

Age-related changes in the pharmacokinetics of marbofloxacin after intravenous administration in buffalo calves (Preliminary study)

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Support by a grant of Agencia Española de Cooperación Internacional y Desarrollo D/011184/07.

ABSTRACT

Buffalo breeding system has a great economic importance in South - America, principally in marginal or sub -tropical lands. Marbofloxacin is a fluoroquinolone developed exclusively for veterinary use. Fluoroquinolones share several pharmacodynamic and pharmacokinetic characteristics such as a wide spectrum of bactericidal activity, a large volume of distribution, low plasma protein-binding and relatively low minimal inhibitory concentrations (MICs) against target microorganisms.

The pharmacokinetics of marbofloxacin was studied in eighteen buffalo calves 2-3, 10 and 20 days old after single i.v. dose of 2 mg/kg body weight. Drug concentration in plasma was determined by high-performance liquid chromatography (HPLC) and the data collected were subjected to a non compartmental kinetic analysis. The results show that, AUC₀₋₈ is significantly greater in youngest animals. Elimination half-life was 8.39 ± 2.74 (2-3 days old), 6.22 ± 0.52 h (10 days old) and 6.42 ± 0.52 h (20 days old). Volume of distribution was relatively high in all age groups (V_{ss} 1.75 ± 0.36 ; 1.65 ± 0.24 L/kg and 2.01 ± 0.22 respectively). Total body clearance (Cl) increased with age from 2.75 ± 1.01 mL/kg/min (2-3 days old) to 3.34 ± 0.85 mL/kg/min (10 days old) and 3.76 ± 0.17 mL/kg/min. As a consequence of increased body clearance, area under the plasma concentration vs. time curve decreased with age (AUC₀₋₈ 830.11 ± 257.3 ug-min/mL in 2-3 days old to 591.8 ± 91 ug-min/mL in 10 days old and 532 ± 24 ug-min/mL in 20 days buffalo calves). Although many anatomical and physiological changes occur in the maturing ruminant, modifications in young animal's pharmacokinetics are most probably related to changes in body composition. Considering the drug's pharmacokinetic profile of marbofloxacin would appear to be a good therapeutic tool for the treatment of most of the infections produced by Gram-negative and Gram-positive susceptible bacteria in buffalo calves. Further studies are required to understand the kinetics at different ages.

INTRODUCTION

Buffalo breeding system has a great economic importance in South-America, principally in marginal or sub-tropical lands. Marbofloxacin is a fluoroquinolone developed exclusively for veterinary use. Fluoroquinolones share several pharmacodynamic and pharmacokinetic characteristics such as a wide spectrum of bactericidal activity, a large volume of distribution, low plasma protein-binding and relatively low minimal inhibitory concentrations (MICs) against target microorganisms¹⁻⁵. The aim of the present study was to investigate Age-related changes in the pharmacokinetics of marbofloxacin after intravenous administration in buffalo calves.

MATERIALS AND METHODS

The pharmacokinetics of marbofloxacin was studied in eighteen buffalo calves 2-3, 10 and 20 days old after single intravenous dose of 2 mg/kg body weight. Body weight was 39.33 ± 1.52 , 50.25 ± 2.06 , 54 ± 3.54 kg respectively. Drug concentration in plasma was determined by high-performance liquid chromatography (HPLC) and the data collected were subjected to a non compartmental kinetic analysis^{1,5}.

RESULTS AND DISCUSSION

Mean \pm SD marbofloxacin plasma concentration-time profiles after intravenous administration are shown in Fig. 1 and pharmacokinetic parameters in table 1. The results show that, AUC_∞ is significantly greater in youngest animals. Volume of distribution was relatively high in all age groups, compared with Buffalos steers³. Total body clearance (Cl) increased with age. As a consequence of increased body Cl, area under the plasma concentration vs. time curve decreased with age^{2,5}. Although many anatomical and physiological changes occur in the maturing ruminant, modifications in young animal's pharmacokinetics are most probably related to changes in body composition^{2,4,5}.

Considering the drugs pharmacokinetic profile of marbofloxacin would appear to be a good therapeutic tool for the treatment of most of the infections produced by Gram-negative and Gram-positive susceptible bacteria in buffalo calves. Further studies are required to understand the kinetics at different ages.

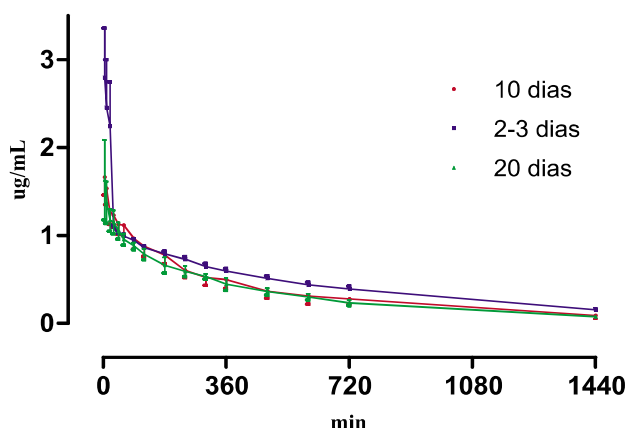


Figure 1: Mean \pm SD marbofloxacin plasma concentration-time profiles after intravenous administration (2 mg/kg) in buffalo calves 2-3, 10 and 20 days old.

PK parameters	2-3 days old		10 days old		20 days old	
	X	S.D.	X	S.D.	X	S.D.
T _{1/2β} (h)	8.39	2.74	6.22	0.52	6.42	0.52
AUC _∞ (μg-h/mL)	830.11*	257.3	591.8	91.02	532	24
V _{ss} (L/kg)	1.75	0.36	1.65	0.24	2.01	0.22
Cl _t (mL/min/kg)	2.75	1,01	3.34	0,85	3.76	0.17
* P> 0.05						

Table 1: Pharmacokinetic parameters after intravenous administration (2 mg/kg) of marbofloxacin in buffalo calves 2-3, 10 and 20 days old.

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Keyword: buffalo calves, pharmacokinetic, marbofloxacin. age-related changes
