Evaluation of Respiratory Rate Measurements Derived from Blood Pressure Waveforms in Telemetered Dogs
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Abstract

Introduction: The objective of the study was to evaluate the potential extraction of a respiratory rate (RR) measurement from a standard arterial blood pressure (BP) signal and compare these values to those obtained from the RIP (Respiratory Inductive Plethysmography) system. Positive (theophylline, a respiratory stimulant) and negative (dexmedetomidine, a respiratory depressant) reference compounds were used to more accurately produce respiratory endpoints. Methods: Male beagle dogs were instrumented with minimally invasive telemetry devices for measurements of blood pressure and heart rate. The RIP system was used during the study for measurements of respiratory rate, tidal volume and minute volume. Single doses of vehicle, theophylline (15, 30, 50 mg/kg, PO) and dexmedetomidine (2.8 and 5.6 µg/kg, IM) were administered via a crossover dosing paradigm (n=6). Telemetry data were collected continuously for 6 (dexmedetomidine) and 24 hours (theophylline) post dose. Results: As expected, oral administration of theophylline increased respiratory rate and minute volume, while intramuscular administration of dexmedetomidine decreased respiratory rate and minute volume in conscious dogs. Neither of compounds had an effect on tidal volume. The results reveal that the magnitude of the respiratory rate values derived from BP waveforms did not correlate well with those obtained from the RIP system. Discussion: The generally lower respiratory rates derived from BP waveforms compared to those detected by the RIP system suggests the indirect method as configured in this study, was not sensitive enough to identify every breath through the chest movements of the animals. Post-study X-ray images of the animals identifying the precise locations of the BP catheter tips were found to be located less advanced than anticipated in the femoral artery. This most likely contributed to the lack of sensitivity respiratory rates derived from BP waveforms compared to those detected by the RIP system. Additional studies with BP catheter tip placement closer to the chest (i.e., to the level of the abdominal aorta) are needed to fully characterize and take advantage of this new method for respiratory rate measurement.

Introduction

The objective of this nonclinical laboratory study was to evaluate the potential extraction of a respiratory rate (RR) measurement from a blood pressure (BP) signal and compare these values to those obtained from the RIP (Respiratory Inductive Plethysmography) system in dogs using positive (theophylline, a respiratory stimulant) and negative (dexmedetomidine, a respiratory depressant) reference compounds.

Methods

Three male beagle dogs (24-38 months of age and weighing 9-13 kg) fitted with telemetry jackets and respiratory bands have been previously implanted with telemetry transmitter (BayTel, FT, EMKA, Paris, France) and received theophylline (15, 30, and 50 mg/kg) and dexmedetomidine (0.0028 and 0.0056 mg/kg, IM) with a minimum washout period of 2 days between doses. A crossover dosing paradigm was used for both reference compounds. telemetry data were recorded with the animal in its cage using emka iDX data acquisition system. Telemetry data were continuously recorded for 2 hours pre-dose and 6-24 hours post-dose. Heart rate, blood pressure, respiratory rate, tidal volume, and minute volume were analyzed from the last (fourth 15-minute) period of every hour to minimize the influence of TK blood sampling and dosing procedures. Blood samples (approximately 0.5 mL in vacutainer containing EDTA) were collected at 0.5, 1, 3, 6, and 24 (theophylline only) hours post dose for drug plasma concentration determinations.

Results

Theophylline:

RIP System: Respiratory rate was increased following theophylline with maximum vehicle-adjusted mean increases of 15 (44%) and 13 bpm (36%) after 30 and 50 mg/kg, respectively (Figure 1A). The effects on respiratory rate peaked at approximately 3 hours post dose and returned to the baseline levels at approximately 8 hours post dose. Minute volume was also increased following theophylline (data not shown). Theophylline had no effects on tidal volume.

BP Derived: There were no effects on derived respiratory rates after 15 and 30 mg/kg. Derived Respiratory Rate was increased with a maximum vehicle-adjusted mean increase of 13 bpm (36%) after 50 mg/kg (Figure 1B). The effects on derived respiratory rates peaked at approximately 3 hours post dose and returned to the baseline levels at approximately 8 hours post dose.

Dexmedetomidine:

RIP System: Respiratory rate was decreased following dexmedetomidine with a maximum vehicle-adjusted mean decrease of 32 (102%) and 38 bpm (123%) after 0.0028 and 0.0056 mg/kg, respectively (Figure 2A). The effects on respiratory rate achieved trough levels at approximately 30 minutes post dose.

BP Derived: Derived Respiratory rate was increased with a maximum vehicle-adjusted mean decreases of 32 (102%) and 38 bpm (123%) after 0.0028 and 0.0056 mg/kg, respectively (Figure 2B). The effects on derived respiratory rate reached levels at approximately 30 minutes post dose.

Conclusions / Discussions

The major purpose of the study was to evaluate an indirect method of respiratory parameter capture, deriving those endpoints from the arterial blood pressure waveforms. These derived values were compared to respiratory rates measured directly from a commercially available EMKA sourced RIP system (Respiratory Inductive Plethysmography), using standard pharmacological tools known to affect respiratory variables. As expected, oral administration of theophylline increased respiratory rate and minute volume, and intramuscular administration of dexmedetomidine decreased respiratory rate and minute volume in conscious dogs. Neither of compounds had an effect on tidal volume. Based on the results with theophylline and dexmedetomidine, it appears that the magnitude of the respiratory rate values derived from BP waveforms did not correlate well with those obtained from the RIP system as shown in the regression plots (Figure 4). It should be noted that the values derived from the BP waveforms were typically lower than those detected by the RIP system. The generally lower respiratory rates measured from BP waveforms suggests the indirect method as configured in this study was not sensitive enough to identify every breath through the chest movements of the animals. This summarization was further confirmed by post study X-ray images (Figure 7A) of the animals identifying the precise locations of the BP catheter tips. Located less advanced than anticipated in the femoral artery most likely contributed to the lack of sensitivity respiratory rate measurements derived from BP waveforms. Additional studies will be required comparing respiratory rate derived from BP vs RIP were conducted using noisy-implanted animals with BP catheter tip placement closer to the chest (i.e., to the level of the abdominal aorta) and further optimizing mean respiratory rates of 20.7 and 20.2 bpm from RIP and BP, respectively. The improved correlations for the absolute respiratory rate values between BP and RIP were evident from the regression plot with a R2 value of 0.73 as shown in Figure 6B. It is concluded that the placement of BP catheter tips proximal to the thoracic diaphragm is critical in accurate respiratory rate measurements from BP signals using jacket telemetry in dogs.