Dexamethasone Iontophoresis in the Equine Tibiotarsal Joint

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The use of iontophoresis as a therapeutic modality for treating horses is presently anecdotal. We used iontophoreseis to deliver 24 mg of dexamethasone-sodium-phosphate (DEX-P) to the tibiotarsal joint of 6 adult horses. At the end of a 40 min treatment period, we failed to detect dexamethasone either in synovial fluid or blood. Iontophoresis was ineffective delivering DEX-P into the joint at the selected electrode drug concentration. Additional studies are necessary to determine the limitations of iontophoresis as a treatment modality in horses. Authors’ addresses: Dept. of Physical Therapy, East Tennessee State University College of Public and Allied Health, Johnson City, TN 37614. Dept. of Large Animal Clinical Sciences, University of Tennessee College of Veterinary Medicine, Knoxville, TN 37901; Dept. of Pharmacology, College of Medicine, East Tennessee State University, Johnson City, TN 37614. © 1999 AAEP.

1. Introduction
Iontophoresis is a drug delivery method where a physiologically acceptable electrical current is used to drive charged particles into the body. Using an electrode with similar polarity to the charge on the drug, the drug is forced through the skin by electrostatic repulsion. Iontophoresis provides a unique method for programmed drug delivery.

Glucocorticoids have significant anti-inflammatory and immunosuppressive actions. Localized delivery of glucocorticoids would be expected to reduce their adverse effects. Dexamethasone-21-phosphate (DEX-P), a negatively charged prodrug of dexamethasone (DEX), is used in rehabilitation medicine with the aim of alleviating local inflammation.1

Iontophoresis has recently been introduced into veterinary medicine; however, there is no kinetic data supporting the efficacy of this procedure in the horse. The purpose of this study was to quantify DEX–P and DEX delivery into the tibiotarsal joint and local vascular compartments, following DEX-P iontophoresis.

2. Materials and Methods
Six adult horses of mixed breed (431–485 kg) were used. DEX-P (6 ml, 4 mg/ml) was delivered by iontophoresis (4 mA for 40 min) from the cathode, over the medial surface of the tibiotarsal joint. Synovial fluid was collected at the end of the 40 min delivery period and a blood sample from the medial saphenous vein, proximal to the joint, was obtained for DEX-P analysis.

Due to the potential for conversion of DEX-P to DEX, the concentrations of both compounds were determined in the synovial fluid and blood samples using high performance liquid chromatography.
Standard curves were determined by adding DEX and DEX-P to normal equine synovium and plasma. Drug concentrations were determined from peak-area ratios of known DEX and DEX-P concentrations. The internal standards were beclomethasone and betamethasone-phosphate, respectively. Data are expressed in µg/ml, and reported as means ± standard deviations.

3. Results
The lowest level of sensitivity for DEX and DEX-P detection in plasma and synovial test fluid was 0.391 µg/ml. No DEX or DEX-P could be detected in synovial fluid or venous blood from the horses tested in this study. Conversion of DEX to DEX-P was demonstrated following in vitro incubation and repeated freeze-thaw cycles. Fifty percent of DEX-P was converted to DEX during a 2.5 hr incubation period. Additionally, 20% of DEX-P was converted to DEX after the first freeze-thaw cycle. The aggregate results of the standard curves for DEX and DEX-P were linear in plasma and synovium over the range 0.39 to 12.5 µg/ml (r = 0.92 to 0.99).

4. Discussion
The clinical interest in DEX-P iontophoresis as a parenteral route of drug delivery in human and veterinary medicine has increased. Clinical investigations in human medicine have focused primarily on subjective outcome assessments.1 No pharmacokinetic investigations under clinically relevant conditions have been conducted. This investigation demonstrates a method and the need for detecting DEX-P and DEX, as conversion of the prodrug (DEX-P) to the active form (DEX) was confirmed.

DEX-P or DEX could not be detected in the synovial fluid or effluent blood. Iontophoresis does not appear to be effective in delivering DEX-P to the synovium at the present electrode drug concentration used in this study. The potential for delivery of DEX-P to periarticular tissue was not examined, but the lack of detectable concentrations of DEX-P or DEX in local venous blood suggests that periarticular delivery was insignificant. Related research with the anionic anti-inflammatory drug ketoprofen, demonstrated that iontophoresis achieves therapeutically relevant concentrations at superficial muscle sites, but that deeper muscle and articular sites may be beyond the potential of current iontophoretic parameters.2 Additional studies need to be performed to determine the efficacy of iontophoresis as a treatment modality used in horses.

References