

Pharmacokinetics of oral phenazopyridine in goats with obstructive urolithiasis

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Introduction

Phenazopyridine, an azo dye and urinary bladder analgesic widely used in human medicine, is commonly used for ancillary pain management in the treatment of goats with obstructive urolithiasis. Despite its common use in these patients, there are no published studies on the pharmacokinetic parameters, safety, or efficacy of phenazopyridine in caprine patients. The aim of this study was to determine the pharmacokinetic parameters of oral phenazopyridine administration in goats with obstructive urolithiasis following tube cystostomy surgery.

Materials and methods

Six male caprine patients, ages 3 months to 4 years, were used in this study. Clinically afflicted goats were patients of an academic veterinary institution and were diagnosed with obstructive urolithiasis based on history, physical examination and abdominal ultrasound findings. Each patient underwent a tube cystostomy surgery to facilitate correction of the obstructive urolithiasis. Following surgery, oral phenazopyridine (95 mg tablets) was administered at a dose of 4 mg/kg every 12 hours. Plasma and urine samples were collected over a 48-hour period following the first dose. Phenazopyridine concentrations were determined using high performance liquid chromatography (HPLC) with UV detection. A standard curve was validated for both sample types using plasma and urine from phenazopyridine-free goats, spiked with an analytic standard from 0.01-5 µg/mL ($R^2 > 0.99$, interday CV < 4%, intraday CV < 6% for plasma; $R^2 > 0.98$; interday CV < 12%; intraday CV < 6% for urine). For plasma, the limit of detection was 0.01 µg/mL, and the limit of quantification

was 0.05 µg/mL. For urine, the limit of detection was 0.05 µg/mL, and the limit of quantification was 0.1 µg/mL. Concentrations of phenazopyridine in study plasma and urine samples were then determined and plotted on linear and semi-logarithmic graphs for analysis and visual assessment of the model fit for downstream pharmacokinetic analysis. The pharmacokinetic parameters were determined using non-compartmental analysis.

Results

The mean (geometric) terminal elimination plasma half-life ($T_{1/2}$), maximum plasma concentration (C_{max}), and area under the curve (AUC) were 1.26 hours (0.42-3.20 hours), 0.33 µg/mL (0.21-0.70 µg/mL), and 0.69 hr* µg/mL (0.10-2.99 hr* µg/mL), respectively. The concentration of phenazopyridine in urine samples was below the limit of assay detection (0.05 µg/mL) in all but one sample.

Significance

Phenazopyridine was rapidly eliminated from plasma and did not concentrate at detectable levels in the urine after oral administration. Additional investigations of phenazopyridine metabolites and oral bioavailability, as well as pharmacokinetic studies in healthy goats, are needed prior to recommendation for clinical patients.

