Anesthetic management of a dog with severe subaortic stenosis and mitral valve disease complicated with atrial fibrillation undergoing ovariohysterectomy

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Abstract

The anesthetic management in patients with subaortic stenosis and mitral valve disease should involve intensive monitoring and the anesthesiologist's main concern is to ensure oxygen delivery and tissue perfusion. Since anesthetic procedures in such patients are rare, there is no previous report about the anesthetic management. A 5.5-year old, 32-kg Boxer, suffering a severe heart disease due to a final stage subaortic stenosis and mitral insufficiency, was anesthetized for an ovariohysterectomy to remove an ovarian tumor that was producing high-volume ascites. Methadone (0.3 mg kg^{-1}) was administered intramuscularly (IM) for pre-anesthetic medication, etomidate (1.3 mg kg^{-1}) and midazolam (0.2 mg kg^{-1}) were used for the induction of anesthesia and after endotracheal intubation, anesthesia was maintained with sevoflurane vaporized in oxygen and air. Fentanyl (5–10 µg kg^{-1} h^{-1}) and paracetamol (15 mg kg^{-1}) were administered to improve analgesia. Previous persistent atrial fibrillation was refractory to medication (digoxin, diltiazem, and pimobendan) and continued during the anesthetic procedure. Dobutamine (1.5–5 µg kg^{-1} minute^{-1}) helped to maintain mean arterial blood pressure above 60 mmHg. Epidural morphine (0.1 mg kg^{-1}) and incisional bupivacaine (2 mg kg^{-1}) were administered at the end of surgery to provide postoperative analgesia. Anesthesia was otherwise uneventful, and recovery was considered excellent.

Keywords: Anesthesia, Atrial fibrillation, Dog, Mitral, Subaortic stenosis.

Introduction

Anesthesia in severe cardiac patients is challenging and has special considerations due to their inability to ensure an adequate cardiac output (CO) despite physiological compensatory mechanisms. In addition to physical examination and a complete blood work, including blood count, chemistry panel, and electrolytes, the assessment of the electrocardiogram, blood pressure, thoracic radiographs, and echocardiogram should be accomplished to the patients suffering from heart disease (Congdon, 2014; Robinson and Borgeat, 2016). Heart diseases affect in a variety of ways, the cardiovascular function and anesthetic drugs should be considered based on the cardiovascular-sparing effects. Although there are some general principles applicable to patients with cardiovascular disease, some considerations should be taken to adapt the anesthetic plan depending on the patient's cardiovascular status.

Anesthetic management in the patients with subaortic stenosis (SAS) and mitral valve disease (MVD) should involve intensive monitoring while avoiding significant change in heart rate (HR), sinus rhythm, blood pressure, and intravascular volume. Thus, the anesthesiologist's main concern is to prevent the increase in myocardial oxygen demand and decreased tissue perfusion (Robinson and Borgeat, 2016).

There are no reported cases of anesthesia in a dog presenting the aforementioned heart diseases, thus this case report describes the anesthetic management of a dog with severe chronic and degenerative heart disease undergoing an ovariohysterectomy.

Case Details

A 5.5-year-old Boxer bitch weighing 32 kg was referred to the Veterinary Teaching Hospital with lethargy, anorexia, and abdominal distension. Two weeks before, the dog had been presented to the referring veterinarian with a suppurative mass over the stifle and abdominal distension. Prior to the surgical removal of the mass (diagnosed as a mastocytoma) and due to the previous history of heart disease, a thorough examination of the heart condition was suggested. The echocardiography showed a severe SAS with a pressure gradient of 108 mmHg and mitral insufficiency associated to thickening of the valve with severe dilation of the left chambers of the heart. Ejection fraction, Simpson Method, and fractional shortening, Teizchold Method, were decreased (40.1% and 19.6%, respectively). Systolic function was reduced, and pulmonary hypertension was not observed. Thereafter, the referring veterinarian prescribed ciprofloxacin [250 mg twice a day (BID)], prednisone [10 mg once a day (QD)], benazepril (10 mg BID), and

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furosemide (40 mg BID) orally, and referred the patient to the Teaching Hospital.

On presentation at the Hospital, the dog was depressed, had weak peripheral pulse and positive jugular pulse. Auscultation revealed a heart murmur (III/VI) and the electrocardiography showed atrial fibrillation (AF) and left bundle branch block, usually associated with left cardiac chambers enlargement. HR was 250 beats per minute (bpm). Among other age-related findings (and not associated to the current complain), the chest radiographs showed cardiomegaly with a vertebral heart score of 13, dorsal displacement of the trachea, and the presence of interstitial-alveolar pattern in the proximal third of the seventh intercostal space in the lateral projection, and at the right medium and caudal lobes in the ventrodorsal projection, most likely to be cardiogenic pulmonary edema. Other findings were costochondral calcifications, deforming spondylosis, and bony bridges among sternebrae. Additionally, on abdominal radiographs, there was loss of peritoneal detail, most likely representing peritoneal effusion. Hence, abdominocentesis was performed and six liters of modified transudate were obtained. Afterward, ultrasound of the abdomen revealed the presence of a mass close to the right kidney suggestive of ovarian tumor. No other findings were remarkable, with the exception of iliac lymphadenopathies. Evaluation of the ovarian mass with cytology of a fine needle aspirate obtained from the ovarian revealed an adenocarcinoma. The presence of abdominal effusion is a common clinical sign with this type of tumor in the bitch (Bertazzolo *et al*., 2012). Based on the clinical findings, ovariohysterectomy was proposed, as an alternative to humane euthanasia, and eventually the owners gave their informed consent for the surgical procedure.

Initially, digoxin (0.125 mg BID; Digoxina 0.25 mg, Kern Pharma), diltiazem (15 mg BID; Diltiazem Sandoz 60 mg, Sandoz Farmaceutica), and pimobendan (6.125 mg BID; Vetmedin 5 mg, Boehringer Ingelheim) were added to the previous oral treatment. A stage D of valvular disease was considered as there were signs of heart failure refractory to the therapy (Atkins *et al*., 2009). Surgery was scheduled for 2 weeks later. In between, digoxin check-up showed normal values (1.8 ng ml^{-1}).

The dog was fasted the night before the surgery although *ad libitum* water was available. Two hours before surgery, all the prescribed medications were given orally with the exception of furosemide (Seguril 20 mg 2ml^{-1}, Aventis; 1 mg kg^{-1}) given intravenously (IV). On preoperative physical examination, the patient was on a poor body condition, presented a cardiac murmur (III/VI), AF, and bundle branch block with tachycardia (170-200 bpm), a considerable abdominal distension with positive ascitic wave and positive jugular pulse. Most remarkable findings in blood work were an increase of uremia (125 mg dl^{-1}), hypoproteinemia (4.1 g dl^{-1}), hypoalbuminemia (2.2 g dl^{-1}), and hypocalcemia (8.8 mg dl^{-1}); the remaining parameters were within the normal range for the species. It was classified as an American Society of Anesthetists physical scale of IV. Methadone (Semfortan 10 mg ml^{-1}, Dechra; 0.3 mg kg^{-1}) was administered IM for pre-anesthetic medication. After 20 minutes, mild sedation was achieved and 500 ml of transudate were obtained via abdominal drainage. Both an 18G and a 22G catheter were placed in the cephalic vein and the dorsopedal artery, respectively. After 5-minute preoxygenation (5 l minute^{-1}) by mask, anesthesia was induced with etomidate (Etomidato-Lipuro 2 mg ml^{-1}, B.Braun; 1.3 mg kg^{-1}) and midazolam (Dormicum 15 mg 3 mL^{-1}, Roche; 0.2 mg kg^{-1}) administered IV over 2 minutes, and the trachea was intubated with a 10-mm internal diameter cuffed endotracheal tube and connected to a rebreathing circuit. An intravenous dobutamine (Dobutamina 250 mg 20 ml^{-1}, Inibsa) infusion at 1.5 µg kg^{-1} minute^{-1} was started immediately after anesthetic induction. Anesthesia was initially maintained with 2% sevoflurane (SevoFlo, Abbott) vaporized in 100% inspired oxygen. Once transferred to the theatre, the patient was connected to an anesthesia workstation (Julian, Dräger) and anesthesia was maintained with end tidal concentrations of sevoflurane (Et$_{SEVO}$) between 1.3% and 1.7% vaporized in oxygen and air (80% and 20%, respectively).

Ranitidine (Zantac 10 mg ml^{-1}, GlaxoSmithKline; 1 mg kg^{-1}) and diphenhydramine (Antihistamínico 25 mg ml^{-1}, Syva; 1 mg kg^{-1}) were administered subcutaneously after anesthetic induction to prevent the potential histaminergic effects of the mastocytoma (London and Seguin, 2003). In addition, cefazolin IV (Cefazolina 1 g, Normon; 22 mg kg^{-1}) was administered as a prophylactic antibiotic.

Persistent tachycardia (220–240 bpm) with AF and left bundle branch block were observed throughout the surgery. Mean arterial pressure remained steady (70–80 mmHg) by adjusting the continuous rate infusion (CRI) of dobutamine (1.5–5 µg kg^{-1} minute^{-1}). Oxygen saturation of hemoglobin (> 95%) and body temperature (37.5˚C–38.5˚C), were within physiologic ranges during the whole procedure. An air-warming blanket was used (Bair Hugger, 3M) during the surgery. Moderate hypercapnia (46–62 mmHg) was allowed during spontaneous ventilation to avoid the potential negative effects of mechanical ventilation, such as the rise in intra-thoracic pressure, which may affect the right heart venous return, limiting the cardiac filling and therefore, decreasing CO (Dugdale, 2007).

An intravenous CRI of fentanyl (Fentadon 0.05 mg ml^{-1}, Dechra; 5–10 µg kg^{-1} h^{-1}) was deemed to improve intraoperative analgesia and reduce inhalatory anesthetic requirements. Fluid therapy with Lactated Ringer's solution (Lactato-RingerVet 500 mL, B.Braun) was adjusted to 1–2 ml kg^{-1} h^{-1} depending on fentanyl infusion to avoid fluid overload. In addition, 15 mg kg^{-1} of paracetamol (Paracetamol Kabi 10 mg ml^{-1}, Fresenius Kabi) were administered

over 20 minutes IV as a part of a multimodal analgesic approach.

Once the surgery finished, a subcutaneous injection of bupivacaine (2 mg kg^{-1}; Bupivacaina 0.5%, B.Braun) was used in the surgical wound and an epidural administration of morphine (Cloruro Mórfico 1%, B.Braun; 0.1 mg kg^{-1}) diluted with saline (Fisiovet 100 ml, B.Braun; total epidural volume 0.2 ml kg^{-1}) were performed to provide postoperative analgesia. Total general anesthesia and surgery times were 73 and 56 minutes, respectively.

Arterial blood gases at the end of surgery revealed acidemia (pH = 7.19) due to an expected respiratory acidosis (PaCO$_2$ = 60.4 mmHg). No other findings were relevant, thus no further actions were considered.

The dog was uneventfully recovered from anesthesia and was transferred to the intensive care unit (ICU). There, enoxaparin (Clexane 60 mg 0.6 ml^{-1}, Aventis; 0.8 mg kg^{-1}) was administered every eight hours as well as all the aforementioned cardiac medication. The dobutamine infusion was gradually reduced until finally discontinued 35 hours after anesthesia's end. Non-invasive mean arterial pressure remained above 60 mmHg at all the times. Analgesia was assessed every hour with the Short Form of the Glasgow Composite Measure Pain Scale, and buprenorphine (Buprecare 0.3 mg mL^{-1}, Divasa-Farmavic; 15 µg kg^{-1} SC) was administered every 8 hours. Although depressed mood, stance in the ICU was otherwise uneventful and the patient was discharged 2 days after the surgery.

Discussion

An anesthetic management using sedative and anesthetic drugs with cardiovascular-sparing effects, associated with a multimodal analgesic approach and cardiovascular support, allowed adequate cardiovascular stability in this case. The main complications observed were a moderate hypercapnia and cardiac arrhythmias associated with the cardiac condition. Eventually, the overall outcome of the patient was satisfactory.

SAS is the most common form of aortic stenosis in the dog and Boxer is one of the breeds predominantly affected (O'Grady *et al*., 1989; Kienle *et al*., 1994; Hollmer *et al*., 2008). In this case, the CO is highly dependent on HR because the outflow obstruction in the aorta impedes stroke volume (SV) to increase (Scarabelli and Bradbrook, 2016). The prognosis is based on the pressure gradient along the valve and common drugs used to treat the clinical signs are beta-adrenergic receptor blockers. Dogs with SAS and mild pressure gradients (16–35 mmHg) commonly may experience no morbidity but SAS with moderate (36–80 mmHg) to severe (>80 mmHg) gradients lead to left ventricle (LV) failure, pulmonary edema and high risk of sudden death (O'Grady *et al*., 1989; Kienle *et al*., 1994; Reilly *et al*., 2013). In the current case, the pressure gradient was 108 mmHg and the SV was reduced leading to an overall reduction in CO. In

addition, a cardiac defect such as the MVD which is usually found with SAS (Kienle *et al*., 1994) was also present. The MVD produces insufficiency, reduced CO, and maladaptive compensatory mechanisms. Therefore, methadone was chosen for pre-anesthetic medication as opioids have limited cardiovascular effects, but they also have inhalant anesthetic's minimum alveolar concentration sparing effects in dogs (Credie *et al*., 2010; Williamson *et al*., 2017).

Methadone was expected to provide adequate perioperative sedation and analgesia (Hunt *et al*., 2013). Moreover, it may decrease the HR, but maintaining CO, and increasing SV, which reduces oxygen myocardial consumption (Perkowski and Oyama, 2015). Therefore, methadone may be desirable as tachycardia and AF increase myocardial oxygen demand and reduce CO.

Etomidate was used for anesthetic induction as it produces minimal cardiovascular depression, i.e., HR, blood pressure, left ventricular pressures, contractility, and myocardial oxygen remains unchanged after its administration (Nagel *et al*., 1979; Carter *et al*., 2017). Anesthetic induction with etomidate may produce some adverse effects like excitement, myoclonus or vomiting (Muir and Mason, 1989), thus midazolam was combined to counteract these effects. Most likely, midazolam may reduce the dose of etomidate as when it is combined with other common induction agents such as propofol or alfaxalone (Liao *et al*., 2017). Although midazolam may reduce systolic blood pressure during co-induction with propofol in healthy dogs, values remained within an acceptable range (Hopkins *et al*., 2014). Additionally, propofol or alfaxalone could have been chosen to induce anesthesia but they might affect negatively systemic vascular resistance (SVR) (Scarabelli and Bradbrook, 2016), while etomidate has a better cardiovascular profile (Sams *et al*., 2008; Rodriguez *et al*., 2012).

Isoflurane and sevoflurane are suitable volatile agents for maintenance of anesthesia as both provide similar clinical effects (Bennett *et al*., 2008). Sevoflurane produces a more rapid anesthetic induction (Johnson *et al*., 1998; Cantalapiedra *et al*., 2000) and faster recovery from anesthesia (Eger, 1994). Some studies have suggested that both isoflurane and sevoflurane produce similar cardiovascular depression, but the latter producing a lesser respiratory depression (Galloway *et al*., 2004). However, evidence of clinically relevant differences between quality and speed of recovery between isoflurane and sevoflurane anesthesia in dogs remains controversial; some studies showed a faster recovery using sevoflurane (Lopez *et al*., 2009) while others found no differences in recovery times (Johnson *et al*., 1998; Cantalapiedra *et al*., 2000; Love *et al*., 2007).

Sevoflurane causes dose-dependent hypotensive effects associated with vasodilation, decreases in myocardial contractility and left ventricular afterload (Eger, 1994; Hettrick *et al*., 1996). Considering the diagnosed

reduction in myocardial contractility with severe ventricular dysfunction, together with the likely further reduction produced by sevoflurane in the present case, the administration of dobutamine was considered from the beginning of the anesthesia. Dobutamine has dose-dependent positive inotropic effects and may increase blood pressure without affecting left atrial pressure or afterload (Goya *et al*., 2018). This drug increases arterial pressure and enhances myocardial contractility in isoflurane-anesthetized dogs with surgically induced mitral insufficiency (Goya *et al*., 2018). Thus, the inotropic effect counteracted the cardiovascular effect without increasing afterload. The use of vasoconstrictors (e.g., phenylephrine and norepinephrine) increases SVR, which therefore would increase left atrial pressure (Scarabelli and Bradbrook, 2016) and, for that reason they were not considered in this case. Intravenous infusion of fentanyl was not only administered to enhance intraoperative analgesia but also further reduce Et_{SEVO} (Reilly *et al*., 2013; Suarez *et al*., 2017). In the present case, Et_{SEVO} was maintained between 1.3% and 1.7% to reach an acceptable depth of anesthesia which means a reduction of 20%–40% of the MAC of sevoflurane required to prevent purposeful movements in dogs (Yamashita *et al*., 2012).

Recommendations on the administration of antihistaminergic drugs to avoid cardiorespiratory effects of histamine through actions on H1 and H2 receptors in patients with mastocytoma is still controversial. Preventive treatment has been recommended (London and Seguin, 2003) but more recently, its true efficacy has been questioned in anesthetized dogs undergoing excision of mast cell tumors (Sanchez *et al*., 2017). Both diphenhydramine and ranitidine were given following the former recommendations while no adverse effects were expected after their administration.

Moreover, AF is a common arrhythmia associated with severe atrial enlargement and severe mitral regurgitation in dogs. The characteristic uncoordinated atrial activity impedes atrial contraction leading to reduced CO further aggravated in the presence of tachycardia. Usual treatments include digoxin, beta-blockers, and calcium channel blockers to slow AV conduction (Miyamoto *et al*., 2001; Congdon, 2014). Lidocaine has been used to treat satisfactorily vagally associated AF (Moise *et al*., 2005; Pariaut *et al*., 2008) and reduces the sevoflurane MAC in dogs (Wilson *et al*., 2008). However, lidocaine may cause cardiovascular depression in dogs (Robinson and Borgeat, 2016) and increases in HR, pulmonary arterial pressure, and stroke index (Nunes de Moraes *et al*., 1998). Conversion to sinus rhythm with lidocaine in patients suffering an underlying severe cardiac disease is not always possible (Congdon, 2014). In addition, AF was already refractory to medical therapy in the current case, thus lidocaine and any further cardiovascular depression associated to it was avoided. Amiodarone is a class III antiarrhythmic used to treat AF but has been related to adverse effects such as increased blood histamine

concentrations producing skin reactions, tachycardia, hypotension, and bronchospasm (Cober *et al*., 2009); therefore, it was considered inappropriate in the present case.

Paracetamol is a centrally acting analgesic with weak anti-inflammatory properties but less gastrointestinal and cardiovascular side effects compared with nonsteroidal anti-inflammatory drugs (NSAIDs) (Jahr and Lee, 2010). It is not as widely used in veterinary patients as in human medicine, probably because of its toxic effects in cats and scarce reports of its use in dogs. However, paracetamol might be useful in a multimodal analgesic approach (Mburu *et al*., 1998; White *et al*., 2017). Although other NSAIDs commonly used in dogs such as meloxicam or carprofen could have been used in the present case, the side effects of these drugs, such as the gastrointestinal, renal, or increase in bleeding, were considered (Luna *et al*., 2007). Furthermore, common situations associated with anesthesia, such as hypotension or hypovolemia, can enhance the NSAIDs' adverse effects on renal function (Lomas and Grauer, 2015).

Bupivacaine is a potent amide type local anesthetic with a long duration of action widely used in veterinary medicine (Webb and Pablo, 2009). It was administered incisional in this patient to improve postoperative analgesia. Although intra-peritoneal administration of bupivacaine could have enhanced the analgesic effect (Carpenter *et al*., 2004; Campagnol *et al*., 2012), the presence of ascites discouraged it.

Finally, the epidural administration of morphine was considered to complete the multimodal analgesic approach as it provides postoperative analgesia without causing further hemodynamic depression in the dogs (Naganobu *et al*., 2004; Kona-Boun *et al*., 2006; Perez *et al*., 2013). The more hydrophilic nature of morphine provides a longer duration of the analgesic effect when given epidurally compared to other opioids with higher lipophilicity (e.g., fentanyl), thus with a faster systemic absorption (Valverde *et al*., 1992). Combination of morphine with local anesthetics by the epidural route prolongs analgesic effects but may produce some cardiorespiratory depression considered acceptable for healthy patients (Kona-Boun *et al*., 2006) but potentially harmful for an hemodynamic unstable patient such as the one in this case.

In conclusion, a multimodal analgesic approach, a reduced concentration of sevoflurane for anesthetic maintenance and cardiovascular support under spontaneous ventilation, together with intensive monitoring, were able to maintain an adequate anesthesia in a severe cardiac patient undergoing ovariohysterectomy.

Conflict of interest

The authors declare that there is no conflict of interest.

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