30-Day Oral Acetaminophen Tolerance in Adult Horses

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Abstract

There are no controlled studies of acetaminophen toxicity in horses. The objective was to test the hypothesis that oral acetaminophen administered at a dosage 25% higher than that sometimes used in horses would result in measurable hepatic toxicity as seen in humans and other species. Six healthy adult horses were administered 25 mg/kg acetaminophen powder in corn syrup twice daily for 30 days. Three other horses served as negative controls receiving only corn syrup. Jugular venous blood samples were obtained on days 7 and 1 before treatment; on treatment days 1, 2, 5, 8, 12, 15, 19, 22, 26, and 30; and on days 3 and 7 after treatment ceased. Samples were analyzed the same day for complete blood counts and plasma biochemistry concentrations including hepatic and renal indices. Repeated measures analysis of variance and post hoc Tukey's test were used to identify differences between treatment groups at a significance level of P<0.05. On all sampling days, there were no differences between treated and untreated horses (P>0.05), and all measured values were within the normal range for this laboratory. It was concluded that acetaminophen at this oral dosage was not toxic in any measurable manner to the 6 horses receiving the drug in this way. It is postulated that the use of twice daily 20 mg/kg orally should be safe for periods less than 30 days in healthy horses.

Introduction

The use of acetaminophen (paracetamol outside the USA) has remained rare in equine practice. West et al. (2011) reported the use of acetaminophen in a badly founded obese Welsh gelding which had become poorly-responsive to conventional non-steroidal anti-inflammatory drugs (NSAIDs). Foreman et al. (2016) showed acetaminophen efficacy in a reversible model of equine foot lameness. However, there remain no referred blinded controlled documentations of acetaminophen toxicity in horses. The objective was to test the hypothesis that oral acetaminophen administered at a dosage 25% higher than that sometimes used clinically in horses would result in measurable hepatic toxicity as seen in humans and other species.

Materials and Methods

All materials and methods used for this study were performed under the approval and authority of the University of Illinois Institutional Animal Care and Use Committee (Protocol #17107). Subjects: Nine healthy adult horses (3 WB, 3 STB, 3 TB, 1 QH, 1 Arabian; age mean 14.4±4.4, median 14, range 5-21 years; 2 geldings, 7 mares; mean wt 509±114 kg) were assigned randomly to negative control (n=3) or acetaminophen treatment (n=6) groups. Complete physical, hematological, serum biochemical, and lameness examinations were performed to ensure that each subject was normal before drug administration. Subjects were negative for equine infectious anemia using agar gel immunodiffusion. A minimum of 7 days of stall rest acclimatization was allowed after admission and before any trials were begun.

Six horses were administered generic acetaminophen (Wal-Mart brand “Equate” caplets or tablets) orally in a paste at a dosage of 25 mg/kg twice daily for 30 days. Horses were weighed twice weekly and daily drug doses were adjusted to changes in body weight the day following new weights. As negative controls, 3 horses received no medication but received the same syrup used to make the acetaminophen paste orally twice daily. Blood samples were analyzed the same day for complete blood counts and plasma biochemistry concentrations including hepatic and renal indices. Repeated measures analysis of variance and post hoc Tukey’s test were used to identify differences between treatment groups at a significance level of P<0.05.

Results

At no time before, during, or after acetaminophen administration did these horses have elevations of liver or renal indices, nor did the initial indices change throughout the experiment. There was no apparent effect of acetaminophen administration on horses compared to the negative controls. Selected blood indices are graphed in Figures 1-3.

Discussion

The analgesic effects of acetaminophen (N-acetyl-p-aminophenol) are thought to be mediated via serotonin and cannabinoid pathways. Acetaminophen is well-absorbed (91%) from the small intestine in horses but more poorly in dogs (45%) (Kearley, et al. 2010). It is metabolized via hepatic glucuronidation in horses but there are no pharmacodynamic data and, until now, no toxicity data in horses. The more commonly-used non-steroidal anti-inflammatory drugs (NSAIDs) work by inhibiting one or both of the isoenzymes of cyclooxygenase (COX), but pan-COX inhibitors often result in horses in gastric and colonic ulcers and renal disease. If acetaminophen can be shown to be safe and efficacious in horses, it could be used as an alternative to conventional NSAIDs for horses suffering from NSAID-toxicity or requiring adjunctive pain relief.

Acknowledgments: This study was supported in part by Grant 338.1994 Jul 13. Foreman J, Foreman C, Bergstrom B. Acetaminophen/paracetamol efficacy in a reversible model of equine foot pain. Proc 62nd Annl Conv Am Association Equine Pract 2016: 295-296. Foreman J, Foreman C, Bergstrom B. Acetaminophen/paracetamol efficacy in a reversible model of equine foot pain. Proc 62nd Annl Conv Am Association Equine Pract 2016: 295-296. N.C., U.S.A. 14261 and 16055) has documented the effects of feeding on oral drug bioavailability in horses. Dr. Foreman has housed horses in these same stalls for over 90 consecutive days when horses were wearing special boots which can be damaged by pasture turnout exercise, with no adverse effects to the horses from being housed inside during that period of time. No adverse effects due to chronic housing were observed in these horses; one horse had a cranial cervical nerve lesion which she had had prior to admission to this study.

Conclusions

It was concluded that this dose, 25% higher than that commonly used in horses with clinical lameness, did not cause renal, hepatic, or red blood cell injury to the horses studied in this experiment. The slightly lowered dosage (20 mg/kg twice daily) used more commonly should be safe for most healthy horses for up to 30 days.

References