

A comparison between two blood level studies following oral dosing in horses with either Trimethoprim/Sulfadiazine Powder (UNIPRIM) or human generic SMZ tablets.

Michael G. Pay, BVetMed FRCVS

Macleod Pharmaceuticals Inc., 2600 Canton Court, Suite C, Fort Collins CO 80525

Summary

Trimethoprim/Sulfadiazine Powder (UNIPRIM) gave 50% higher Trimethoprim levels and greater persistence compared to the SMZ tablets, even after five doses of the human generic tablets. The explanation could be that in the case of SMZ tablets, not only was the dose split into two but the Trimethoprim in human tablets is micronized and these fine particles adhere to roughage.

It took the human tablets an extra two days to reach comparable sulfa blood levels compared to the TMP/SDZ powder.

In horses Sulfadiazine also penetrates tissues from the bloodstream to a greater extent than Sulfamethoxazole and achieves a larger volume of distribution.

These findings may explain the quicker clinical response that is being reported with Uniprim.

Introduction

Veterinarians in the field are reporting quicker clinical response to Trimethoprim/Sulfadiazine powder (TMP/SDZ) compared to the use of human generic Trimethoprim/Sulfamethoxazole (TMP/SMZ) tablets. This paper offers some possible explanations for these findings.

Methods

The results of Brown, Gronwall and Castro (1) have been compared with bioavailability data obtained at Macleod Pharmaceuticals Inc. (2) using Uniprim Powder.

Brown et al dosed a group of six horses with human SMZ tablets at 30 mg/kg active, divided into two daily doses. The horses were dosed a total of five times.

In the bioavailability study conducted at Macleod, twenty horses were dosed orally with TMP/SDZ powder on the feed at 30 mg/kg active in one dose.

In both experiments, blood samples were taken from the jugular, Brown et al over a period of 60 hours, and Macleod over a period of 24 hours. In both experiments serum levels of trimethoprim and sulfonamide were obtained by HPLC analysis.

Results

Trimethoprim levels.

Figure 1 gives the serum results on the first day. The maximum concentration (Cmax) reached for the SMZ tablets was 0.26 mcg/mL and for TMP/SDZ powder it was 0.85 mcg/mL.

Figure 2 compares blood levels on the third day for SMZ tablets when the Cmax was 0.57 mcg/mL compared to 0.85 mcg/mL on day one for TMP/SDZ powder.

A minimum M.I.C. level of 0.5 mcg/mL was maintained for 5 hours on day 1 with TMP/SDZ powder, but only for a few minutes on the third day with SMZ tablets.

Sulfonamide levels.

Figure 3 compares the first day for both treatments. The SDZ in Uniprim had a Cmax of 20.0 mcg/mL and the SMZ had a Cmax of 13.7 mcg/mL.

Figure 4 compares the third day of SMZ tablets with the first day of Uniprim treatment. The Cmax of SMZ was 17.4 mcg/mL.

Discussion

The divided dose of human tablets would partly account for the low levels of Trimethoprim. However, the Trimethoprim in human generic tablets is finely micronized. It is possible that these fine particles adhere to roughage and are not available for absorption as described by van Duijkeren (3). This may explain why TMP levels were 50% higher with TMP/SDZ (UNIPRIM) than human SMZ tablets even after 5 doses.

The sulfonamide blood levels of the human tablets took a further 48 hours to reach levels comparable with those of Uniprim.

The work of Brown, Kelly, Stover, and Gronwall (4) and Brown et al (1) has clearly demonstrated that sulfadiazine has a greater volume of distribution in the horse than sulfamethoxazole with resulting higher tissue levels.

Conclusion

Trimethoprim/Sulfadiazine powder (UNIPRIM) gave 50% higher TMP blood levels and reached comparable sulfonamide levels 2 days earlier than human generic tablets. These findings could explain the apparent quicker clinical response when using Uniprim.

References

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