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RESEARCH PAPER

Alfaxalone for total intravenous anaesthesia in bitches undergoing elective caesarean section and its effects on puppies: a randomized clinical trial

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Abstract

Objective To evaluate the effects and reliability of alfaxalone constant rate infusion (CRI) in comparison to isoflurane to maintain anaesthesia in bitches undergoing elective caesarean section.

Study design Prospective, randomized, 'blinded' clinical trial.

Animals Twenty-two client-owned bitches and 94 puppies.

Methods Bitches were randomly assigned to receive an alfaxalone CRI [0.2 mg kg^{-1} $minute^{-1}$ intravenously (IV), and once the last puppy was delivered, the dose was halved; $n = 11$] or 2% (vaporizer dial setting) isoflurane ($n = 11$) for maintenance of anaesthesia. All dogs were induced with alfaxalone (3 mg kg^{-1}) IV. Additional alfaxalone (0.3 mg kg^{-1} IV) was administered if the depth of anaesthesia was inadequate and the total dose was calculated. Bitches were mechanically ventilated. Analgesia was administered after the delivery of puppies. Physiological variables were recorded every 5 minutes. The bitches' recovery times were also recorded. Quality of induction and recovery were evaluated. Puppies' vigour was evaluated with a modified Apgar score at 5 and 60 minutes after birth. Puppies' survival rates at 24 and 48 hours and at 15 days were recorded. Data were analysed using an ANOVA, Student's *t*-test or Wilcoxon rank-sum test.

Results The rescue dose of alfaxalone was higher ($p = 0.01$); bitches' recoveries were longer ($p < 0.001$) and puppies' Apgar scores were significantly lower at 5 and 60 minutes ($p < 0.001$ and $p = 0.003$, respectively) with alfaxalone than with isoflurane. However, no significant differences were found for puppies' survival between groups.

Conclusions and clinical relevance Alfaxalone CRI seems to be a possible protocol for puppies and bitches undergoing elective caesarean sections. However, bitches recovered more slowly and puppy Apgar scores were lower in comparison to isoflurane.

Keywords alfaxalone, Apgar score, bitch, caesarean section, total intravenous anaesthesia.

Introduction

During caesarean section, the anaesthetic technique must provide optimal conditions both for the dam and for the foetus. Unfortunately, all anaesthetics cross the placenta and the foetus blood–brain

barrier, leading to foetal depression and may result in poor survival (Clarke et al. 2014).

Several studies have been performed to determine the optimal anaesthetic protocol during caesarean sections. Luna et al. (2004) compared the effects of four anaesthetic protocols on the puppies' neurological and cardiorespiratory variables and concluded that the best anaesthetic technique was epidural local anaesthesia. Nevertheless, epidural injection may require some degree of sedation for administration and can be sometimes contraindicated. When epidural anaesthesia was unsuitable, of the protocols studied, propofol appeared to be the most appropriate induction agent prior to maintenance with an inhlation agent, to maintain puppy neurological reflexes of the protocols studied (Luna et al. 2004)[1].

Isoflurane commonly is used to maintain anaesthesia for caesarean section in several species. In dogs, it was positively associated with puppies' vocalization, a sign of vigour and good survival score (Moon-Massat & Erb 2002). Nevertheless, in sheep, volatile agents may produce maternal and foetal hypotension and acidosis (Palahniuk & Schnider 1974; Okutomi et al. 2009). In addition, besides the environmental pollution that inhalant anaesthetics may produce (Zuccherelli 2007), chronic exposure to halogenated agents at low dose might affect the staff's health (Shirangi et al. 2008).

The new water-soluble formulation of alfaxalone was successfully proposed as an alternative to propofol to induce anaesthesia in bitches and produced better Apgar scores in puppies (Metcalfe et al. 2008; Doebeli et al. 2013). Alfaxalone in combination with alfadolone (Althesin; Glaxo, UK) was used to maintain anaesthesia in 90 women undergoing caesarean section (Gulotta et al. 1980). This steroid anaesthetic had no effect on the Apgar score, uterine tone, maternal–foetal metabolism, cardiocirculatory and respiratory stability. The authors also considered using Althesin as an alternative anaesthetic in order to avoid chronic staff exposure to volatile anaesthetics.

Alfaxalone CRI in dogs results in a rapid recovery and a good muscle relaxation (Ambros et al. 2008; Suarez et al. 2012). It is rapidly metabolized and eliminated by the body (clearance rate = 59 mL minute^{-1} kg^{-1}; Ferré et al. 2006). It has a high margin of safety and minimal cardiovascular effects (Morgaz Rodríguez et al. 2012). Although it was used for induction of anaesthesia in dogs undergoing caesarean section, alfaxalone has not yet been evaluated to maintain anaesthesia during this procedure.

The objectives of this study were to compare isoflurane and alfaxalone administration in client-owned bitches undergoing elective caesarean sections by evaluating the maintenance of anaesthesia (quality and cardiorespiratory functions), recovery from anaesthesia (duration and quality) and the effects on puppies (Apgar, survival and mortality scores).

We tested the hypothesis that, for maintenance of anaesthesia, alfaxalone CRI (0.2 mg kg^{-1} minute^{-1}, and, after puppies' delivery, 0.1 mg kg^{-1} minute^{-1}) would result in better scores (see earlier) than isoflurane (2%) anaesthesia in bitches as well as in their puppies.

Material and methods

Animals

This randomized (1:1), blinded, parallel-group clinical study has been approved by the Ethic Committee of VetAgro Sup, France (no. 1302). Legal and ethical requirements have been met with regard to the humane treatment of animals in accordance with the Euroguide, and good clinical practice of veterinary care was respected. Informed client consent was obtained for each animal included in the study.

Eligible dogs were healthy bitches enrolled to undergo elective caesarean sections. Ultrasound examinations were performed and progesterone venous concentrations were measured daily from 59 days post-ovulation. Aglepristone 15 mg kg^{-1} (Alizine; Virbac, France) was administered if progesterone concentrations were between 6 and 15 nmol L^{-1} and if there was no evidence of foetal distress (puppies' heart rate >200 beats minute^{-1}, calculated using the M-mode in the ultrasound machine). The surgery was then planned for the following day. Criteria for exclusion from the study were complications related to surgery or anaesthesic administration occurring during the procedure.

Bitches' recovery time was the primary outcome on which the sample size calculation was based. R statistical software (R Core Team; R Foundation for Statistical Computing, Austria; http://www.R-project.org/) was used to calculate it. To detect a difference of recovery time of 20 minutes between the two groups (time empirically chosen based on our experience; SD = 15 minutes) with a two-sided

[1][Correction added on 7 March 2016, after first on-line publication: Part of the Introduction has been removed on this version]