Impact of milk yield on pharmacokinetics of six intramammary drugs – a population approach

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Abstract

The aim of the research was an examination of potential impact of milk yield on the intercompartmental clearance – distribution clearance as well as determination of the variability of obtained pharmacokinetic parameters by the population approach using a two-compartmental structural model. Blood perfusion has a considerable impact on physiology of the udder and kinetics of drugs that are distributed in this organ. The research was performed on healthy Holstein-Friesian and Polish Black-White cows at the age of 4-10 years. Determination of antibiotics (ampicillin, amoxicillin, cefoperazone, penicillin G prokaine, cloxacillin, cefacetril) concentration was carried out after their every intramammary administration to one quarter of the udder. A population pharmacokinetic model was created to fit milk concentration data. General milk yield of a single cow was used as a variable. A population analysis was conducted using non-linear mixed-effect modeling. The impact of milk productivity was set solely by reference to intercompartmental clearance only in case of penicillin G, cloxacillin and ampicillin. It, has been found that milk yield, depending on a drug, influenced the distribution clearance of the drug to varying degrees. It means indirectly that increased perfusion of the udder has a different impact on drug distribution from the udder to the bloodstream.

Key words: intramammary, population, pharmacokinetics, antibiotic

Introduction

Intramammary administration (IMM) of veterinary drugs has been widely applied especially in dairy cows on breeding farms. Currently, observational analysis founded on frequent sampling and calculations, is based exclusively on a structural model (e.g. compartmental model) without simultaneous variables analysis that can modify pharmacokinetic parameters of IMM drugs, and dominates (Allore and Erb 1999, Stockler et al. 2009). One of the pharmacometric methods combining the impact of dependent and independent variables is population pharmacokinetics. One of its applications is the usage of structural model as well as typical values