Pharmacokinetics of dexmedetomidine in anaesthetized horses: comparison between repeated subcutaneous administration and continuous rate infusion

Di Cesare F., Draghi S., Amari M., Rabbogliatti V., Brioschi F.A., Villa R., Ravasio G., Cagnardi P.
Dept. of Veterinary Medicine and Animal Sciences, University of Milan, Lodi, Italy

Introduction: Balanced anaesthesia, with the combined administration of an inhalant anaesthetic and a sedative, such as dexmedetomidine (DEX), represents a valid approach to improve the clinical outcome and the recovery quality in horses. To this aim DEX can be administered by different routes: intravenous, continuous rate infusion (CRI) or intramuscular. More rarely it is administered by subcutaneous route and to date, no pharmacokinetic data are available for equine patients regarding DEX following subcutaneous administration within a balanced anaesthetic protocol. The study aimed to determine DEX serum concentrations in anaesthetized horses, to define its pharmacokinetic profile following repeated subcutaneous administration in comparison to CRI, and to report the possible occurrence of side effects with these routes.
Patients and Methods: Twenty adult, client-owned, non-food producing horses undergoing general anaesthesia for diagnostic procedures were randomly assigned to CRI group (intravenous administration of DEX at 1 µg/kg/h up to the end of the diagnostic procedure) or SC group (DEX at 2 µg/kg every 60 minutes up to the end of the diagnostic procedure). The length of diagnostic procedures influenced the duration of CRI and the number of SC administrations. Serum DEX concentrations were determined by intra-laboratory validated HPLC-HRMS Orbitrap analysis. Pharmacokinetic analysis was carried out with a non-compartmental approach (Phoenix® WinNonLin 8.3).
Results: In the CRI and SC group DEX maximum concentrations (C_{max}) were 0.83 ± 0.27 ng/mL and 1.14 ± 0.71 ng/mL, respectively, reached at a time (T_{max}) of 57.00 ± 13.37 minutes and 105.50 ± 29.85 minutes. Mean residence time to the last measurable concentration (MRT_{last}) was 11.71 ± 6.18 and 55.77 ± 19.65 minutes for CRI group and SC group, respectively. The elimination half-life was 94.81 ± 69.84 minutes for SC group and 17.97 ± 9.95 minutes in CRI group, but determined in 7 out of 10 horses. No signs of adverse effects were recorded in both groups.
Conclusions: The pharmacokinetic profile of DEX determined following repeated SC administrations was comparable to that by CRI, without signs of side effects. Additionally, considering DEX concentrations, the SC route would be able to balance the cardiovascular alterations in the anaesthetized horse and to improve the quality of recovery from anaesthesia in equine patients.