LOCAL ANTIBIOTIC THERAPY IN EQUINE INFECTIONS

THE OLD AND THE NEW

SK Hart, BVMS (Hons); JG Barrett, DVM, PhD, DACVS; KE Sullins, DVM, MS, DACVS
Marion duPont Scott Equine Medical Center,
Virginia-Maryland Regional College of Veterinary Medicine
Leesburg, Virginia, USA 20176

INTRODUCTION

Orthopaedic and soft tissue infections are an important cause of morbidity and mortality in equine patients. Postoperative infection rates in horses are reported to be 10% to 53%[1] in musculoskeletal surgery, and 10%[2] to 37%[3] in gastrointestinal surgery.

Systemic Antibiotic Therapy:

- Prohibitive cost
- Risk of organ toxicity; narrow therapeutic range
- Delivery to area of infection can be unpredictable
- Biofilm formation may result in bacteria being up to 1000 times more resistant to antibiotics
- Increased prevalence of multi-resistant bacteria limits antibiotic choices

Local Antibiotic Therapy:

- Associated with decreased morbidity, hospital stay and cost of treatment in humans[4]
- Excellent outcomes in treatment of orthopaedic infections in horses
- Established methods: regional limb infusion, direct injection in to synovial structure, antibiotic-impregnated polymethylmethacrylate (PMMA), and continuous infusion in to synovial structures
- Newer methods include the use of biodegradable antibiotic delivery devices, calcium sulphate-dextran sulphate beads and a cross-linked dextran gel

AIMS

To present a concise discussion of the currently available local antibiotic therapeutic modalities, and the advantages and disadvantages of each.
Introduce several newer methods of delivering local antibiotics in high concentrations, and the applications in orthopaedic and soft tissue surgery.

CONCLUSIONS

- Local antibiotic therapy can play an important role in the management of severe orthopaedic and soft tissue infections in the horse. The use of these modalities may decrease total hospital stay and improve outcome in select cases.
- There are a number of different applications for local antibiotic therapy. Newer biodegradable, biocompatible formulations provide an improved method of delivery.

NEWER METHODS OF LOCAL ANTIBIOTIC DELIVERY

Several novel methods of local delivery of antibiotics are now available. These include the use of biodegradable, biocompatible matrices in the form of antibiotic-impregnated cross-linked dextran gel.

Cross-linked dextran gel **is an injectible gel that is biocompatible, fully biodegradable and nonimmunogenic.**

- **A sustained release composition comprising an antibiotic or combination of antibiotics, and a water-soluble complexing polymer of sufficient molecular weight that it forms a gel when mixed (Figure 1).**
- **The gel combined with different antibiotics (amikacin, vancomycin, or amikacin-clindamycin) is widely used in the treatment of diabetic foot infections in humans, with excellent results.**
- **Amikacin-, vancomycin-, or amikacin/clindamycin-impregnated R Gel® has been evaluated experimentally in horses. The gel was implanted via surgical incisions in the necks of horses, and capillary ultrafiltration probes were used to collect interstitial fluid to measure elution of the antibiotics.**
- **Concentrations greater than 2000 times the MIC of vancomycin (4µg/ml), and greater than 1000 times the MIC of amikacin (4µg/ml) were achieved.**
- **Mean concentration remained above MIC for vancomycin at the incision for 10 days, and at 1.5cm from the incision for 8 days. Mean concentration remained above MIC for amikacin at the incision for 10 days and at 1.5cm from the incision for 7 days.**
- **Use in clinical cases: soft tissue and orthopaedic infections, including incision infections, orthopaedic implant infections, chronic draining wounds, poll evil (supra-atlantal bursitis) and sinus infections (Figure 2).**
- **Potential for other anti-infectives (primarily anti-fungals) to be incorporated in to the cross-linked dextran gel also exists.**

Figure 1: R Gel®. Provided in two syringes, which are conjoined, and reciprocation for 2 – 3 minutes results in a viscous gel being formed.

Figure 2: Use of antibiotic-impregnated cross-linked dextran gel in clinical cases. A – Chronic Draining tract of the right hind heel bulbs; B – Draining tract of the face; C – Septic extensor carpi radialis tendon shealth.

ESTABLISHED METHODS OF LOCAL ANTIBIOTIC DELIVERY

Routine methods of local antibiotic delivery include regional limb infusion, continuous intra-synovial infusion, direct injection of an appropriate antibiotic in to a synovial structure, or use of antibiotic-impregnated polymethylmethacrylate (PMMA).

Regional limb infusion: administration of antibiotic solution in to the vasculature of the distal limb isolated by a tourniquet → high concentration and pressure gradients, and a significantly greater local concentration of antibiotic compared to what could be achieved using systemic antibiotics alone. Intravenous (Figure 5) and intraosseous techniques used.

Advantages:
- Inexpensive, simple, effective

Disadvantages:
- Thrombophlebitis (IV)
- Diffuse oedema/ cellulitis affects access (IV)
- Discomfort during infusion

Continuous intra-synovial infusion of antibiotics: most commonly a balloon infusion system, consisting of an administration pump, flow control tubing, an air filter, intra-articular catheter and introducer (Figure 6).

Advantages:
- Constant delivery of antibiotics to an infected area ensures antibiotic concentrations are maintained up to 100 times the MIC
- No significant detrimental effects on the synovial membrane or articular cartilage[6]

Disadvantages:
- Can be difficult to maintain; may need to be replaced because of complications.[6]
- Systemic absorption → systemic dose must be adjusted[9]

Figure 5: Intravenous regional perfusion of the distal limb.

Figure 6: Continuous Intra-synovial infusion in a septic digital flexor tendon sheath.

Figure 7: Direct intra-articular infection in to the palmar pouch of the distal interphalangeal joint.

Direct injection: achieves sufficiently high concentrations (greater than the minimum inhibitory concentration, or MIC) for up to 48 hours.[5] Typically easy to perform; however, in fractious horses, for multiple injections, or in presence of extensive soft tissue damage, it may be more difficult (Figure 7).

Antibiotic-impregnated PMMA: widely used in the local treatment of orthopaedic infections. Has been used for decades to augment systemic antibiotic therapy, is effective in providing high local antibiotic concentrations, inexpensive and simple to manufacture.

Disadvantages:
- Variable antibiotic elution
- Construction of the PMMA involves an exothermic reaction
- PMMA is non-biodegradable, and a second surgery may be required if removal of the beads is necessary
- Prolonged elution of sub-therapeutic concentrations of antibiotics has been associated with the development of resistance in humans
- PMMA exhibits low biocompatibility

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