Orally administered enrofloxacin, a quinolone antibiotic, was shown to cause cartilage damage similar to that observed in immature animals of other species. The damage was characterized by synovial joint effusion and lameness, erosion and cleft formation in articular cartilage, and histological evidence of chondrocyte damage and loss of proteoglycans. Authors' address: Triangle Equine, PO Box 4707, Cary, NC 27513 (Vivrette), Department of Anatomy, Physiological Sciences and Radiology (Bermingham, Papich), and Department of Microbiology, Pathology and Parasitology (Bostian), College of Veterinary Medicine, North Carolina State University, 4700 Hillsborough St., Raleigh, NC 27606. © 2001 AAEP.

1. Introduction

Quinolones are broad spectrum gyrase-inhibiting antibiotics that have been shown to cause articular cartilage damage in immature dogs, rodents, rats, and other species. Typically, quinolone arthropathy is associated with acute disease of weight-bearing joints with fissures in Zone 2 of the articular cartilage, loss of chondrocytes, and cartilage erosion.1 Studies on the effects of quinolone antibiotics on articular cartilage in the horse are limited. An in vitro study using cartilage explants did not demonstrate cartilage damage, although proteoglycan synthesis was reduced at high doses.2

Previous studies at North Carolina State University (NCSU) have investigated the pharmacokinetics of intravenous and oral enrofloxacin in foals.3 The results of that study determined that for IV administration, mean ± SD total area under the curve (AUC0-infinity) was 48.54 ± 10.46 µg × h/ml, clearance was 103.72 ± 0.06 ml/kg/h, half-life (t½β) was 17.10 ± 0.09 hours, and apparent volume of distribution was 2.49 ± 0.43 l/kg. For oral administration, AUC0-infinity was 58.47 ± 16.37 µg × h/ml, t½β was 18.39 ± 0.06 hours, maximum concentration (Cmax) was 2.12 ± 0.51 µg/ml, time to Cmax was 2.20 ± 2.17 hours, mean absorption time was 2.09 ± 0.51 hours, and bioavailability was 42 ± 0.42%. Compared with adult horses given 5 mg of enrofloxacin/kg IV, foals have higher AUC0-infinity, longer t½β, and lower clearance. Concentration of ciprofloxacin was negligible. Using a target Cmax to minimum inhibitory concentration ratio of 1:8 to 1:10, computer modeling suggests that 2.5 to 10 mg of enrofloxacin/kg administered q 24 h would be effective in foals, depending on minimum inhibitory concentration of the pathogen.

This study was designed to study the effects of the quinolone antibiotic enrofloxacin on articular cartilage in neonatal foals.

2. Materials and Methods

Four neonatal foals (Quarter Horse, Standardbred, Arabian, and Thoroughbred crosses) were used in the experiment. The average weight of the foals was 54.18 kg. In a separate experiment, the foals
were administered a single dose of enrofloxacin intravenously at 5 mg/kg, and, after a washout period, PO at 10 mg/kg for pharmacokinetic evaluation of the drug. After the oral pharmacokinetic study, enrofloxacin was administered at 10 mg/kg PO once daily for 8 doses beginning at 2 weeks of age. The mares and foals were kept in a 12 × 12 foot box stall at night, and were turned out (60 × 60 foot corral or 2 acre pasture) during the day. The foals were monitored for clinical signs of lameness and joint distention. At the end of the experiment, synovial fluid was collected from distended joints. The foals were euthanized and a complete necropsy was performed.

3. Results
Three of the 4 foals became moderately to severely lame during the experimental period. There was moderate to severe joint distention, primarily in the tibial-tarsal joints. Synovial fluid cytology from distended joints revealed decreased viscosity, suppurative to chronic inflammation, and there were mildly elevated protein concentrations. On gross examination, articular cartilage damage was found in all the foals and included cartilage roughening and superficial to full-thickness erosions of the tibial-tarsal, femoral-tibial, or the humeral-radial joints. Histological examination also revealed lesions in all the foals and included mild chondrocyte necrosis, cleft and vesicle formation limited to Zone 2 of the articular cartilage, and surrounding loss of proteoglycans.

4. Discussion
The results of this study indicate that neonatal foals are sensitive to cartilage damage induced by quinolones. The mechanism of quinolone-induced arthropathy has not been identified, but the acute nature of the lesions suggests primary damage to chondrocytes or extracellular matrix.1 Severe lameness, as seen in the experimental foals, has been observed in dogs receiving quinolones, and is thought to be associated with profound synovial effusion. In other experimental models of quinolone arthropathy, lameness is not a clinical finding.4 Treatment of sepsis and other infectious disease of neonatal foals usually involves administration of broad spectrum antibiotics. The results of this experiment suggests that administration of quinolone antibiotics, such as enrofloxacin, should be reserved for cases where therapy with other classes of antibiotics is unsuccessful, and antimicrobial sensitivity results indicate that quinolones are the only therapeutic option. Pharmacokinetic values, obtained after completion of this experiment, indicated that in certain circumstances, lower doses of enrofloxacin than those used in this study may be used based on pathogen susceptibility.3 The effects of lower doses of enrofloxacin on articular cartilage of neonatal foals have not been determined. Until such studies are performed, it cannot be assumed that lower doses of enrofloxacin do not cause articular cartilage damage in foals.

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References