

Pharmacokinetics of Hydromorphone in Dogs after Intravenous Bolus and Delivered Subcutaneously with the RxActuator Mini-Infuser® Infusion Pump

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## INTRODUCTION

There are few therapeutic options to treat moderate pain in dogs on an out-patient basis. The aim of this study was to describe the pharmacokinetics of hydromorphone in dogs following either intravenous (IV) bolus or subcutaneous (SC) infusion via a wearable subcutaneous pump.

## METHODS

Seven adult dogs (four male, three female; weighing  $10.8 \pm 2.0$  kg) received  $0.2 \text{ mg kg}^{-1}$  hydromorphone IV, followed 3 days later by a SC infusion using a commercially available wearable pump (RxActuator Mini-Infuser® wearable subcutaneous constant rate infusion pump) at  $0.01 \text{ mg kg}^{-1} \text{ hr}^{-1}$  for 48 hours in a prospective study. Venous blood samples were obtained at predetermined time points up to 8 hours (IV administration) or 58 hours (after infusion). Plasma hydromorphone concentrations were analyzed using liquid chromatography with mass spectrometry detection, using a method validated for canine plasma. Pharmacokinetic parameter estimates were obtained with noncompartmental methods, using commercially available pharmacokinetic modeling software (Phoenix® WinNonLin®, version 8.3). Descriptive statistics were used.

## RESULTS

Following IV administration, clearance was  $56.45$  ( $47.07$ – $88.10$ )  $\text{mL min}^{-1} \text{ kg}^{-1}$ ; volume of distribution at steady state was  $4.01$  ( $2.57$ – $7.70$ )  $\text{L kg}^{-1}$ . Area under the curve was  $59.05$  ( $37.84$ – $70.82$ )  $\text{hr} \cdot \text{ng mL}^{-1}$ . Terminal half-life was  $1.47$  ( $1.34$ – $2.04$ ) h. Following SC infusion, maximum concentration was  $8.08$  ( $6.21$ – $9.97$ )  $\text{ng mL}^{-1}$ ; time to maximum concentration was  $6.00$  ( $2.00$ – $12.00$ ) h. Area under the curve was  $244.22$  ( $152.55$ – $282.72$ )  $\text{h} \cdot \text{ng mL}^{-1}$ . Terminal half-life was  $7.35$  ( $3.25$ – $16.07$ ) h.

## CONCLUSION

The RxActuator Mini-Infuser® pump delivered a consistent rate of hydromorphone over approximately 48 hours, with plasma concentrations exceeding those associated with analgesia (approximately 4 ng mL<sup>-1</sup>). Larger studies in clinical patients are warranted to further determine the analgesic effects of hydromorphone delivered as a subcutaneous infusion.

## SPEAKER INFORMATION

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