Arthritis

BY CHRISTY WEST

Doxycycline Antibiotic For Arthritis?

Osteoarthritis is the most common human joint disorder in the world, and in the equine industry it's the most economically important disease," said Ashlee Watts, DVM, a graduate student at Cornell University, during the 2007 American Association of Equine Practitioners Convention, held Dec. 1-5 in Orlando, Fla. "It's the primary cause of decreased athletic function and wastage in racehorses."

Many medications have been tried to treat this common condition, and Watts discussed the relatively new option of doxycycline for arthritis. Doxycycline is a semisynthetic antibiotic that's related to tetracycline and has been used in horses since the 1990s. It's also used to treat Lyme disease, and one study on that disease noted that horses given the medication along with other antibiotics "never went better," despite being negative for Lyme disease, suggesting a possible anti-inflammatory effect. Therefore, researchers decided to investigate its possible use against osteoarthritis.

Doxycycline might indeed be therapeutic for osteoarthritis, laminitis, and neuropathy (nerve dysfunction), and it might be useful for prophylaxis in high-risk cases.

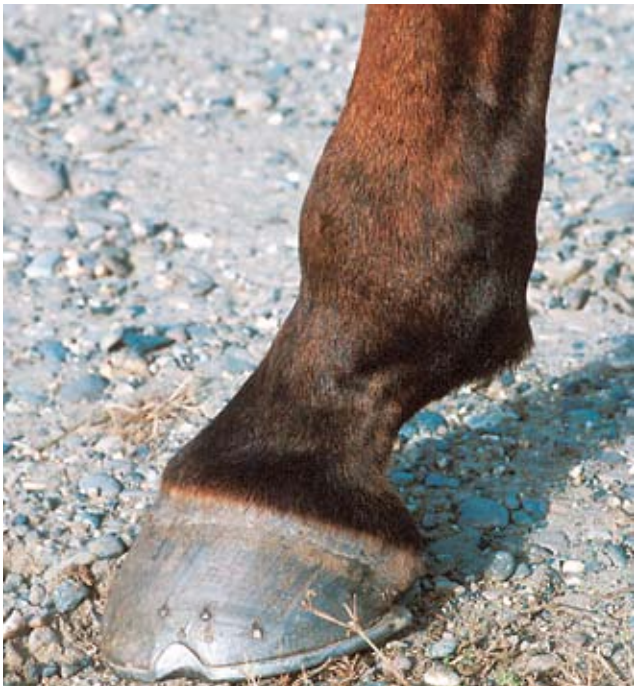
Previous laboratory research found that at concentrations as low as 0.0462 microliters (µg/mL) in synovial (joint) fluid and plasma, doxycycline could inhibit the expression of matrix metalloproteinases 3 and 13 (MMP 3 and 13). Various MMP enzymes have been implicated in osteoarthritic and laminitic disease processes, so inhibiting them might help slow these disease processes. However, antibiotics shouldn't be used at antimicrobial levels (which are substantially higher than 0.0462 microliters (µg/mL) without good reason, because this might promote antibiotic-resistant bacteria strains.

To determine if oral dosing could deliver enough doxycycline (0.0462 µg/mL) to joints without having antimicrobial effects, researchers fed six healthy horses 5 mg/kg (half the recommended antimicrobial dose) every 12 hours via nasogastric tube for two days. This dosing strategy was, indeed, effective at achieving therapeutic concentrations in the joints, Watts reported; levels reached 0.1943 µg/mL by one hour after administration and increased thereafter.

Thus, doxycycline might indeed be therapeutic for osteoarthritis, laminitis, and neuropathy (nerve dysfunction), and it might be useful for prophylaxis in high-risk cases. Possible concerns with doxycyline use include photosensitization (horse becomes overly sensitive to light) and whether it can be performance-enhancing in addition to disease-modifying.

"Further in vivo studies are warranted to determine if MMP activity is inhibited in vivo and to fully elucidate a medication protocol," she concluded.

(Lisa Fortier, DVM, PhD, Dipl. ACVS, associate professor of veterinary clinical sciences at Cornell University, was the principal investigator on the study.)



DR. NANCY S. LOVING

Swelling in the fetlock joint due to osteoarthritis.

Treatments for Osteoarthritis

Osteoarthritis has a major impact on pain and athleticism of horses, and many medications are used to combat it. At the 2007 American Association of Equine Practitioners Convention, held Dec. 1-5 in Orlando, Fla., an in vitro study comparing commercial preparations of hyaluronic acid (HA, Hylartin V) and the corticosteroid triamcinolone acetate (TA, Vetalog), in terms of two measures of joint health, were presented. Elysia Schaefer, DVM, a graduate student and second-year equine surgery resident at the University of Illinois, presented the study results.

"Hyaluronic acid is an important component of cartilage that helps maintain hydrostatic pressures to resist weight-bearing forces," she explained. "Corticosteroids inhibit the production of inflammatory mediators (some of which can break down cartilage) and leukotrienes (which sustain inflammatory reactions), which are in part responsible for pain. They also block production of pro-inflammatory cytokines."

The study was carried out on normal chondrocyte (cartilage cell) pellets from six horses that were stimulated to break down the cartilage matrices by using interleukin-1 (a degadation protein). Researchers found that only the HA product significantly increased proteoglycan synthesis (proteoglycan is a necessary

component of cartilage), while both products significantly increased glycosaminoglycan content of cartilage (which works to protect against the progression of arthritis).

"In this study, there was no significant interaction when combining HA and TA," noted Schaefer. "Both a high dose of HA (2 mg/mL) and of TA (0.6 mg/mL) had a protective effect on interleukin-1-stimulated chondrocytes."

Myristol's Effects on Clinical Joint Disease

The results of a blinded, controlled study on the effects of the neutraceutical Myristol on lameness caused by osteoarthritis (OA) were discussed by Kevin Keegan, DVM, MS, Dipl. ACVS, associate professor of equine surgery at the University of Missouri.

The product contains cetyl myristoleate, glucosamine hydrochloride, methylsulfonylmethane, and hydrolyzed collagen. "Each individual ingredient has shown some positive effect in either human clinical trials or *in vitro* (in the lab) in horses," said Keegan.

For the study, 39 horses in Missouri and Florida were selected for naturally occurring osteoarthritis that caused Grade 2-4 lameness on a scale of 0-4. Horses were either in the control group (no Myristol) or the treated group, which received 4 ounces of Myristol daily for 14 days, then 2.67 oz daily for 28 days (42 total days of supplementation). Lameness exams at Days 1, 14, 28, and 42 were used to assess the efficacy of the supplement.

Researchers found that treatment with Myristol significantly improved lameness score, lameness at the walk, response to joint flexion, lameness after flexion, and quality of life compared to controls.

"We conclude that oral administration of Myristol had beneficial clinical effects on horses with naturally occurring OA," said Keegan. "The most apparent beneficial effects were in parameters related to joint flexion. For many of these horses, this was a significant improvement in their quality of life."

Surpass vs. Bute for Arthritis

David Frisbie, DVM, PhD, Dipl. ACVS, associate professor of veterinary clinical sciences at Colorado State University (CSU), discussed a study comparing clinical efficacy and joint health parameters of Surpass (topical liposomal diclofenac cream) to those of the commonly used oral non-steroidal anti-inflammatory medication phenylbutazone (Bute).

In 24 horses, carpal (knee) osteoarthritis was induced in one knee, and the horses were split into one control and two treatment groups. One treatment group got 7.2 g of Surpass on the affected joint every 12 hours for five days, while the other received 2 g of Bute orally once a day for five days. Horses were exercised on a high-speed treadmill daily, and lameness, tissue scores, biochemical scores, and biomarker scores were used to evaluate the efficacy of treatment.

Frisbie reported that the Bute- and Surpass-treated limbs got significantly better in terms of lameness scores. The cartilage glycosaminoglycan content in the Surpass-treated limbs was better than with Bute (meaning the cartilage was better hydrated and lubricated). There were also improvements in bone sclerosis (hardening) of the radial carpal bone and total erosion scores in the Surpass-treated joints.

"Both Surpass and Bute had symptom-modifying effects, but Surpass alone had disease-modifying (curing) effects," Frisbie summarized. "Diclofenac liposomal cream (Surpass) applied to a joint with experimental osteoarthritis provides a significantly better outcome than a similar joint treated with systemic phenylbutazone."