Why is Oral Prednisone Ineffective for Treatment of Heaves?

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Prednisone tablets are ineffective for the treatment of heaves, but dexamethasone preparations relieve airway obstruction within three to seven days. Prednisone is ineffective because it does not reach the blood as its active metabolite prednisolone. Authors’ addresses: Department of Large Animal Clinical Sciences, Michigan State University, East Lansing, MI 48824-1314 (Peroni, Jackson, Jefcoat, Derksen, and Robinson); California Animal Health and Food Safety Laboratory, University of California–Davis, Davis, CA 95616 (Stanley and Kollias-Baker). © 2000 AAEP.

1. Introduction
In 1999 Jackson et al.1 compared the effects of prednisone with environmental management to environmental management alone for the treatment of heaves. They reported that oral prednisone has no additional benefit. To be effective, oral prednisone must be absorbed and metabolized to the active drug prednisolone. The present study had two objectives: 1) to compare prednisone tablets with intravenous dexamethasone for treatment of heaves; and 2) to measure serum prednisolone levels after oral administration of prednisone and prednisolone.

2. Materials and Methods
A. Objective 1
Six heaves-susceptible horses were stabled until they developed airway obstruction. In each part of the randomized three-part study, horses received a different treatment for ten days. Treatments were prednisone tablets (2.2 mg/kg q 24 h), intravenous dexamethasone (0.1 mg/kg q 24 h), or no medication. During the trial, the horses’ management was not changed. Severity of airway obstruction was measured by the maximal change in pleural pressure during tidal breathing ($\Delta P_{\text{pl}_{\text{max}}}$).2

B. Objective 2
Each of five horses received five drug formulations in a Latin square design study. Treatments were prednisone tablets (50 mg/tablet), prednisone solution (1 mg/ml), prednisolone tablets (20 mg/tablet), prednisolone syrup (3 mg/ml), or intravenous prednisolone sodium succinate (50 mg/ml), all at a dose of 2.2 mg/kg. The latter was administered as a positive control. A high-performance liquid chromatography (HPLC) method with mass spectrometry detection was used for the qualitative and quantitative determination of prednisone and prednisolone. Data were analyzed by repeated measures ANOVA,
with drug and time as main factors with statistical significance set at $p < 0.05$.

### 3. Results

Before horses received prednisone, dexamethasone, or no medication, they had severe airway obstruction: $\Delta P_{pl_{\text{max}}} = 56.2 \pm 10.2$ (mean $\pm$ SEM); $44.3 \pm 9.3$ cm H$_2$O; and $40.6 \pm 5.8$, respectively. On days 3, 7, and 10 of treatment, $\Delta P_{pl_{\text{max}}}$ was $19.5 \pm 2.9$, $12.1 \pm 0.9$, and $12.3 \pm 1.4$ cm H$_2$O, respectively with dexamethasone; $60.2 \pm 9.2$, $49.1 \pm 3.4$, and $36.1 \pm 11.3$ cm H$_2$O with prednisone; and $51.3 \pm 8.8$, $39.4 \pm 6.9$, and $38.7 \pm 9.0$ cm H$_2$O with no medication. There were no significant differences between prednisone administration and no medication at any time. At days 3, 7, and 10 of dexamethasone treatment, $\Delta P_{pl_{\text{max}}}$ was significantly less than before treatment and also less than with prednisone or with no medication at each of these time periods.

Prednisolone was detectable in serum immediately after intravenous administration of prednisolone sodium succinate, peaked around 1000 ng/ml at 12 min, and was below levels of detection (5.0 ng/ml) by 24 hr. Similarly, oral administration of prednisolone tablets or liquid yielded serum prednisolone levels of 240–650 ng/ml at 15 min, with peak concentrations of 377–1032 ng/ml at 30–45 min. Levels were below detection by 24 hr. When horses received oral prednisone tablets or liquid, prednisolone never reached detectable levels in the serum. Small amounts of prednisone (<130 ng/ml) were detected.

### 4. Discussion

Intravenous dexamethasone was first demonstrated to be effective for treatment of heaves by Rush et al., and both Traub-Dargatz et al. and Jackson et al. have suggested that prednisone is ineffective. The current study confirms those findings. Intravenous dexamethasone relieves airway obstruction within three days and the effect is maximal after seven days. Because potent systemically administered corticosteroids may have side effects, practitioners tend to use oral prednisone as the first choice for treatment of heaves. This is not an effective treatment. At no point in the study was the prednisone treatment different from no medication.

In order for the drug prednisone to be effective after oral administration it must be absorbed from the gastrointestinal tract and converted to the active drug prednisolone by the liver. Although trace serum levels of prednisone were detected, prednisolone never appeared in the serum. Our data do not allow us to determine if prednisone is poorly absorbed, rapidly excreted, or not converted to prednisolone by the liver. However, it is clear that prednisone is unlikely to have any anti-inflammatory effect when administered by mouth. Oral administration of prednisolone is likely to be beneficial because it is rapidly absorbed and achieves serum levels close to those that result from intravenous administration.

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### References


