Effect of Age on the Pharmacokinetics of Meloxicam in ISA Brown Chickens (*Gallus gallus domesticus*).

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Abstract

The Non-Steroidal Anti-Inflammatory drug (NSAID) meloxicam has been deemed a safe and effective treatment for numerous inflammatory conditions and injuries from extensive pharmacokinetic and pharmacodynamic studies in various mammalian species. However, there is a lack of meloxicam pharmacokinetic information in avian species. This leads to pharmacokinetic data being extrapolated from mammals in order to administer and treat birds. This often leads to ineffective pain relief or overdoses that can be fatal for birds. Due to this void in literature this study was designed to increase the basic pharmacokinetic knowledge in birds but to also determine if age affects the pharmacokinetics of meloxicam in ISA Brown chickens. Meloxicam was injected intravenously (IV) at 2 mg/kg in 20 healthy ISA Brown chickens (*Gallus gallus domesticus*). One group consisted of 10 ISA brown chickens that were 18 weeks old, the second group consisted of 10 ISA Brown chickens that were 24 months old. Serial blood samples were withdrawn from a catheterised vein from each ISA Brown chicken into a heparinised vial at 0, 10, 20, 30 minutes, 1, 4, 8, 10, 12 hours after the administration of meloxicam.

The pharmacokinetics for ISA Brown chickens were calculated using the non-compartmental model, which was analysed using the mean data from each group of ISA Brown

chickens. The elimination half-life, steady state volume of distribution and mean resident time were significantly higher in the 24 month old ISB Brown chickens compared to the 18 week old ISA Brown chickens. Overall, the results indicate that as an ISA Brown chicken ages the pharmacokinetics of meloxicam show some significant changes in crucial pharmacokinetic parameters. The differences in the pharmacokinetic parameters may ultimately affect the efficacy of meloxicam when treating 'geriatric' birds due to possible age-related health issues in the liver and kidneys, which are major organs involved in processing drugs.

KEYWORDS: Meloxicam, non-steroidal anti-inflammatory drugs, ISA Brown chickens, analgesia, pharmacokinetics.

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List of abbreviations

AIC – Alkaline Information Criterion

AA - Arachidonic acid

AUC – Area under the curve

AUMC – Area under the moment curve

BIC – Bayesian Information Criterion

BMR – Basal Metabolic Rate

C_{lb} – Body (systemic) clearance

CNS – Central nervous system

C_{p0} – Concentration at time zero

COX-1 – Cyclooxygenase 1

COX-2 - Cyclooxygenase 2

CYP - Cytochrome P450

$t_{1/2\alpha}$ – Distribution half-life

α – Distribution rate constant

DAD – Diode array detector

ED – Electrochemical detector

$t_{1/2\beta}$ – Elimination half-life

β – Elimination rate constant

GI – Gastrointestinal

GFR - Glomerular filtration rate

$t_{1/2}$ – Half-life

HPLC – High Performance Liquid Chromatography

IM – Intramuscular

IT – Intrathecal

IV – Intravenous

LC/MS – Liquid chromatography/Mass spectrophotometer

LOD – Limit of detection

LLE – Liquid-liquid extraction

LLD – Lower limit of detection

LLQ – Lower limit of quantification

MAT - Mean absorption time

MEC – Mean effective concentration

MRT – Mean residence time

C_{max} - Maximum concentration

NSAIDs – Non Steroidal Anti-inflammatory drugs

OA – Oral administration

C_p – Plasma drug concentration at any time

SPE – Solid phase extraction

SC – Subcutaneous

TXA_2 and TXB_2 – Thromboxane

C_L - Total clearance

V_{dt} – Total volume of distribution

V_d – Volume of distribution

V_{dc} – Volume of distribution, central compartment

V_{dp} – Volume of distribution, peripheral compartment

V_{ss} – Volume of distribution, steady state

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To my parents

Andrew and Fiona Gildersleve

I cannot truly express how much your unconditional love and support has meant to me. Throughout this journey you have reminded me of the Lord's love and grace. And that I can do all things through Him who strengthens me.

To my papa

Late David Henry Pledge

Even though you were not here to see me accomplish this goal. Your passion for science lives on through me, and I hope I have done you proud.

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