Compounding Iron Dextran with NSAIDs for Use in Piglets at Time of Processing

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SUMMARY

The objective of this project was to evaluate whether the mixing (compounding) of NSAIDs (anti-inflammatory/analgesic agents), such as meloxicam or flunixin meglumine, with iron dextran for administration to piglets at the time of processing has any effects on the availability of the NSAID. In a series of experiments, we evaluated the stability and systemic availability of both NSAIDs when mixed with iron dextran in the same bottle for administration to piglets at the time of processing. We also evaluated the effects of this practice on iron dextran's ability to increase piglet hemoglobin concentrations. We found that the amount of NSAID recovered from the bottle was reduced beginning shortly after mixing. We also found that blood drug levels measured in piglets for each NSAID when compounded with iron dextran was significantly lower than when each NSAID was administered alone to piglets. We did not find any significant effects of mixing NSAIDs with iron dextran on iron dextran's ability to increase hemoglobin following administration to piglets. The overall conclusion from these experiments is that the mixing of NSAIDs with iron dextran in the same bottle for administration to piglets at the time of processing results in a suspected drug interaction that reduces the shelf-life of the formulation and the amount of NSAID available for therapeutic effects.

INTRODUCTION

When NSAIDs (anti-inflammatory/analgesic agents) such as meloxicam or flunixin meglumine are administered to piglets at the time of processing, it is tempting to mix or compound the NSAID with iron dextran to be delivered in a single injection, thereby reducing the number of injections to the piglet. Technically the practice of mixing two different products in the same syringe/bottle is not allowed under the Canadian Quality Assurance program, nor is the compounding of drugs for food animal use acceptable to the Canadian Global Food Animal Residue Avoidance Databank, but we are aware that this practice does occur and therefore it seems prudent to evaluate possible drug interactions that could affect the absorption and availability of either the NSAID or iron. The study was carried out using three separate experiments and performed at the University of Guelph, with the following objectives i) to evaluate the bioavailability of meloxicam (Metacam® 20 mg/mL Solution for Injection, Boehringer Ingelheim Canada LTD) and flunixin meglumine (Banamine®, Merck Animal Health) when compounded with iron dextran (Dexafer-200®, Vetoquinol) and administered to newborn piglets of approximately 5 days of age, ii) to evaluate the effect of compounding these agents on iron dextran's ability to increase piglet hemoglobin concentrations, and iii) to evaluate the storage life by measuring concentrations of the NSAIDs at various times after mixing with iron dextran.

RESULTS AND DISCUSSION

Measurement of recoverable flunixin meglumine and meloxicam when compounded in iron dextran was accomplished using high performance liquid chromatography. Our results showed that recoverable levels of either NSAID were reduced, beginning as early as 2 hours post-mixing, and with over 30% reduction in recoverable flunixin meglumine concentrations and over 10% reduction in meloxicam concentrations by 24 hours post-mixing. These findings suggested a probable drug interaction that could result in reduced NSAID being available for systemic absorption when administered to piglets. In the first of our two live animal experiments, we found no significant effects of compounding either NSAID with iron dextran on measured blood hemoglobin levels, indicating no significant effects on the iron status of the pig. The results of our bioavailability study (n= 8 piglets per group) comparing blood NSAID levels for flunixin meglumine and meloxicam when administered to piglets alone versus compounded in iron dextran did show notable findings. Piglets receiving flunixin meglumine were dosed intramuscularly at 2.2 mg/kg either as the NSAID alone or when compounded with iron dextran. Piglets receiving meloxicam were also dosed intramuscularly at 0.4 mg/kg as the NSAID alone or when compounded with iron dextran. Multiple blood samples collected shortly after dosing to 72 hours post-dosing were analyzed for meloxicam or flunixin meglumine using validated mass spectroscopy methods. Results showed significantly reduced concentrations of both NSAIDs when compounded with iron dextran compared to levels noted when NSAID was given alone rendering the compounding of NSAIDs with iron dextran not bioequivalent to NSAIDs administered alone.

CONCLUSION

The results of our study show that the mixing of meloxicam or flunixin meglumine with iron dextran likely produces a drug interaction, which does not appear to affect iron dextran's ability to maintain adequate hemoglobin concentrations, but does reduce the availability of the NSAID for absorption into the systemic circulation. The clinical ramifications of the reduced blood NSAID levels when compounding with iron dextran require additional efficacy studies to evaluate whether adequate analgesia is being provided at the current NSAID concentrations in the compounded formulation. Importantly, if flunixin meglumine or meloxicam is mixed with iron dextran for administration to piglets at the time of castration and processing the compounded product needs to be used right away.

ACKNOWLEDGEMENTS

This project was funded through the Ontario Farm Innovation Program and Ontario Pork.