Theriogenology 96 (2017) 10–15

Contents lists available at ScienceDirect

Theriogenology

journal homepage: www.theriojournal.com

Puppy survival and vigor associated with the use of low dose medetomidine premedication, propofol induction and maintenance of anesthesia using sevoflurane gas-inhalation for cesarean section in the bitch

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ARTICLE INFO

Article history:
Received 24 July 2016
Received in revised form
19 March 2017
Accepted 22 March 2017
Available online 23 March 2017

Keywords:
Cesarean section
Medetomidine
Propofol
Apgar score
Puppy survival
Dog

ABSTRACT

The safety of an anesthetic protocol consisting of medetomidine hydrochloride (7 μg/kg iv) as premedicant, propofol, (1–2 mg/kg iv) as induction agent and sevoflurane, at 2% in oxygen for maintenance of anesthesia was studied in 292 cesarean sections (CSs) and 2232 puppies delivered. Medetomidine effects were reversed using atipamezole hydrochloride at 50 μg/puppy sc immediately following delivery and in the bitch iv immediately following surgery. The protocol's safety for puppies was expressed using survival immediately, 2 h and 7 d after delivery, and Apgar scores (measurement starting 15 min after delivery of the last puppy). The maternal survival rate was established immediately, 2 h and 7 d after cesarean section (CS). The CSs included 148 on Boerboel, 84 on English bulldog and 60 on other purebred bitches, which resulted in 1378, 541 and 313 puppies, respectively. Boerboel, English bulldog and other purebred bitches yielded 97.39%, 96.67% and 91.69% live puppies at delivery, 95.43%, 88.35% and 89.78% alive by 2 h and 89.19%, 79.11% and 84.03% alive by 7 d. Sixteen (1.16%), 32 (5.59%) and 4 (1.28%) malformed Boerboel, English bulldog and other purebred puppies were euthanized. Thirty five, 18 and 26, Boerboel, English bulldog and other purebred puppies were stillborn respectively, of which 12, 9 and 15, respectively had been discovered dead upon ultrasound examination immediately before CS. After correction for fetuses found dead on ultrasound examination and malformed euthanized puppies, 98.21%, 95.60% and 94.30% of Boerboel, English bulldog and other purebred puppies survived until 2 h and 91.78%, 87.17% and 88.26% until 7 d. Two-hour survival rates are negatively correlated to the proportion of puppies in a litter with scores of 8 or below ($r = 0.14$, $P = 0.01$, $n = 292$ litters) and tends to be positively correlated to the lowest Apgar score in a litter ($r = 0.11$, $P = 0.05$, $n = 292$ litters). This study shows that medetomidine hydrochloride in the protocol used is a safe premedicant in bitches prior to cesarean section and is associated with good puppy vigor as well as 2 h and 7 d puppy survival rates. The use of medetomidine as premedicant permitted use of less than half the dose of propofol usually required as induction agent.

1. Introduction

The ideal anesthetic protocol for cesarean section (CS) should provide adequate muscle relaxation, analgesia and narcosis for optimal operating conditions, be safe for the bitch [1] and should not affect the viability and survival of the puppies [2,3]. Additional recommendations include using drugs with a short duration of action [4] and using drugs that are reversible [5]. Induction using propofol and maintenance of anesthesia using isoflurane is widely accepted and associated with good outcome [3,6–11]. The use of alpha2-adrenergic agonists before anesthesia for CS, however, is controversial. The alpha2-adrenergic agonist xylazine, is not recommended in patients undergoing CS because it was identified as a risk factor for increased puppy mortality [11,12], associated with

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http://dx.doi.org/10.1016/j.theriogenology.2017.03.021
0093-691X/

increased risk of death in the dog [13,14] and caused severe maternal and neonatal cardiovascular depression [15].

The greatest objection to the use of the alpha2-adrenergic agonists is the cardiopulmonary effects that include transient hypertension followed by mild hypotension, bradycardia, increased systemic vascular resistance, reduced cardiac output, and respiratory depression [16]. In more recent surveys of anesthetic mortality in the dog however, premedication with medetomidine prior to anesthesia for routine surgery, was not identified as an increased risk factor for mortality [17] and data from human literature has shown that dexmedetomidine is associated with a reduction in all causes of mortality when used for non-cardiac, cardiac and vascular surgery [18,19]. No studies in veterinary medicine have been conducted on the use of medetomidine for CS.

This study assessed puppy vigor and survival following medetomidine, propofol and sevoflurane anesthesia for elective CS.

2. Materials and methods

The protocol was approved by the Animal Ethics Committee of the Faculty of Veterinary Science, University of Pretoria, (Onderstepoort, South Africa) (protocol number V048-14). During hospitalization all experimental animals were housed and fed commercial dry pellets twice daily and had access to water *ad-lib*. All the bitches were taken out twice daily for walks.

This is a retrospective, descriptive study that included 292 CSs in 256 privately owned bitches that underwent a CS and were selected from the general obstetric population because of increased obstetric risk. The duration of the study was from May 2012 until August 2015. High-risk pregnancies in the current study were considered those occurring in bitches from breeds with a high risk of complicated parturition [20], with a history of dystocia [21], or with known very large litters [22]. A trial of labor (attempt at spontaneous unassisted labor) was declined by all the owners of the bitches in the current study. From this subpopulation of bitches, only those destined for elective CS and for which the day of onset of cytological diestrus (D0) had been determined, were included. For all the cesarean sections, the bitches were admitted 3–4 d prior to the predicted parturition date calculated as 57 d following D0. During these days the bitches were observed for signs of impending parturition (panting, inappetence, nesting behavior, tenesmus) and by 6 hourly vaginal speculum examinations to assess the cervix. The decision on when to perform a CS was based upon the first appearance of any degree of dilatation of the cervix. All but two singleton pregnancies were excluded from the current study and were assigned to another study. This was done because some singleton pregnancies fail to progress normally [23]. Once the decision to perform a CS was made, an ultrasound examination of the abdomen was performed to establish if there were any dead fetuses (absence of detectable heartbeat). The bitches were weighed before surgery. In all bitches, fluid administration (Ringer lactate, Fresenius Kabi, Midrand, South Africa) commenced starting at induction and continued for 1½–2 h following induction for surgery until the set amount of fluids (35 ml/kg bw) had been infused and the hematocrits before and after CS determined as previously described [24]. The anesthetic protocol used in the current study included the alpha2-adrenergic agonist medetomidine hydrochloride (Domitor®, Zoetis Animal Health, Sandton, South Africa) at 7 μg/kg iv as premedicant, followed one min later by propofol (Fresenius propoven®1%, Fresenius Kabi, Midrand, South Africa), (1–2 mg/kg iv) as induction agent. The propofol was administered as follows, the calculated dose of 2 mg/kg was drawn up in syringe and 1 mg/kg/iv was administered as a bolus. The remaining propofol was used as top-up if required. This was followed by immediate intubation and inhalation of room air. Following surgical preparation (averaging 3–5 min), the bitch was connected to a closed circuit anesthetic machine with 2% sevoflurane (Sevoflo®, Safeline Pharmaceuticals, North Cliff, South Africa) in oxygen for maintenance of anesthesia. The peri-operative use of antibiotics included cefazolin (Zefkol®, Brimpharm, Claremont, South Africa) administered iv at 10 mg/kg at the time of induction followed by oral amoxycillin (Betamox, Be-tabs, Roodepoort, South Africa) at 20 mg/kg b.i.d for five days. The CS was performed in standard fashion as described [25]. Meloxicam (Metacam®, Boehringer Ingelheim, Randburg, South Africa) was administered iv (0.1 mg/kg) intra-operatively as proposed by Ref. [26], immediately after delivery of the last puppy. For 10 English bulldog- and 10 Boerboel litters, the exact time it took to deliver all the fetuses from the uterus (delivery time) and the total surgery times were recorded. The delivery time was the time measured in seconds that it took the surgeon to migrate all the fetuses to the uterine incision on the dorsal aspect of the uterine body, deliver them via the incision, remove the fetal membranes from their faces, sever their umbilical cords and hand them to an assistant. (The delivery time starts with the onset of manipulation of the first fetus and ends when the last fetus is handed to the assistant). The surgical time was the time it took from making the first incision through the abdominal skin until the last suture was placed in closing the skin. The processing of puppies following delivery involved immediate administration of atipamezole hydrochloride (Antisedan®, Zoetis Animal Health, Sandton, South Africa) at the dose of 50 μg/puppy sc, tying off of the umbilicus and applying 10% povidone iodine thereto, drying the puppies, shaking fluids from their airways and placing them in an air-heated incubator set at 35 °C. No oxygen support was offered to the puppies after delivery. Also, immediately after surgery, atipamezole hydrochloride at the dose of 20 μg/kg was administered iv (extra label) to the bitch, following which the remainder of the 35 ml/kg ringers lactate was allowed to infuse. The bitch was observed until the coughing reflex returned and was then extubated and observed until it was established that she was breathing comfortably whilst in sternal recumbency, sitting upright or standing. It was recorded whether the bitches were fully ambulatory 15 min following extubation. After delivery of the puppies the following records were made; total number of puppies delivered, live puppies, dead puppies, deformed puppies and puppies euthanized. The Apgar scores were assessed starting with the first puppy 15 min after the last puppy was delivered according to the method adapted by Ref. [27] and later used by Ref. [28]. The bitch and puppies were discharged usually 2–3 h following surgery.

The puppy survival rate was established immediately after delivery, at 2 h post CS and 7 days post CS and the maternal survival rate was established after delivery of the last puppy, at 2 h and at 7 d post CS. The Glasgow pain scale evaluation was performed at the time of discharging the bitch according to Glasgow Composite Measure Pain Scale to ensure adequacy of pain management [29].

3. Results

A total of 292 CS were performed, 148 on 133 Boerboel bitches, 84 on 68 English bulldog bitches and 60 on 55 other purebred bitches, which resulted in a total of 2232 puppies (1378, 541 and 313, respectively, per breed). Thirty six bitches underwent more than one CS in this study. The ages of 138 of the bitches were known and ranged from 1 to 8 years of age (mean = 3). The parity of 141 were known and ranged from zero to five previous litters (mean = 1). The percent live at delivery for the Boerboel, English bulldog and other purebred's puppies respectively was; 97.39%, 96.67% and 91.69%. The 2 h survival rate respectively was 95.43%, 88.35% and 89.78%. The 7 day survival rate was respectively 89.19%, 79.11% and 84.03%. The numbers of puppies euthanized due to