Effect of the Chronic Systemic Administration of an Injectable Enrofloxacin Solution on Physical, Musculoskeletal, and Histologic Parameters in Adult Horses

Alicia L. Bertone, DVM, PhD; W. Henry Tremaine, BVSc; Delphim G. Macoris, DVM, PhD; Emily J. Simmons, DVM; Kathleen M. Ewert, DVM, MS; and Steven E. Weisbrode, VMD, PhD

The administration of injectable enrofloxacin 5 mg/kg IV q 24 h for 3 weeks was safe in adult horses and did not produce detectable physical abnormalities or joint or tendon disease. Authors’ addresses: Bayer Corp., P.O. Box 390, Shawnee Mission, KS 66201 (Ewert) and Dept. of Veterinary Clinical Sciences, The Ohio State University, 601 Tharp St., Columbus, OH 43210 (all other authors). © 1998 AAEP.

1. Introduction
Enrofloxacin (a fluoroquinolone antimicrobial) is rapidly bactericidal, has a broad spectrum of activity and low bacterial resistance, is effective at low tissue concentrations, and can be administered by mouth or by injection once daily. These features make it an attractive antibiotic for use in horses, particularly for musculoskeletal infections. Systemic fluoroquinolone administration at much greater than 5× the manufacturer’s recommended dosage produced cartilage lesions in juvenile rats, dogs, guinea pigs, rabbits, and nonhuman primates.1–4 An anecdotal report has suggested that cartilage lesions may develop in horses after the oral administration of enrofloxacin.5 Concentrations of enrofloxacin (2–10 µg/ml) that might be achieved following systemic administration (5 mg/kg) did not significantly suppress equine chondrocyte explant metabolism in vitro; however, high concentrations of enrofloxacin (>1000 µg/ml) were toxic.6 Current limited clinical use has not produced reported joint damage, although the safety of the use of enrofloxacin in horses has yet to be scientifically evaluated.

The purpose of this study was to evaluate the clinical safety of the administration of 5, 15, and 25 mg/kg of injectable enrofloxacin given intravenously once daily for 3 weeks (21 days). A specific investigation of the physical parameters, blood parameters, musculoskeletal system (joints and tendons), and lameness was made by using blinded investigators, a random assignment of horses, and a strict adherence to Good Laboratory Practice regulations.

2. Materials and Methods
Twenty-four healthy adult horses of various breeds were used in this study and randomly divided into
four groups as follows: group 1 (n = 6), control (equivalent volume as group 2 of 0.9% NaCl IV q 24 h, for 21 days); group 2 (n = 6), enrofloxacin 5 mg/kg IV q 24 h, for 21 days; group 3 (n = 6), enrofloxacin 15 mg/kg IV q 24 h, for 21 days; and group 4 (n = 6), enrofloxacin 25 mg/kg IV q 24 h, for 21 days. All horses met strict inclusion criteria, including age (3–11 years), a normal physical and lameness examination, soundness at the trot, palpably normal joints, full range of carpal and tarsal joint motion, normal hemogram and blood chemistry profile, acceptable radiographs (four views) of both carpi and tarsocrural joints, acceptable palpation and ultrasound examination of both digital flexor and calcaneal tendons, and no significant lesions on the articular cartilage of both midcarpal and tarsocrural joint surfaces as determined by an arthroscopic examination. For horses accepted into the study, measurements were made for fetlock joint angles (goniometer measurement), cross-sectional areas of the superficial digital flexor, deep digital flexor, and calcaneal tendons, the presence and size of carpal or tarsal osteophytes, and the location and extent of midcarpal and tarsocrural articular cartilage lesions. After all baseline measurements were made, horses were acclimated for 10 days before the administration of enrofloxacin or control solutions. All horses were again verified as normal on physical and lameness examination within 24 h. Injections were made intravenously through a jugular catheter for 21 days. Horses were evaluated daily by physical examination and for lameness at the walk and trot by blinded investigators. All horses were evaluated twice daily for adverse reactions to injections for 30 min after the injection. Subsequent to the completion of the injections, all parameters necessary for inclusion in the study were repeated on each horse. Additionally, articular cartilage and subchondral bone were biopsied from both tarsocrural joints, decalcified, sectioned, and stained with Toluidine Blue for morphologic and staining intensity characteristics. Statistical comparisons were made among groups and across time (before and after injections).

3. Results
Enrofloxacin administered intravenously once daily at 5, 15, and 25 mg/kg for 3 weeks did not produce increased clinical signs of lameness, joint effusion, joint pain, or tendon laxity; nor did it produce measurable changes in osteophyte number or size, tendon size or density, or articular cartilage damage. In the last week of treatment, one horse receiving 15 mg/kg for 21 days developed clinical signs similar to curb (plantar desmitis), but the histology of the plantar ligament was normal. One horse receiving 15 mg/kg and one horse receiving 25 mg/kg developed mild superficial digital flexor tendinitis and tarsal sheath effusion, respectively, without concurrent lameness, 3 days after the 21-day therapy was discontinued. High doses of enrofloxacin (15 and 25 mg/kg) administered by bolus intravenous injection intermittently produced transient neurologic signs. The signs completely resolved within 10 min and the horses suffered no long-term effects. A slower injection (15 mg/kg dose over 15 min) and slower infusion (25 mg/kg in 500 ml 0.9% NaCl over 40 min) ameliorated the neurologic signs. No adverse reaction was ever noted with 5 mg/kg given as an intravenous bolus.

4. Conclusion
Injectable enrofloxacin administered at 5 mg/kg intravenously once daily for 3 weeks did not produce any clinical signs of joint pain, lameness, joint effusion, tendon pain, tendon laxity, or tendon swelling. There were no measurable changes in osteophyte number or size, tendon size or density, or articular cartilage damage.

This project was funded by Bayer Corp. Animal Health, Shawnee Mission, KS.

References