, and when MVP is reached, leakage of perfusate under the tourniquet occurs through the venous system. Tourniquet pressure and width, patient characteristics, site and rate of injection, volume of perfusate, and previous exsanguination determine the effectiveness of a tourniquet.

Use of wide tourniquets (20% wider than the limb diameter), low infusion rates, previous exsanguination, and injection from a site distal to the tourniquet increases the effectiveness of the tourniquet. Nevertheless, narrower tourniquets have been successfully used, although they are regarded as less efficient and more traumatic to the underlying tissues.

Different types of tourniquets, such as elastic rubber tubing, elastic bandages (ie, Esmarch bandage), pneumatic cuffs, and rolled gauze secured with elastic bandage, have been used. Pneumatic tourniquets allow better control of the technique and the pressure is more uniformly applied, so risk of tissue damage is decreased. The Esmarch bandage and a similar rubber bandage, effectively stop venous return after their application at the proximal portion of the metacarpus on anesthetized and standing horses, are commonly used in clinical practice, and are substantially cheaper than pneumatic tourniquets.

Commonly, tourniquets have been used on the distal portion of the limb of horses to control blood loss and provide a bloodless surgical field. On the basis of our clinical experience and published studies, tourniquet periods of up to 2 hours have minimal effects on horses. Severity and frequency of tourniquet-induced complications are diminished or avoided when the tourniquet is applied to a well-muscled region where nerves and blood vessels are protected, when pneumatic tourniquets are used, and when the lowest possible pressure needed to accomplish the desired effect is used. When performing antimicrobial RLP periods of 30 minutes are clinically practical and effective, although longer periods (up to 1 hour) have been used without adverse effects.
The pressure applied by an elastic tourniquet is variable and difficult to standardize. Ideally, the application pressure of a tourniquet should be the minimum pressure necessary to stop bleeding, which has been defined as approximately 100 mm Hg greater than the maximum systolic blood pressure, which is approximately 150 to 170 mm Hg. However, pressure values are not known when using rubber tourniquets, and with pneumatic tourniquets, higher pressure values from 300 to 500 mm Hg are typically used without reported adverse effects.

Systemic hypertension is a unique tourniquet-induced adverse effect described in adult horses. Blood pressure returns to reference range when the tourniquet is removed. In neonatal foals, development of severe tourniquet-induced osteonecrosis has been documented.

### Anesthesia Versus the Standing Position

Regional limb perfusion can be safely accomplished during anesthesia or in a standing horse. General anesthesia may be more comfortable and safer for the surgeon and helps better control the pain that may result from the injection (especially for IORLP), but it is expensive and exposes the horse to additional risks associated with general anesthesia. It is, however, practical for horses undergoing surgical debridement or joint lavage procedures because they can both be performed during the same general anesthetic episode. Regional limb perfusion should be performed after completing any surgical procedure because lavaging the joint can flush the antimicrobial away from the region of interest and surgical incisions cause the perfusate to leak from the vessels.

Regional limb perfusion can be safely accomplished daily during standing with sedation, with or without perineural anesthesia. The compression applied by the tourniquet may be uncomfortable and require an additional dose of sedative, a nerve block, or administration of some local anesthetic solution before the perfusate; this is typical during standing IORLP because of pain elicited by intramedullary pressure. In a standing horse, the tendons are loaded and stressed and are not compressed by the tourniquet, which makes correct application of the tourniquet challenging. To overcome this problem, small gauze rolls can be placed over the digital vessels in the groove between the suspensory ligament and flexor tendons for optimal vessel occlusion. Gauze rolls can also be placed over the cephalic or saphenous veins. Intravenous antimicrobial RLP on standing horses has resulted in satisfactory outcomes, and standing IORLP induces synovial fluid and bone concentrations of antimicrobials in the distal aspect of the limb that exceed the reported MIC of pathogens commonly implicated in orthopedic infections in horses.

### Clinical Applications

The presence of an antimicrobial in synovial fluid after RLP indicates that the drug has diffused through the synovial capillaries into the joint, traversing the synovial membrane, which is a site of bacterial colonization in an infected joint. Synovial fluid antimicrobial concentrations after RLP are not as high as those achieved after direct intra-articular injection, but concentrations as high as 100 times the MIC for periods up to 36 hours have been reported. Compared with systemic antimicrobial administration, RLP results in higher regional concentrations and Cmax/MIC ratios 3 to 30 times the target ratios of systemic administration.

Both IVRLP (administered either into the cephalic vein or into the digital vein at the level of proximal sesamoid bone) and IORLP (administered into the distal third of the metacarpal bone) techniques can be used for perfusion of digital structures of horses. Infusion into the first phalanx is an alternative, although a study of that technique revealed that antimicrobial concentrations in the metacarpophalangeal joint were lower, compared with the other techniques. Higher peak concentrations and area-under-the-curve values were observed in the distal interphalangeal joint after IVRLP, compared with IORLP, but no differences were observed in the metacarpophalangeal joint. For tarsal perfusion, IVRLP into the saphenous vein is preferred to IORLP into the distal portion of the tibia or proximal portion of the metatarsus because higher concentrations are achieved in synovial fluid and the procedure is easier to perform. However, both intraossceous routes adequately deliver the antimicrobial to the tibiotalar joint.

Few studies have investigated antimicrobial concentrations in bone. Bones located in the region subjected to RLP are also perfused, whereas there has been uncertainty regarding bone perfusion after intra-articular administration of antimicrobials; a recent study found that intra-articular injection and RLP results in bone concentrations of gentamicin that are not significantly different. Standing IORLP of the distal portion of the limb results in local gentamicin concentrations in the digital bones that exceed the reported MIC of pathogens commonly implicated in orthopedic infections in horses. Antimicrobial solution can also be directly infused into an infected bone.

Perfusate distribution to various tissues and structures has not been thoroughly studied. Time to reach Cmax and elimination half-life at each synovial digital structure are similar by both routes. Antimicrobial concentrations achieved in the digital tendon sheath are similar or lower than those detected in joints. If different digital joints are compared, similar amikacin concentrations in synovial fluid and synovial membranes are detected. However, significantly higher concentrations of vancomycin are found after IVRLP in the distal interphalangeal joint, compared with the metacarpophalangeal joint. Surrogate variables (such as area under the curve, half-life, and mean residence time) do not appear to differ between joints after digital antimicrobial perfusion.

All studies of regional pharmacokinetics of antimicrobials have been conducted on healthy animals. It is important to note that in septic conditions, vascularization can change substantially, thus changing concentrations and pharmacokinetics of antimicrobials. Systemic administration of antimicrobials has resulted in higher synovial concentrations in acutely inflamed joints, compared with healthy joints. However, Whitehair et al detected lower gentamicin concentrations in synovial fluid of inflamed joints subjected to RLP than those achieved in healthy synovial joints. Because
antimicrobial activity at infected sites can be reduced, pharmacokinetic investigations under septic conditions and more case-series studies would be beneficial.

In the published literature, RLP has been more effective than systemic administration for treatment for experimentally induced joint infections and has resulted in the elimination of infection in clinical cases of infectious arthritis and osteomyelitis. In experimental chronic infections in rabbits, antimicrobial perfusions resulted in negative results of bacteriologic cultures of bones in 70% of the animals, whereas in those treated with systemically active antimicrobials, only 35% yielded negative results. In that study, samples of purulent material aspirated from infected bone during the perfusion contained 100 times the antimicrobial concentration in the serum. The same investigators treated 15 human patients with long-standing (2 months to 38 years’ duration) osteomyelitis with IVRLP, and clinical effectiveness of the technique was proven. The effectiveness of the technique was evaluated in horses by resolving experimentally induced septic arthritis. In that study, the perfused joints had a significant decrease in mean leukocyte count and terminal bacterial cultures of synovial fluid and synovial membranes yielded negative results in 50% of joints, whereas results were positive in 100% of joints treated only via systemic antimicrobial treatment.

The effectiveness of RLP as a sole treatment is difficult to evaluate because it is usually used as an adjunct to conventional treatment (systemic administration of antimicrobials, lavage, debridement, anti-inflammatory, and rest). Treatment strategies and management differ largely among cases, which precludes direct comparisons among clinical reports. However, a successful clinical response in a great variety of clinical cases in which antimicrobial RLP has been performed supports the effectiveness of the RLP technique (Table 1). Survival rates are high (>80%), with many horses returning to riding soundness. Interestingly, 2 horses with implant-associated osteomyelitis healed without removal of the implants, and in 1 horse, a sequestrum was resorbed. In another foal with septic physis of the third metacarpal bone, administration of antimicrobials via RLP resulted in rapid healing of the lesion. We observed a similar response in a 3-week-old foal with an osteomyelitic lesion in the calcaneus that was unresponsive to systemic treatment and healed after RLP with amikacin. In both of these foals, debridement of the infected area was not performed.

There is no established general treatment protocol (ie, dose or number and frequency of RLPS) to obtain a successful outcome with orthopedic infections. From 1 to 9 protocols have been used for clinical cases, and they are usually performed once daily or every 2 or 3 days (Table 1). In humans with long-standing infections, antimicrobials are regionally infused twice daily for 5 to 7 days, which could be indicated when using time-dependent antimicrobials. Some horses have responded after a single perfusion. Factors that determine the effectiveness of RLP include characteristics of the infectious process, duration of the septic process prior to treatment, ability to debride the infected and necrotic tissue, susceptibility pattern of the organism, dose and mechanism of action of the antimicrobial, chronicity and extent of the infection, and the technique used for RLP. Comparative studies have not been conducted to determine the optimal duration of the procedure. The period that the tourniquet should be maintained could be dependent on physiochemical, pharmacologic, and pharmacodynamic characteristics of the antimicrobial; microbiologic factors; and individual factors of the patient and clinical case. In those animals in which the antimicrobial solution is infused slowly, maintenance of the tourniquet for a longer period than the infusion time is preferred to allow the antimicrobial to distribute completely into the tissues.

The prophylactic use of antimicrobial RLP prior to long surgical procedures seems interesting, and its effectiveness has been reported in humans prior to implantation of knee prosthesis. This practice could provide high antimicrobial concentrations at the tissue level when surgically approached. This has not been described in horses, but long surgical procedures, such as complex fractures or difficult arthrodesis, which are associated with a higher risk of infection, might benefit from the prophylactic use of RLP.

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