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RESEARCH PAPER

Effect of dexmedetomidine constant rate infusion on the bispectral index during alfaxalone anaesthesia in dogs

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Abstract

Objective To assess the effect of two rates of infusion of dexmedetomidine on the bispectral index (BIS) in dogs anaesthetized with alfaxalone constant rate infusion (CRI).

Study design Prospective, randomized, 'blinded' experimental study.

Animals Six healthy Beagles (three females and three males).

Methods Dogs received as premedication saline (group D0), 1 μg kg^{-1} (group D1) or 2 μg kg^{-1} (group D2) dexmedetomidine, intravenously (IV). Anaesthesia was induced with alfaxalone (6 mg kg^{-1} to effect IV) and maintained with alfaxalone at 0.07 mg kg^{-1} $minute^{-1}$ and a CRI of saline (D0) or dexmedetomidine 0.5 μg kg^{-1} $hour^{-1}$ (D1) or 1 μg kg^{-1} $hour^{-1}$ (D2) for 90 minutes. BIS, electromyography (EMG), signal quality index (SQI) and suppression ratio (SR) were measured at 10 minute intervals and the median values were calculated. Nociceptive stimuli were applied every 30 minutes and BIS and cardiorespiratory values were compared before and after stimuli. Cardiorespiratory parameters were recorded throughout the study.

Results BIS and EMG values differed significantly among groups, being lower in D2 (71 ± 8) than in D0 (85 ± 10) and D1 (84 ± 9). SQI was always over 90% and SR was zero throughout all the treatments. There were no significant differences between pre- and post-stimulus values of BIS, EMG and SQI for any treatment, although in D0 and D1, heart rate, respiratory rate and arterial pressures increased significantly after the nociceptive stimulus.

Conclusions and clinical relevance Administration of dexmedetomidine (2 μg kg^{-1} + CRI 1 μg kg^{-1} $hour^{-1}$) decreases the BIS values and avoids the autonomic responses of a nociceptive stimulus during alfaxalone anaesthesia at 0.07 mg kg^{-1} $minute^{-1}$ in dogs. However, further studies are needed to verify whether this combination produces an adequate degree of hypnosis under surgical situations.

Keywords alfaxalone, anaesthesia, bispectral index, dexmedetomidine, dog.

Introduction

Anaesthesia is a hypnotic state or level of central nervous system (CNS) depression in which the patient neither perceives nor recalls a noxious stimulus (Prys-Roberts 1987). The term 'depth of anaesthesia' is an abstract one that has been described as referring to planes of anaesthesia characterized by different degrees of hypnosis and analgesia (Guedel 1937). Maintenance of an adequate depth of anaesthesia is vital to prevent intraoperative awareness, to maintain haemodynamic

stability and to reduce intraoperative stress response. Although the target of anaesthetic agents is the CNS, clinical assessment of depth of anaesthesia utilizes indirect parameters such as hemodynamic responses, automatic responses, motor responses (palpebral, corneal reflex, jaw tone) and reflexes (Henao-Guerrero et al. 2009; Morgaz et al. 2009). But the use of these clinical parameters could be inaccurate, because changes in them do not necessarily reflect altered consciousness (Bleijenberg et al. 2011).

Over the last few decades, an effort has been made to find objective measurements of anaesthetic depth. Electroencephalography (EEG) has been used to assess depth of anaesthesia, but its use is not practical in clinical situations because it requires specialized staff. Most recently, the bispectral index (BIS) algorithm has been derived from complex analysis of the EEG waveforms studies in anaesthetized humans (Sigl & Chamoun 1994; Johansen & Sebel 2000). Although the BIS was based on processed EEGs of humans, its validation and efficacy in diverse animal species have been evaluated in numerous studies (Antognini et al. 2000; Greene et al. 2002a,b; Haga & Dolvik 2002; March & Muir 2003).

The BIS estimates the degree of hypnosis in humans and animals and measures the overall response of the CNS to drugs, but not drug concentration (Rosow & Manberg 2001). The BIS is a dimensionless number, computed in real time and scaled between 0 and 100. It is inversely related to anaesthetic depth, with 100 indicative of a normal, conscious state and 0 indicative of an isoelectric EEG or absence of electrical brain activity (Johansen & Sebel 2000). In anaesthetized humans, BIS values of between 40 and 60 are an indication that an optimal level of hypnosis or a surgical plane of anaesthesia has been achieved (Sigl & Chamoun 1994; Johansen & Sebel 2000). BIS values of 55–65 were correlated with an adequate surgical plane of anaesthesia in dogs anaesthetized with sevoflurane (Guerrero 2003).

The cardiopulmonary, sedative, analgesic and isoflurane-sparing effects of dexmedetomidine infusions have been widely reported in dogs (Pascoe et al. 2006; Lin et al. 2008; Uilenreef et al. 2008; Gutierrez-Blanco et al. 2013; Pascoe 2015). Hall et al. (2000) showed that dexmedetomidine, administered as a continuous rate infusion (CRI), decreases BIS values during the intraoperative period when used as an adjuvant during general anaesthesia in humans. However, Ebner et al. (2013) reported that the mean BIS values were not significantly different when dexmedetomidine CRI (0.5 μg kg^{-1} $hour^{-1}$) was used in isoflurane-anaesthetized dogs as compared with isoflurane alone. To our knowledge, there are no data about the effect of dexmedetomidine on the BIS in alfaxalone-anaesthetized dogs.

The aim of this study was to evaluate the effect of two different dexmedetomidine doses, administered as a CRI, on the BIS in dogs anaesthetized with an alfaxalone CRI. We hypothesized that the higher dose of dexmedetomidine would decrease the BIS more profoundly.

Materials and methods

Animals

This study was approved by the University of Córdoba Institutional Animal Care and Use Committee. Six healthy adult Beagles (three females and three males) aged 2.3 ± 0.4 years with a mean body weight of 15.3 ± 2.3 kg were included in this study. A sample size of six was calculated based on detecting a variation in BIS values of 8, assuming a SD of 6, a power of 80% and an alpha error of 0.05 (G*Power 3.1.9.2, Germany). Their health status was assessed by physical examination, haematology and biochemistry. The animals were fasted for 12 hours without solid food and water prior to anaesthesia. These dogs were enrolled simultaneously in cardiorespiratory and anaesthetic study protocols (Quirós Carmona et al. 2014). Each dog received three different IV treatments separated by at least a 7 day washout period.

Study design

Before premedication, an area over the middle point of the frontal bone, 1 cm over the level of the eyes, extending between both zygomatic arches was clipped and shaved. Both cephalic veins were cannulated with a catheter of a suitable size (VasoVet 20 gauge 1.1 × 33 mm; B. Braun Melsungen AG, Germany) and the dogs received crystalloid fluid (NaCl 0.9%; B. Braun Medical SA, Spain) through the right catheter at 10 mL kg^{-1} $hour^{-1}$ throughout the procedure.

The dogs were selected randomly (by drawing from a box which contained three cards for each dog) before the first anaesthesia to establish the treatment order. Dexmedetomidine (Dexdomitor