Increased analgesic options are needed for the continued improvement of equine patient care. Although potent analgesics, the use of opioids used sparingly in horses due to commonly seen adverse effects. Current equine pain management involves mostly non-steroidal anti-inflammatory drugs (NSAIDs) and α2 adrenergic agonists.

To the best of our knowledge, the first study evaluating the analgesic effect of codeine in horses. Limited number of studies evaluating the pharmacologic effects of codeine in horses. Preliminary studies with oral codeine in horses demonstrated similar morphine and morphine-6-glucuronide concentrations to that described in other species. Codeine metabolism in horses is similar to other species with the 6-hydroxylation and 6-glucuronidation of codeine being the major metabolic pathways.

The hypothesis of this study was that oral codeine administration will provide predictable, time-related blood concentrations of parent drug and active metabolites, as well as describe the pharmacodynamics including anti-nociceptive and adverse effects following oral administration.

MATERIALS AND METHODS

Horses

Seven horses were recruited for this study. The horses were between the ages of 4–12 years old and were of various breeds. All horses were of sound body condition and were not currently taking any medications. None of the horses had a history of analgesic use in the previous 30 days.

Drug Administration

The horses were placed in a randomized, balanced 5-way crossover design. Liquid oral saline, and a positive control of 0.2 mg/kg IV morphine were ingested as negative controls. Three oral doses of codeine were ingested at concentrations of 0.3 mg/kg, 0.6 mg/kg, and 1.2 mg/kg. Each dose was administered in a random order. All doses were administered in a liquid form, which was mixed with applesauce.

Blood Sampling


• Potential use as analgesic in equine patients is promising
• Further research to explore analgesic properties of codeine in horses warranted
• Thermal nociceptive data collected thus far suggests codeine may have similar analgesic properties to morphine (0.2 mg/kg IV) dose of morphine (0.2 mg/kg) following administration of all three codeine doses
• Concentrations of morphine metabolites were equivalent to or exceeded those observed following administration of an analgesic

Thermal Nociceptive Data:

To determine the effect of codeine on thermal nociception, a TopCat Metrology UK device was used to measure the thermal nociceptive cut-off temperature (TC). TC was defined as the temperature at which the horse expressed a nociceptive response, such as turning away from or pawing the skin. The thermal threshold (TT) was defined as the temperature at which the skin was exposed to for 30 seconds without nociceptive response. The percent thermal excitation (%TE) was calculated using the formula:

\[ %TE = 100 \times \left( \frac{TT - T_0}{TC - T_0} \right) \]

where TT is the thermal threshold, T0 is the skin temperature, and TC is the thermal nociceptive cut-off temperature.

Behavioral Data:

Behavioral data was collected to determine the effect of codeine on behavioral responses. Measures included:

- Defecation incidence and consistency
- Gastrointestinal borborygmi
- Step counts as an assessment of excitation
- Heart rate and rhythm (Holter monitors)
- Effect on thermal threshold

Defecation data was recorded using a TopCat Metallurgical UK device. Gastrointestinal borborygmi was measured using a Metallurgical TopCat device. Step counts were recorded using a TopCat Metallurgical UK device. Heart rate and rhythm were recorded using a TopCat Holter monitor. The effect on thermal threshold was measured using a TopCat Metallurgical UK device.

Heart Rate:

Heart rate data was collected using a TopCat Holter monitor. Heart rate was recorded at various time points: before bronchoalveolar lavage in horses. Am. J. Vet. Res. 66, 1420–4 (2005).

Step Counts:

Step counts were recorded using a TopCat Metallurgical UK device. Step counts were recorded at various time points: before bronchoalveolar lavage in horses. Am. J. Vet. Res. 66, 1420–4 (2005).

Effect on Thermal Threshold:

The effect of codeine on thermal threshold was measured using a TopCat Metallurgical UK device. The thermal threshold was defined as the temperature at which the skin was exposed for 30 seconds without nociceptive response. The percent thermal excitation was calculated using the formula:

\[ %TE = 100 \times \left( \frac{TT - T_0}{TC - T_0} \right) \]

where TT is the thermal threshold, T0 is the skin temperature, and TC is the thermal nociceptive cut-off temperature.

Pharmacokinetic Data:

Pharmacokinetic data was collected to determine the absorption, distribution, metabolism, and excretion of codeine and its metabolites following oral administration. Blood samples were collected at various time points: before bronchoalveolar lavage in horses. Am. J. Vet. Res. 66, 1420–4 (2005).

Pharmacokinetic data was collected using a TopCat Metallurgical UK device. Blood samples were collected at various time points: before bronchoalveolar lavage in horses. Am. J. Vet. Res. 66, 1420–4 (2005).

Pharmacokinetics:

The pharmacokinetic data was analyzed using a TopCat Metallurgical UK device. The pharmacokinetic parameters determined included:

- Cmax: maximum measured concentration
- Tmax: time of maximum concentration
- Z: terminal slope
- HL: Lambda Z
- AUC: area under the plasma-concentration curve from time 0 to infinity
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Study Summary

The results of this study warrant further research to continue to explore the analgesic properties of codeine in horses. The results also suggest that codeine may have similar analgesic properties to morphine (0.2 mg/kg IV) dose of morphine (0.2 mg/kg) following administration of all three codeine doses. Concentrations of morphine metabolites were equivalent to or exceeded those observed following administration of an analgesic.