Pharmacokinetics of a florfenicol-tyllosin combination after intravenous and intramuscular administration at two dose levels to beagle dogs

Kim Eun Young, Elias Gebru, Joong-Su Lee, Seung-Chun Park

College of Veterinary Medicine, Kyungpook National University, Daegu 702-701, South Korea

Introduction: Florfenicol is a novel broad-spectrum antibiotic belonging to the family of agents that includes thiamphenicol and chloramphenicol. Its equal or even better efficacy, lower toxicity, and less development of resistance as compared with chloramphenicol made florfenicol an attractive antibiotic for use in different animals. Tylosin, a macrolide antibiotic with bacteriostatic action against certain gram-positive and anaerobic bacteria, Mycoplasma spp. and some Rickettsiae, is registered exclusively for veterinary use in several countries. The rationale for a combination therapy with antimicrobial agents is often that pharmacological or pharmacokinetic interactions, leading to improved efficacy or safety profiles, compared with the single components. Florfenicol is combined with tylosin at a 2:1 ratio in a commercial preparation (FTD-inj™, Shinilbiogen Co., Ltd, Korea). We have reported earlier the intramuscular pharmacokinetics of the combination in pigs. The aim of the present study was to investigate the disposition kinetics of florfenicol and tylosin in dogs following intravenous (i.v.) and intramuscular (i.m.) administration the combination product at two different dose levels.

Materials and Methods: A two period cross-sectional study was conducted in six beagle dogs after intravenous (i.v.) and intramuscular (i.m) administration at 2 dose levels (5 and 10 mg/kg body weight for florfenicol, and 2.5 and 5 mg/kg body weight for tylosin). Serum concentrations of both florfenicol and tylosin were determined by high performance liquid chromatography (HPLC) with fluorescence detection. The pharmacokinetic parameters were analysed by non-compartmental methods. Descriptive statistical parameters as mean and standard deviation were calculated, and the student's t-test was applied to test parameters for significant difference between two dose levels.

Results: Significant differences were observed in most pharmacokinetic parameters between the two dose levels of both drugs. Following i.m. route, absorption was rapid and nearly complete for both drugs with a mean absolute bioavailability of 92.7 and 102.9% for florfenicol, and 109.1 and 90.9% for tylosin at lower and higher dose levels, respectively. Following i.v. and i.m. administrations, both drugs had prolonged elimination half life, and the tissue penetration after i.v. injection was high for both drugs with a steady state volume of distribution of 1.71 and 2.81 L/kg for florfenicol and 2.56 and 1.89 L/kg for tylosin at lower and higher dose levels, respectively.

Conclusions: After IV and IM administration of the florfenicol-tylosin combination to beagle dogs, no overt adverse effects were observed. The PK of both drugs were characterized by a rapid and complete absorption, extensive tissue distribution and slow elimination, with significant differences in most PK parameters between the 2 dose levels applied for both drugs. Additional studies that address pharmacodynamic and toxicological issues may be required before recommendations can be made regarding the clinical application of the product in dogs.

References

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