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ALFAXALONE SEDATION FOR CENTRAL VENOUS CATHETERIZATION IN A DOG UNDERGOING HEMODIALYSIS: CASE REPORT

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Abstract

A 5 years old Shar Pei female, diagnosed with acute kidney injury was referred for hemodialysis therapy. The dog was presented with lethargy, lack of appetite, severe weight loss, dehydration (7-10%) and pale mucous membranes. To prevent exacerbation of preexisting comorbidities, in order to sedate a renal patient, a safe anesthesia protocol requires understanding the kidney disease pathology and hemodialysis therapy implications. A central venous catheter (CVC) was placed under a light sedation with additional oxygen therapy. Sedation was induced intravenously with alfaxalone (Alfaxan® multidose), on a peripheral catheter. The dose was titrated until full relaxation of the patient was observed. During the procedure, there were no major hemodynamics changes in the patient. Alfaxalone is a short-acting and rapid duration anesthetic with minimal or no cardiovascular consequences. When given titrated to effect, it represents the best choice for short sedation in central venous catheterization for acute renal patients undergoing hemodialysis.

Key words*: alfaxalone, sedation, CVC, hemodialysis, kidney.*

INTRODUCTION

Sedation is a daily routine in clinical practice, used for minor medical procedures or in premedication prior to general anesthesia, imaging studies or to manage fractious or excited animals. Because of their availability and efficacy, intramuscular (IM) administration of ketamine, opioids, α2-adrenoceptor agonists or their combinations has been widely used for sedation or general anesthesia in dogs (Tamura et al., 2015).

Alfaxalone is a synthetic neuroactive steroid that produces good quality sedation with fast onset, good muscle relaxation, minimal cardiovascular effects and mild respiratory depression when administered intravenously at clinically doses in dogs, making it a clinically acceptable induction agent for unstable canine patients. In dogs, alfaxalone has been demonstrated to have less cardiorespiratory side effects and minimal to none cardiovascular changes when it is used at clinical doses. These hemodynamic changes are dose-dependent. Overdoses can cause increased heart rate, hypotension and hypoventilation (Psatha et al., 2011). Intravenous administration of alfaxalone produces a smooth induction of anesthesia and rapid recovery with dose-dependent cardiorespiratory depression (Kato et al., 2021).

Acute kidney injury (AKI) is characterized by sudden renal parenchymal injury, and is associated with decreased renal function, retention of uremic waste products, fluid, electrolyte and acid-base imbalances. Short-term prognosis of AKI is affected by multiple factors including the etiology (which influences the reversibility of the injury), comorbidities, complications and treatment options (Rimer et al., 2022).

Despite advances in management of AKI and the increased availability of renal replacement therapies, the overall case fatality rate remains high both for dogs managed medically or with hemodialysis. Despite comprehensive diagnostic workup, in a substantial percent of patients with AKI the etiology is unknown at presentation (Rimer et al., 2022).

Central venous catheter (CVC) use is increasingly higher in veterinary practice in the management of critical patients when peripheral venous access is difficult or even

impossible to achieve, and is the primary element in the therapy of patients with acute kidney injury or chronic kidney disease undergoing hemodialysis (HD). Vascular access is the most important basic requirement of successful extracorporeal renal replacement therapy. Hemodialysis is a therapeutic procedure that use the extracorporeal circulation of a patient's blood to improve azotemia, fluid overload, electrolyte and acid-base abnormalities characteristic of the uremic syndrome (Ștefănescu & Viţălaru, 2018).

The aim of this study was to evaluate the dose-dependent sedative and anesthetic effects of IV alfaxalone administered for central venous catheterization in a dog undergoing hemodialysis.

MATERIALS AND METHODS

A 5 years old female Shar Pei, 18 kg body weight, diagnosed with acute kidney injury was referred for hemodialysis therapy. The dog was presented with lethargy, appetite loss, severely weight loss, dehydration (7-10%) and pale mucous membranes. Results from a complete blood cell count (CBC), biochemistry, and urine analysis submitted at that time were abnormal.

Hemodialysis, hydro-electrolytic rebalancing and partial parenteral nutrition were the main parts of the complex therapy. The placement and installation of the central venous catheter is a key factor for the therapeutic success of hemodialysis.

The American Society of Anesthesiologists (ASA) physical status classification system in this study was performed based on physical examination of the dog at presentation and hematology and biochemistry results, imaging diagnostic tests and underlying disease.

Monitored parameters before sedation, as a part of pre-anesthetic evaluation, were: heart rate (HR, beats/minute), peripheral oxygen saturation (SpO_2), respiratory rate (RR, breaths/minute), electrocardiogram (ECG) with 3-leads and rectal temperature (TºC). The blood pressure (BP) was measured using High-Definition Oscillometry (HDO), with the dog placed in sternal recumbency. The systolic (SAP, mmHg), diastolic (DAP, mmHg) and MAP (mean arterial pressure) were monitored. The successful clipping and placing of an peripheral IV catheter was recorded as part of the sedation assessment.

The patient did not receive any premedication, the sedation protocol being initiated with a 3.2 mg/kg IV bolus of alfaxalone. The assigned drug was injected at a rate of 25% of the total calculated dose (0.8 mg/kg) every 15 seconds over the first 60 seconds. The patient was directly induced by alfaxalone bolus administration, followed by CRI at a rate of 0.18 mg/kg/min using an infusion syringe pump for delivery. During sedation the patient received fluid therapy with Ringer (rate and dosage: 10 ml/kg/h) given for hydro-electrolytic rebalancing.

During the CVC placement procedure, vital parameters were measured using a patient monitoring system and additionally assessed with a stethoscope and by observing thoracic movements. Heart rate was measured by thoracic auscultation and lead II-ECG wave. Respiratory rate was obtained by direct observation of thoracic movements. SpO_2 and HR variability were obtained simultaneously using non-invasive pulse oximetric recording. SAP, DAP and MAP were measured on the forelimb using the HDO method, with an appropriately sized cuff placed above the carpus (width 40% of limb circumference - C1 cuff). Rectal temperature was measured with a digital thermometer.

Due to mild respiratory depression (hypoventilation) during the procedure oxygen supplementation via face mask (low-flow oxygen system) was started. The patient was maintained during the CVC placement procedure with CRI of alfaxalone and oxygen. Oxygen supplementation was stopped when the patient no longer presented hypoventilation and SpO_2 returned to physiological parameters.

The anesthetic and cardiorespiratory effects were evaluated before administration and sequentially at every 5 minutes, after the IV administration of alfaxalone until the recovery of the patient. The procedure lasted 20 minutes. All this time the patient was under sedation protocol and any abnormal movements, ECG alteration or other abnormal measurements were noted, recorded and monitored. Recovery from sedation was uneventful.

RESULTS AND DISCUSSIONS

The aim of this study was to evaluate the clinical efficacy and cardio-respiratory effects of alfaxalone as an induction agent for sedation protocol in dogs with severe systemic diseases such as acute kidney injury prior to hemodialysis.

At the admission, the patient had elevated blood biochemistry results on renal interest parameters BUN: 210 (RR: 7-21 mg/dL), CRE: 18.9 (RR: 0.4-1.4 mg/dL). Moderate hyperkalemia appears on the electrolyte imbalance side K^+: 6.8 (RR: 3.4-5.6 mmol/L), low value of CA: 12.6 (RR: 8.6-11.8 mg/dL) and value of PHOS: 18.5 (RR: 2.9-6.6 mg/dL), ALB: 2.0 (RR: 2.6-3.5 g/dL). Results from complete blood cell count (CBC) revealed: HGB: 3.2 (RR: 12-18 g/dL), HCT: 12.76 (RR: 37-55%), MCHC: 28.8 (RR: 31-39g/dL) and RDWc: 12.1 (RR: 14-20%) consistent with anemia. Urinalysis was carried out from urine obtained through ultrasound guided cystocentesis and showed a UPC ratio of >=0.5 to <2.0 (proteinuric), pH of 5.1, microalbumin >=25 mg/L. Based on these results and IRIS AKI Grading criteria, the patient is staged in grade V. Using ASA Physical Status Classification System, the patient was assigned as IV risk class, based on clinical signs and blood work results (a patient with severe systemic disease that is a constant threat to life – unstable renal disease with high uremia).

Prior to sedation, the patient had SAP between 184 to 195 mmHg, DAP 93 to 98 mmHg and MAP between 123 and 130, using HDO. The cardio-respiratory parameters, were: HR with 110 to 113 beats/minute, SpO_2 within 97 to 98%, RR within 25 to 28 breaths/minute and rectal temperature of 37.2ºC. Respiratory sinus arrhythmia was expressed on lead II-ECG, with no other electrical conductivity changes.

The stage of sedation that made the patient relaxed and positioned in lateral recumbency for the CVC procedure was observed 2 minutes after CRI administration of alfaxalone. There were no significant changes in ECG - sinus rhythm and blood pressure SAP: 167 to 173 mmHg, DAP: 80 to 90 mmHg and MAP: 109 and 117. HR decreased slightly to 99-101 beats/minute, RR from 28 to 12 breaths/minute and SpO2 between 96 and 97%.

After starting the CRI administration of alfaxalone, the patient expressed mild respiratory depression. Hypoventilation lasted about two minutes, SpO_2 dropped between 94 and 95% and RR decreased from 12 to 5 breaths/minute. Oxygen supplementation was mandatory and the patient received it via face mask at a flow rate of 5 L/min until the peripheral oxygen saturation was above 97%. It is cited that alfaxalone can cause short-lived hypoxia and oxygen supplementation was applied to the patient (Rodríguez et al., 2012).

Intravenous administration of alfaxalone was able to provide a dose-dependent anesthetic effect and good to excellent short-term sedation when administered as CRI. The CRI dose of 0.18 mg/kg/minute after a bolus dose of 3.2 mg/kg, produced adequate sedation without causing severe cardiorespiratory depression but a clinically acceptable decrease in vital parameters such as HR, RR and BP. Transient respiratory depression was noted and managed on time for the medical procedure to be performed safely for the patient, with no clinical implications.

In the present study, the dog exhibited mild muscular tremors and paddling during the early period of recovery from IV alfaxalone sedation.

CONCLUSIONS

The pharmacokinetic and pharmacodynamic properties of alfaxalone including its rapid onset and short duration of action with high total body clearance, resulted in little accumulation following IV administration.

The bolus dose of alfaxalone required for sedation and adequate neuro-depressive effect was 3.2 mg/kg IV and a total dose of 3.6 mg/kg (0.18 mg/kg/minute) administered in CRI for 20 minutes of procedure for central venous catheterization, provides clinically useful and effective sedation without causing severe cardiorespiratory depression, but a mild respiratory distress with no clinical implications was noted for this patient. An important factor that must be considered in patients with grade V AKI undergoing sedation for the CVC procedure, is that the clinical status may have a negative impact on the effects of anesthetic agents on homeostasis.

When it is used as a sedation agent in compromised dogs, alfaxalone seems to have a suitable cardiovascular pharmacodynamic profile with a mild respiratory side effect, that can be managed with thorough monitorization.

In conclusion, a dose-dependent anesthetic effect and smooth recovery were obtained with IV administration of alfaxalone in bolus following titration of the dose in a CRI on a patient that was not premedicated.

This protocol provided adequate neuro-depressive effect and effective sedation causing mild and transient respiratory distress with no severe cardiac depression or other clinical implications, for central venous catheterization.

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