

Determination of milk concentrations and pharmacokinetics of salicylic acid following acetylsalicylic acid (aspirin) administration in postpartum dairy cows

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Introduction

The objectives of this descriptive study were to 1) describe the pharmacokinetics of salicylic acid (SA) in the milk and plasma of postpartum dairy cattle following oral administration of acetylsalicylic acid (ASA) (aspirin); 2) to estimate a recommended milk withdrawal period for dairy cattle treated with ASA; and 3) to determine the impact of ASA administration on plasma prostaglandin E₂ metabolite (PGEM) concentrations. Administration of non-steroidal anti-inflammatory drugs, such as the widely available drug aspirin, or acetylsalicylic acid (ASA), may improve health and milk production in postpartum dairy cows. However, plasma pharmacokinetic data for salicylic acid (SA), the active metabolite of ASA, are unrepresentative of lactating dairy cows and current treatment regimens, and there are currently no published milk residue and minimal pharmacodynamic data available for ASA or SA in dairy cows.

Materials and methods

Primiparous (n = 3) and multiparous (n = 7) postpartum Holstein dairy cows received 2 oral treatments with ASA at 200 mg/kg bodyweight, 24 h apart. Concentrations of SA in plasma and milk from 0 h through 120 h after ASA administration were analyzed using ultra performance liquid chromatography triple quadrupole mass spectrometry and milk withdrawal periods were estimated using the United States Food and Drug Administration Milk Discard App in R. Two withdrawal periods were estimated: 1) a whole-herd treatment scenario with no dilution factor and 2) an individual animal treatment scenario with a bulk tank factor included in analysis. Plasma PGEM concentrations in samples from 0 h to 24 h after ASA administration were determined using a commercially available competitive ELISA.

Results

Relevant pharmacokinetic parameters included the following: C_{max} 96.6 µg/mL (50.4 to 139.6 µg/mL), T_{max} 2.4 h (2.0 to 6.0 h), AUC_{0-∞} 978.4 h*µg/mL (786.16 to 1,403.99 h*µg/mL), and T1/2 11.5 h (9.7 to 12.8 h). Milk SA concentrations were initially undetectable in all cows at 48 h after the last ASA treatment. Secondary peaks were observed in plasma at 58 and 82 h after the last treatment and in milk at 87 h after the last treatment. In the absence of a tolerance for SA in milk, the estimated milk withdrawal periods were 156 h for the whole herd treatment scenario and 120 h for the individual animal treatment scenario. Plasma PGEM concentrations were reduced compared to baseline for up to 12 h after ASA administration, with the greatest reduction observed at 2 h (-49.3%).

Significance

Pharmacokinetic and milk withdrawal data from this study will inform future recommendations for extra-label use of aspirin in postpartum dairy cows. Data from this study suggest that the current milk withhold recommendation for dairy cattle administered ASA may need revision to 120 h (5 d) and that ASA administration may mitigate postpartum inflammation through reduction in prostaglandin production for up to 12 h after treatment. Further research is required to determine the basis for the secondary SA peaks and to elucidate the long-term effects of ASA administration on dairy cow health.

