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CASE REPORT

Dexmedetomidine Related Bradycardia Leading to Cardiac Arrest in a Dog

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ABSTRACT

A 2-year-old, mixed breed female dog (16 kg) underwent an exploratory laparotomy following ultrasonographic diagnosis of foreign body and a segment of small intestine intussusceptions. The patient was classified as an ASA II. Ketamine (1mg/kg, IV), and dexmedetomidine (2.5 µg/kg, IV), and morphine (0.6 mg/kg, SC) were given as anesthetic premedication. Propofol (0.1 mg/kg, IV) titrated to a total amount of 4 ml (2.5 mg/ kg) was given for intubation. Asystole was occurred. Cardiac resuscitation was then conducted immediately. Atipamezole (0.1 ml) was injected, but showed no response on ECG. Atropine (0.02 mg/kg) was then injected, and a second dosage was given. Two-three mins later, the heart rate at 84 beats/min. The NIBP showed 203/132 with MAP 153 mmHg, and the SpO₂ showed 95% after the cardiac function was regained. Dexmedetomidine related bradycardia leading to cardiac arrest has been suggested in this case.

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INTRODUCTION

Dexmedetomidine is widely used in various clinical indications including anxiolytic, analgesia, and sedation that reflect them suitable as adjuncts in anesthesia. One of the benefits in using dexmedetomidine is that it causes minimum respiratory effect (Gerlach and Dasta, 2007). However, the common adverse reactions associated with dexmedetomidine in a Phase III study in 401 patients were hypotension (30%), hypertension (12%), nausea (11%), bradycardia (9%), and dry mouth (3%) (Bhana *et al.*, 2000). Among all the adverse effects, hypotension (22.7%) and bradycardia (4.4%) were the most commonly reported in a dexmedetomidine registry (Dasta *et al.*, 2004). The ISO-sparing effect of dexmedetomidine has been proven in canine as well as feline patients. A study in feline patients using dexmedetomidine from different routes (constant rate infusion or epidural) showed that dexmedetomidine could reduce isoflurane MAC (Souza *et al.*, 2010). Herewith, we presented a case with linear foreign body and discussed the possible causes of cardiac arrest during anesthesia.

HISTORY

A 2-year-old, crossbred female dog (16 kg) was admitted to the Veterinary Medicine Teaching Hospital of

National Chung Hsing University for the treatment of 5-day standing vomiting and defecation with fabric specks. The patient's vaccination record was current, had no history of allergic reaction(s) to any medications or foods, and no previous anesthesia record was available.

During the initial physical examination, the mucosal membranes were normal (pink and moist), and the capillary refill time was <2 seconds. The body condition score was 4/9. The rectal temperature was 38.3°C. The dog was panting with the pulse rate at 100 beats/min. Distended bowels were noted in palpation. Blood examination revealed leukocytosis (30,300/µl; reference range, 6,000-18,000/µl) with left shift (3030/µl; reference range, 0-450/µl). Serum electrolytes analysis revealed hyponatremia (123 mmol/L; reference range, 140-155 mmol/L), hypokalemia (3.0 mmol/L; reference range, 3.6-5.8 mmol/L) and hypochloremia (73 mmol/L; reference range, 96-124 mmol/L).

A dilated plicated loop containing a few round gas shapes at the right side of abdomen was observed by abdominal radiology and a linear foreign body was suspected. Ultrasound examination found the linear foreign body and a segment of jejunal intussusception.

An exploratory laparotomy for removal of the linear foreign body was planned. Prophylactic antibiotics such as ampicillin and metronidazole were administered to the patient. The patient was classified as an ASA II patient

(patient with mild systemic disease). Ketamine (1mg/kg, IV) and dexmedetomidine (2.5 µg/kg, IV), and subcutaneous morphine (0.6 mg/kg, SC) were given as anesthetic premedication. Propofol (0.1 mg/kg, IV) titrated to a total amount of 4 ml (2.5 mg/kg) was given for intubation. A 9.5-mm cuffed endotracheal tube was placed in the trachea. The anesthesia was maintained using isoflurane in oxygen (flow rate, 0.5L/min). When the end-tidal concentration of isoflurane gradually increased to 0.5%, the heart rate was decreased from 149 to 79 beats/min and the ECG showed sinus arrhythmia. Ten minutes later, the heart rate decreased dramatically to 29 bpm and the SpO₂ dropped to 83%. An asystole then occurred. At the time of cardiac arrest, the isoflurane concentration was 1.2% with oxygen. Cardiac resuscitation was then conducted immediately. Isoflurane was turned off and 100% oxygen was given (2L/min) until extubation. Atipamezole (0.1 ml) was injected through intravenous catheter, but the patient still showed no electronic cardiac response on ECG monitor. Atropine (0.02 mg/kg) was then injected intravenously, and a second dosage was given subcutaneously. The patient was resuscitated with the heart rate at 84 beats/min 2-3 minutes later. The NIBP showed 203/132 with MAP 153 mmHg, and the SpO₂ showed 95% after the cardiac function was regained.

DISCUSSION

Several cases have been reported that dexmedetomidine is potential to cause cardiac arrest in human patients (Gerlach *et al.*, 2009; Gerlach and Murphy, 2009) that have been discussed in several aspects. Firstly, the correlation between the cardiac arrest and the decrease cardiac output or the myocardial infarction associated with dexmedetomidine has been mentioned. In the latter report, the possibility that in certain genetically predisposed individuals, stimulation of α₂-adrenoreceptors by dexmedetomidine may cause profound myocardial ischemia and myocardial dysfunction due to coronary vasoconstriction. Secondly, the combination of multiple drugs may also augment the bradycardia (Zhang *et al.*, 2010). Opioids are also potent stimulants of vagal tone through the inhibition of sympathetic outflow, and this action may combine with dexmedetomidine to result in hypotension and bradycardia. Propofol administration should also be considered another potential cause of bradycardia. Propofol can cause bradycardia through β₂-adrenergic receptors block or through M₂-acetylcholine receptor activation. However, the clinical occurrence of bradycardia with propofol (in the absence of concomitant opioid administration) has been reported only in preexisting myocardial depression or as a part of the propofol infusion syndrome (PRIS). In the present case, the patient had received the combination of morphine and dexmedetomidine, following propofol for the induction. The cardiac arrest occurred shortly after intubation procedure which could stimulate the vagal tone activity and then worsen the bradycardia, leading to the cardiac arrest.

The mechanism of sedative effect of dexmedetomidine takes place in the brain called locus ceruleus, in which dexmedetomidine stimulates alpha 2 receptors on the presynaptic neurons. The activation of the alpha 2 adrenergic receptor will then inhibit adenylyl cyclase. Following a complex cascade, an efflux of potassium through calcium-activated potassium channels and an inhibition of calcium into calcium channels in nerve terminals then occur. The change in membrane ion conductance leads to a hyperpolarization of the membrane, which suppresses neuronal firing in the locus ceruleus as well as its activity in the ascending noradrenergic pathway. To sum up, the net effect is decreased in norepinephrine release from presynaptic neurons with inhibition of postsynaptic activation, which attenuates central nervous system excitation. Additionally, the ISO-sparing effect of dexmedetomidine has been proven both in canine (Uilenreef *et al.*, 2008) and feline (Souza *et al.*, 2010) patients. Epidural dexmedetomidine 3 µg/kg in dogs reduced isoflurane MAC by 29%. In cats, a slight increase in epidural dexmedetomidine dose (4 µg/kg) reduced 47% requirement of isoflurane, suggesting that a small increase in epidural dexmedetomidine dose resulted in a larger sparing effect in cats under isoflurane anesthesia, or that dexmedetomidine might have a greater effect in cats than in dogs. In the present case, the cardiac arrest occurred when the isoflurane reached to the highest level. Due to the sparing effect and isoflurane, the increasing isoflurane concentration might be one of the reasons that led to cardiac arrest.

It is concluded that the present case of cardiac arrest was associated with dexmedetomidine premedication to supplement isoflurane general anesthesia and a prompt cardiac resuscitation resulted in complete recovery. It appears that combined anesthetic factors led to severe bradycardia and cardiac arrest and a care must be taken while using dexmedetomidine as premedication for isoflurane anesthesia in dogs.

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