Medical Therapy in Equine Wound Management

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KEYWORDS

- Equine • Wounds • Antibiotics • Regional limb perfusion • Intraosseous perfusion
- Antibiotic-impregnated polymethylmethacrylate beads

KEY POINTS

- Acute superficial wound infections are usually the result of one dominating microorganism, whereas chronic or deep wound infections of horses are often polymicrobial.
- The most common organisms for subcutaneous tissue wounds are *Staphylococcus* species, which tend to be deceptive in onset and provoke a chronic inflammatory response.
- Traumatic synovial structure wound infections are typically gram-negative enteric genera, *Streptococcus*, and *Staphylococcus.* Polymicrobial infection is common.
- Regional and intraosseous perfusion maximizes efficacy of antibiotics by concentrating the antibiotic in a confined area to promote a concentration gradient.
- Antibiotic-impregnated polymethylmethacrylate beads are predominantly helpful for wounds that have a poor blood supply and for wounds containing surgical implants that must remain in place.

INTRODUCTION

The primary objective for the medical management of wounds is preventing infection and creating an optimum environment for wound healing with the reestablishment of an epithelial cover and recovery of tissue integrity, strength, and function. The goal in antimicrobial therapy is to administer an appropriate drug regimen so that pathogens are killed or curbed to the extent that they are purged by the host's immune system and no longer impede wound healing. The appropriate drug is determined by identifying the principal pathogens within the wound and associated antibiotic sensitivities. Regrettably, inappropriate use of antibiotics is likely a major cause for the widespread emergence of resistant pathogenic bacterial organisms.[1,2]

PROPHYLACTIC USE OF ANTIBIOTICS

Administration of prophylactic antibiotics to horses undergoing a clean surgical procedure of short duration is not indicated, except when the development of a surgical site infection (SSI) would be performance limiting or life threatening.[3] Although many factors contribute to SSI, studies suggest that the incidence of infection in horses after clean surgical procedures is very low.[4,5] Horses that have elective arthroscopy without receiving perioperative prophylactic antibiotics have a 0.5% incidence of septic arthritis versus a 0.9% incidence for horses undergoing arthroscopy that receive antibiotics perioperatively.[4,5] However, antimicrobial prophylaxis is indicated if the equine surgical patient is at high risk of infection; that is, when the likelihood of occurrence of infection exceeds 5% without prophylactic antimicrobial use.[3]

The use of antimicrobial drugs should not replace meticulous aseptic and atraumatic surgical technique. These include atraumatic handling of tissue, good hemostasis, preservation of blood supply, strict aseptic technique, accurate apposition and minimum tension on tissue, use of appropriately sized suture material, and obliteration of dead space. Risk factors of infection include surgical procedures that are clean-contaminated or contaminated, surgical times that exceed 60 minutes, anesthetic plane depths that may affect perfusion and oxygenation of tissues, and the presence of orthopedic implants.[6–12]

Suitable use of prophylactic antimicrobial drugs depends on the accurate selection of appropriate antibiotics, dosing regimen, and duration of use. An antibiotic with a narrow spectrum of activity should be selected for use to preserve the patient's normal flora and decrease the risk for development of antimicrobial resistance. Prophylactic antimicrobial therapy should begin preoperatively so that the concentrations of the drug in serum and tissues lasts for the duration of surgery and exceeds the minimum inhibitory concentration for organisms likely to be encountered.[13,14] The current recommendation is for the preoperative dose to be administered within 60 minutes of skin incision and for readministering during surgery if the procedure extends beyond 2 half-lives of the antibiotic.[14] The antibiotics used prophylactically most commonly in equine medicine, penicillin and gentamicin, reach peak concentrations at the surgical site between 15 and 30 minutes after intravenous (IV) administration, with concentrations declining rapidly thereafter.[15–17] The half-life of potassium penicillin G (20,000 IU/kg, IV) in horses is approximately 40 minutes, whereas that of gentamicin sulfate (6.6 mg/kg, IV) is approximately 90 minutes.[15–17]

For humans, prophylactic antibiotic therapy should be continued for no more than 24 hours postoperatively irrespective of whether the surgery was clean, clean-contaminated, or contaminated.[18–20] Prolonged administration of prophylactic antibiotics can result in increased morbidity, including a 33% greater rate of hospital infection, a 15% greater incidence of surgical wound infection, and may contribute to antimicrobial resistance.[18–20] There is no difference in the rate of SSI between horses that received antibiotics for less than 36 hours after exploratory celiotomy versus horses treated more than 36 hours, nor is there a benefit in administrating antibiotics for 120 hours rather than 72 hours, to prevent incisional infections after surgery for an acute abdominal crisis.[21,22]

THERAPEUTIC USE OF ANTIBIOTICS

Systemic administration of antibiotics is warranted when the degree of infection exceeds the efforts of local control of the bioburden and signs of local soft tissue infection or systemic infection are apparent.[23] Because the indication for systemic antibiotic therapy is not always clear, antimicrobial drugs are often administered

empirically, as a routine adjunct to the management of open wounds or when the wound is at high risk of becoming infected, such as with puncture wounds, devitalized tissue, open fractures, or has entered a body cavity or a synovial structure[24–26] (see Elsa K. Ludwig and Philip D. van Harreveld's article, "Wounds Over Synovial Structures," and Randy B. Eggleston's article, "Wound Management: Wounds With Special Challenges," in this issue).

A long delay between the onset of injury and treatment increases the risk that contamination will progress to colonization and infection. Debridement, irrigation, and topical therapies are fundamental to reducing the bacterial burden and disrupting biofilms (see Karl E. Frees' article, "Equine Practice on Wound Management: Wound Cleansing and Hygiene," and Britta S. Leise's article, "Topical Wound Medications," in this issue). Bacteria that become embedded in an extracellular polymeric substance (biofilm) are slow or nongrowing, but can delay wound healing because bacteria in biofilms have enhanced virulence, are protected from the immune response of the host, and are more likely resistant to antimicrobials.[27]

Bacteria cultured from acute and chronic wounds show a significantly higher potential for biofilm formation than bacteria isolated from skin. *Pseudomonas aeruginosa* and *Enterococcus faecium* are the bacteria species most commonly isolated from equine wound and skin samples, respectively. *Staphylococcus* was the most commonly isolated genus isolated from either environment.[28] Although bacterial colonization of a wound does not necessarily prevent wound healing, the presence of multiple bacterial species capable of biofilm formation suggests that bacteria may be surviving and proliferating within biofilm and subsequently hindering wound healing.[28,29]

Ideally, a wound exudate for bacterial culture and antibiotic sensitivity testing should be collected before instituting therapy. The sample should be harvested from deep within the wound rather than from its contaminated surface.[30] This enables targeting the microorganisms with a narrow-spectrum antimicrobial drug. Selected antibiotics should reflect the microbial predilection while considering the prevalence of antimicrobial resistance and the importance of using a narrow-spectrum antibiotic based on antibiotic sensitivity testing of bacterial isolates.[28,31,32] If clinical signs of infection evolve, final selection of the antibiotic is based on the results of culture and sensitivity tests.

For wounds of subcutaneous tissue, the most commonly cultured organisms are *Staphyloccus* sp, which tend to be insidious in colonization and provoke a chronic inflammatory response.[33,34] The less commonly found organisms involved in wound infection are *Streptococcus,* gram-negative aerobes, anaerobes, and *Corynebacterium pseudotuberculosis*. Penicillin, or trimethoprim-sulfonamide, or a combination of both, are often used empirically to treat acute or superficial wound infections while awaiting results of culture and sensitivity. Puncture wounds, including those involving synovial cavities, are frequently best treated with a beta-lactam antibiotic along with an aminoglycoside, such as gentamicin sulfate or amikacin sulfate because infections are often polymicrobial.[22–26,28,30–33] Ceftiofur sodium or enrofloxacin are generally reserved for infections resistant to penicillin and aminoglycosides.[22,33] Enrofloxacin is not recommended for use in young horses because it can rapidly lead to noninflammatory arthropathy in immature animals.[35] High doses of penicillin and metronidazole are recommended for treating deep fascial cellulitis, septic myositis, or pyonecrotic processes associated with *Clostridium* sp.[22,32] Antibiotic treatment of clostridial infection is typically required for weeks and discontinuation is based on the health of the affected tissues and negative culture results. *S* sp infections typically are more antibiotic sensitive, so treatment is commonly shorter (10–14 days).

Wounds of muscle typically respond very well to antimicrobial therapy, needing only a short course of treatment. Open drainage of muscle wounds, which is not difficult at

most sites, speeds resolution of infection particularly with intramuscular abscesses. Clostridial myonecrosis can rapidly cause severe systemic illness but with aggressive surgical debridement and aeration, local and systemic antibiotic therapy often resolves infection within days.[33]

For traumatic wounds of a synovial structure complicated by infection, the most commonly cultured organisms are gram-negative enteric genera, *Streptococcus* and *Staphylococcus.* Polymicrobial infection is common[33,35] (see Elsa K. Ludwig and Philip D. van Harreveld's article, "Wounds Over Synovial Structures," in this issue). Postoperative infection of a synovial structure typically involves *Staphylococcus, Streptococcus, Enterobacter, Pseudomonas*, or other enteric genera.[33,35] Administration of both a cephalosporin and gentamicin or amikacin is indicated for treatment of an infected synovial structure; enrofloxacin alone is a reasonable alternative in adult horses.[32] Metronidazole may be additionally administered for wounds on the distal aspect of the limb or other wounds likely to have fecal contamination or the presence of obligate anaerobes. Synovial structures usually require treatment for weeks using parenterally administered antibiotics initially that may be switched to oral administration after substantial improvement is seen. Intrasynovial lavage and antibiotic infusion are indicated and repeated, if needed. Regional perfusion for wounds at or distal to the carpus or tarsus is indicated and repeated, if needed.[36]

Traumatic wounds involving bone or physeal cartilage typically involve *Enterobacter, Streptococcus, Staphylococcus,* and in young foals, gram-negative enteric genera[33] (see Randy B. Eggleston's article, "Wound Management: Wounds With Special Challenges," in this issue). For postoperative osseous infections, *Streptococcus zooepidemicus, Staphylococcus aureus,* or another *Streptococcus* species is most commonly isolated.[9] The antibiotic treatment options are the same as for synovial structures. Weeks or months of antibiotic therapy is usually required for resolution of infection of bone or physeal cartilage.

The intravenous route should be used initially for systemic administration of antibiotics because the desired serum concentration of a drug is more predictable than when the drug is administered by other routes. The antibiotic can be administered orally or intramuscularly after an adequate concentration of the drug in the blood has been achieved by intravenous administration. Regional intravenous perfusion is particularly useful in the management of infected wounds on the distal aspect of limbs of horses, as it provides a high concentration of the antimicrobial drug at the target. Multiple surgical debridements of a wound may be necessary. The implantation of antibiotic-impregnated polymethylmethacrylate (PMMA) beads into a wound are particularly important when complete debridement is not possible or when surgical implants must remain.[36]

The duration of treatment of any wound infection is primarily dictated by the patient's response to therapy. The benchmarks that indicate a positive response include resolution of systemic signs of inflammation, continued improvement in comfort and function, reduction and ultimately resolution of the localized signs of inflammation and purulent discharge, negative culture result, and a normal rate of wound healing. Administration of antimicrobial drugs should not be continued once there is clinical and microbiologic evidence that an infection has been eliminated.[37]

REGIONAL INTRAVENOUS ANTIBIOTIC DELIVERY

Regional intravenous delivery of antibiotics may be pivotal for resolution of well-established infections, wounds of inadequately perfused tissue, biofilm-infected wounds, and wounds involving surgical implants that must remain in place. Targeted

modes of antibiotic delivery may even preclude the need for systemic antibiotic therapy in certain cases.

Regional intravenous limb perfusion with antibiotics maximizes efficacy of treatment while minimizing the cost of the drug and the risks of toxicity and development of antibiotic resistance. Therapeutic concentrations of antibiotic can be achieved even in poorly perfused wounds or those with necrotic tissue, because the drug diffuses down a concentration gradient from the vascular space to the interstitial space. Regional intravenous perfusion is most effective with concentration-dependent antibiotics, such as aminoglycosides, although it may also be effective with time-dependent antibiotics, such as penicillins and cephalosporins. For susceptible pathogens, a single treatment may be adequate when administered in concert with systemic antimicrobial therapy.[38]

As most regional intravenous limb perfusions are usually performed in the standing horse, the patient should be sedated and the site of catheter placement desensitized with regional anesthesia. A palmar nerve block for digital perfusion via a palmar digital vein improves patient comfort and reduces movement during perfusion. A ring block may be used for regions with complicated or multifaceted innervation. The level of sedation necessary is dictated by the horse's temperament and severity of pain and achieved by choice and dose of the sedative.

To prepare for regional intravenous limb perfusion, the skin should be clipped and aseptically prepared, as for a routine IV catheterization. A sterile IV catheter, such as a butterfly, or short over-the-needle catheter, is used for a single treatment. It is convenient to use an indwelling IV catheter for repeated treatment. Catheter gauge and length vary according to vein diameter and shape. An extension set can be affixed to the hub of the catheter, which is glued or taped to the skin with adhesive tape. It is best to place and secure the catheter before applying the tourniquet, because securing the catheter may take several minutes and the tourniquet must be removed 30 minutes after placement.

Tourniquets limit the antibiotic to the perfused area, thereby creating local concentrations of the antibiotic in tissues and fluids that significantly exceed those achieved after systemic administration. An Esmarch or pneumatic tourniquet is applied firmly and then secured so that it occludes venous outflow for the duration of the 30-minute procedure.[39,40] Adhesive tape or a bandage should be applied to secure the Esmarch bandage after application.

Where possible, a pair of tourniquets proximal and distal to the wound and catheter/cannula site should be used to isolate the infected area and nearby vein. Narrow rubber tourniquets and elastic bandages are not suitable for this procedure.[39] The proximal tourniquet prevents escape of the antibiotic into the systemic circulation during perfusion. The distal tourniquet limits the volume of tissue being perfused. A tourniquet that is applied too lightly or that loosens allows the antibiotic to exit the area and escape into systemic circulation before the procedure is completed, which prevents achieving locally high antibiotic concentrations at the site of the infection. If using a palmar/plantar digital vein for IV perfusion, the tourniquet should be applied in the mid-metacarpal/tarsal region. If using the cephalic/saphenous vein because of local swelling distally, apply the tourniquet to the distal aspect of the radius/tibia.

The antibiotic solution should be immediately infused after applying the tourniquets. To reduce the hydrostatic pressure during infusion, and reduce the risk of extravascular leakage and perivascular inflammation, blood is allowed to flow without restrictions from the extension set until it slows to a drip, or alternatively, a volume of blood equal to the intended infusion can be aspirated. The antibiotic solution is infused

slowly over 1 to 2 minutes, then the drug within the extension set is emptied into the catheter by infusing a small bolus of air.

The tourniquet is removed after 30 minutes. The catheter is removed unless repeated perfusion is anticipated. Firm digital pressure is applied to the venipuncture site or the site is securely wrapped for a few minutes. The venipuncture site is then covered with a sterile dressing and light pressure wrap. Maintenance of an indwelling catheter is the same as for IV catheterization at any other site. More perivascular swelling may be present for 24 to 48 hours after catheter removal, but no other adverse effects are seen in most cases. Using a topical nonsteroidal anti-inflammatory drug (NSAID) (eg, 1% diclofenac liposomal cream) may be of value if an indwelling catheter was not placed and the site may need to be used again.[41,42]

The dose of amikacin used is prescribed by the size of the perfused area: 500 to 1000 mg for smaller areas like the digits through the palmar or plantar vein, or 2.0 to 2.5 g when perfusing the distal aspect of the limb via the cephalic or saphenous vein for the carpus or tarsus. Other commonly administered drugs and dosages that can be incorporated into a regional limb perfusion route in an adult horse include gentamicin: 100 to 300 mg; Na/K penicillin: 10 million to 20 million units; ceftiofur: 2 g; enrofloxacin: 700 mg (1.5 mg/kg); and marbofloxacin: 300 mg (0.67 mg/kg). Enrofloxacin may cause vasculitis at therapeutic dosages, so is best reserved for documented enrofloxacin-sensitive infections with no other reasonable options. Bactericidal drugs (eg, aminoglycosides, penicillins, cephalosporins, metronidazole, rifampin, and quinolones in adult horses) are best used to treat severely infected wounds rather than using bacteriostatic drugs (eg, chloramphenicol, tetracyclines, sulfonamides, macrolides, and trimethoprim-sulfonamide combinations).[36,38,42,43]

Volumes commonly administered are 20 to 30 mL for perfusion of the digit via a digital vein; 60 mL for larger areas, such as the carpus/tarsus, distal aspect of the limb; and up to 100 mL for distal limb perfusion via the cephalic/saphenous vein. However, lower perfusion volumes with higher drug concentrations, such as 500 mg gentamicin diluted in 10 mL with sterile isotonic saline solution for perfusion of the distal aspect of the limb via a palmar digital vein may be equally effective.[33,34] Lower perfusion volumes also may reduce the risk of extravascular leakage and perivascular inflammation caused by high hydrostatic pressures associated with larger volumes.[34,44]

A disadvantage of regional limb perfusion with antibiotics is that intravenous perfusion is difficult or impossible when soft tissue swelling obscures the desired vein.[39] There is potential for phlebitis and local tissue necrosis with IV perfusion, particularly when the procedure is repeated or if perivascular leakage occurs. Regional limb perfusion is limited to wounds at or below the carpus or tarsus because a tourniquet must be applied proximal to the site and there is limited residual effect after the tourniquet is removed.[22,39,42]

For intrasynovial injections into a joint space, tendon sheath, or bursa, it is important to use meticulous aseptic technique to avoid further contamination of the synovial structure while injecting an antibiotic. Improved effectiveness of the antibiotic can be achieved if the joint space is lavaged liberally beforehand. Although constant-rate infusion of antibiotic is described for synovial injections in horses, clinical response and long-standing effect seem analogous to individual-dose intrasynovial injection.[45] Commonly administered antibiotics using this route for adult horses include amikacin: 500 to 1000 mg; gentamicin: 150 to 500 mg; ceftiofur: 150 mg; cefazolin: 250 to 500 mg; and Na/K penicillin: 2 million to 5 million units.[38]

INTRAOSSEOUS REGIONAL LIMB PERFUSION

Intraosseous (IO) perfusion is indicated when there is severe soft tissue swelling, edema, or when the veins are not easily accessed. Intraosseous perfusion involves drilling a hole through cortical bone into the medullary cavity. A site is selected that has the greatest and most reachable medullary cavity nearest the wound and that lies just under the skin, requiring little or no surgical dissection to access. The distal aspect of tibia or proximal third of the metatarsus are commonly chosen as sites for IO perfusion of the tarsus. The horse is sedated and the drill site desensitized using regional anesthesia. Hair is clipped and skin is aseptically prepared. Using aseptic technique, a 1-cm incision is made through skin, subcutis, and periosteum over the infusion site, taking care to avoid nerves, vessels, and tendons. The soft tissue is gently retracted with a pair of hemostatic forceps and a 4-mm-diameter uni-cortical hole is drilled through the cortex. The hole is subsequently tapped to 5.5 mm in diameter, if a self-tapping screw is not used, and a 5.5-mm 20-mm cannulated bone screw is inserted so that it provides direct access to the medullary cavity. The male end of a catheter extension set is attached to the Luer lock adapter inserted into the cannulated screw. Alternatively, the male adapter end of an IV delivery set can be carefully wedged into a 4-mm-diameter bone hole.[46]

Tourniquets are applied proximally and distally before antibiotic perfusion to isolate the wound and cannula site to prevent the escape of the infused antibiotic into the systemic circulation. The distal tourniquet limits the volume of tissue being perfused, and thus dilution of the antibiotic in the extracellular fluid. For wounds at or distal to the metacarpo/metatarsophalangeal joint, a single tourniquet is applied proximal to the site. For standing horses, 2 to 3 mL of a local anesthetic solution is infused into the medullary cavity to reduce discomfort caused by the increase in intramedullary pressure during infusion. With tourniquets occluding blood flow proximally and distally, the antibiotic, diluted in 60 mL sterile isotonic saline solution is slowly infused into the medullary cavity over 10 minutes, from where it is absorbed into the regional vasculature. The tourniquet is removed 30 minutes after completing the infusion.

If planning to repeat the IO infusion, the port in the bone screw is capped and covered with a sterile dressing and protective bandage; otherwise the cannulated screw is removed and skin is either closed or left to heal by second intention. In either case, the site is covered with a sterile dressing and light pressure wrap. Localized soft tissue swelling can be expected at the site for a few days after IO perfusion, as can a small amount of serosanguinous discharge when the skin incision is not closed primarily. No treatment other than basic postsurgical wound care is required.

ANTIBIOTIC-IMPREGNATED POLYMETHYLMETHACRYLATE BEADS

Antibiotic-impregnated polymethylmethacrylate (PMMA) beads are predominantly helpful for treatment of wounds that have a poor blood supply and for those containing surgical implants that must remain in place. They may also be useful for treatment of infected wounds in problematic patients that make other forms of antibiotic delivery and wound care challenging or unachievable. Locally high antibiotic concentrations can be sustained in the wound, which may allow discontinuation of systemic antibiotic therapy.[38]

The antibiotic, preferably in lyophilized form, is mixed with the dry PMMA polymer at a rate of 1 to 4 g antibiotic to 20 g polymer. The liquid monomer is applied in a powder-to-liquid ratio of 2:1, and mixed thoroughly for 1 minute. If using a bead mold, 3 strands of size 0 braided polyester suture material can be placed over one-half of the mold, and both halves of the mold are filled with the PMMA mixture. The mold is closed

and clamped tightly, allowing the beads to take an appropriate size and spherical or cylindrical shape for the wound and then put aside to harden for at least 10 minutes. A bead mold that forms 6-mm-diameter beads is optimal for treatment of most infected wounds. When using more than one antibiotic, a separate batch of PMMA beads should be made for each drug. Metronidazole may be mixed with hoof acrylic (Equilox; Equilox International, Pine Island, MN) for treatment of polymicrobial infections.[38]

The size and number of antibiotic-impregnated PMMA beads implanted in a wound are determined by the dimensions of a wound. When the beads are placed into the wound, they release sustained therapeutic concentrations of the antibiotic into the surrounding fluid and tissue for several days or weeks. Unless the beads are being implanted while the horse is anesthetized, the horse is sedated and local or regional anesthesia is used to desensitize the wound. The beads may be held in place by partially suturing the wound or by maintaining a sterile dressing over the wound. If the beads are not used immediately after formulation, they should be stored in a sterile, airtight container away from direct light until implanted.

Because the PMMA beads do not biodegrade, they may need to be removed after treatment, depending on the type of wound, ease of the bead removal, and the likelihood of them causing functional impairment if left in place. The beads may be left in place unless they are causing persistent foreign body reaction and drainage, are likely to interfere with future athletic function, or need to be replaced with fresh antibiotic-impregnated beads. Removing the beads can be difficult after approximately 10 days because they become encapsulated by fibrous tissue as the wound heals. Intrasynovial use of PMMA beads is not advised, because it may cause synovial irritation and pain, but if used, the beads should be removed as soon as the infection is resolved, and at most in fewer than 10 days[38] (see Elsa K. Ludwig and Philip D. van Harreveld's article, "Wounds Over Synovial Structures," in this issue).

NONSTEROIDAL ANTI-INFLAMMATORIES

Inflammation is a normal part of the wound-healing process, and is important for the removal of contaminating microorganisms. In the absence of effective decontamination, however, inflammation may be prolonged. Both bacteria and endotoxins can lead to the prolonged elevation of proinflammatory cytokines, such as interleukin (IL)-1 and tumor necrosis factor-α, and lengthen the inflammatory phase leading to chronicity and failure to heal. Prolonged inflammation within a wound also leads to an increased concentration of matrix metalloproteases, a family of proteases that can degrade the extracellular matrix. Accompanied by the increased protease content in a chronically inflamed wound, the concentration of naturally occurring protease inhibitors can decrease. This shift in protease balance in chronic wounds can cause growth factors that promote healing to be rapidly degraded.[47,48]

NSAIDs are commonly administered to wounded horses for the treatment of inflammation and for pain management. These drugs inhibit the activity of cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) enzymes and thereby the synthesis of eicosanoids, such as prostaglandins, thromboxanes, and leukotrienes. It is likely that most of the analgesic effects of NSAIDs are related to a reduction in inflammation and swelling without affecting the central nervous system.[49] Selective inhibition of COX-2 enzymes in the horse may provide anti-inflammatory, analgesic, and antipyretic effects without causing adverse effects on the gastrointestinal system, such as right dorsal colitis, which is attributed to COX-1 enzyme inhibition.[49]

Some NSAID drugs are thought to be clinically more effective for ameliorating musculoskeletal pain, and others are believed to be more effective for ameliorating visceral pain. For example, flunixin meglumine is considered to be more effective than phenylbutazone for controlling abdominal, uterine, and ophthalmic pain, whereas phenylbutazone is believed to be more effective in controlling musculoskeletal pain. Nevertheless, flunixin can reduce musculoskeletal inflammation and pain, and phenylbutazone is clinically effective for treatment of visceral pain.[50–53]

There are few data to suggest that short-term administration of NSAID drugs has a negative impact on healing. However, the question of whether long-term administration of NSAID drugs interferes with wound healing remains unanswered. In animal models, systemic use of ibuprofen has demonstrated effects on wound healing that include decreased numbers of fibroblasts, weakened wound breaking strength, reduced wound contraction, delayed epithelialization, and impaired angiogenesis.[54–57] The effects of administering an NSAID drug to equine patients during the early phase of wound healing have not been investigated extensively. One study examining incisional healing found that oxyphenbutazone administered to horses at a loading dose 12 mg/kg for 2 days and then a maintenance dose of 6 mg/kg for 5 days significantly reduced wound inflammation and formation of granulation tissue.[58]

The most common use of NSAIDs is for treatment of musculoskeletal and abdominal pain. The NSAIDs most commonly administered to horses are phenylbutazone, flunixin meglumine, and more recently, the selective COX-2 inhibitors carprofen, meloxicam, and firocoxib.[59] Dosages for NSAIDs commonly used in horses are as follows: phenylbutazone 2.2 to 4.4 mg/kg, every 12 hours, intravenous or oral; flunixin meglumine 0.25 to 1 mg/kg, every 8 to 24 hours, intravenous, oral, or intramuscular; carprofen 0.7 mg/kg, every 24 hours, intravenous or oral; ketoprofen 2.2 mg/kg every 24 hours, intravenous; meloxicam 0.6 mg/kg every 24 hours, oral; or firocoxib 0.1 mg/kg, every 24 hours, oral.[53]

DIMETHYLSULFOXIDE

Dimethylsulfoxide (DMSO) is an effective anti-inflammatory, analgesic, and enzyme activator/inhibitor.[60–62] Significantly decreased white blood cell counts in the synovial fluid of joints with chemically induced synovitis treated with DMSO have been reported.[63] DMSO may also possess some bacteriostatic properties as a result of its effect on the immune response and the reduction of endotoxin-induced tissue damage.[60,62] Increased blood flow through experimental skin flaps and the presence of vascular dilation with DMSO application has also been reported.[62] DMSO appears to assist other treatments in attempts to reduce wound-associated limb edema. A 20% solution using medical-grade 90% DMSO in 250 mL Lactated Ringer's Solution with 1 to 2 g of amikacin added has been described as a perfusate.[64] Such properties provide rationale for its use in conjunction with an antibiotic for regional limb perfusion.

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