Comparative pharmacokinetics and pharmacokinetic/pharmacodynamic analysis by nonlinear mixed-effects modeling of cefquinome in nonpregnant, pregnant, and lactating goats after intravenous and intramuscular administration

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Resumen

Cefquinome is a fourth-generation cephalosporin that is used empirically in goats. Different physiologic factors like pregnancy or lactation could determine the pharmacokinetic behavior of drugs in the organism. The objectives of this study are to (a) compare the pharmacokinetics of cefquinome after intravenous and intramuscular administration in adult nonpregnant (n = 6), pregnant (n = 6), and lactating goats (n = 6), at a dose of 2 mg/kg, with rich sampling by nonlinear mixed-effects modeling, (b) conduct a pharmacokinetic/pharmacodynamic analysis to evaluate the efficacy of the recommended posology in goats with different physiological states, and (c) determine the optimal posology that achieve a PTA value ≥ 90%, taking into account a T > MIC ≥ 60% of a MIC value ≤ 0.25 μg/ml, in the different subpopulations of goats for both routes. Gestation significantly increased Ka and V1, while reduced F0, Cl, and Q. On the other hand, lactation significantly increased V1 and reduced Tk0. Cefquinome concentrations achieved in placental cotyledon, amniotic fluid, and fetal serum indicate a minimal penetration across the placental barrier. Moreover, milk penetration of cefquinome was minimal. The total body clearance of cefquinome for goats was 0.29 L kg−1 hr−1, that is apparently higher than the reported for cows (0.13 L kg−1 hr−1) and pigs (0.16 L kg−1 hr−1). So, the optimal dose regimen for cefquinome after intravenous and intramuscular administration required higher dose and frequency of administration compared with recommendations for cows or pigs. Therefore, 2 mg kg−1 8 hr−1 and 5 mg kg−1 12 hr−1 could be used for IV and IM routes, respectively, for the treatment of respiratory infections caused by P. multocida and M. haemolytica, but only 5 mg kg−1 12 hr−1 by both routes should be recommended for Escherichia coli infections.

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