Anesthesia Case of the Month

History
A 4-year-old spayed female mixed-breed dog was brought to the Dentistry Service at the University of Wisconsin’s Veterinary Medical Teaching Hospital for examination of a fractured left maxillary fourth premolar. Results of a CBC and serum biochemistry profile were within reference limits, and complete dental cleaning and a root canal were scheduled for the next week. On the day of the procedure, the dog weighed 19 kg (42 lb) and was bright, alert, and responsive. Results of a complete physical examination were unremarkable aside from the dental abnormalities. The dog was classified as American Society of Anesthesiologists status II because of the mild dental disease.

The dog was premedicated with morphine sulfate (15 mg, IM) and acepromazine maleate (0.2 mg, IM). Anesthesia was induced with thiopental sodium (250 mg, IV) and maintained with isoflurane (2%) administered in oxygen via an 11-mm cuffs endotracheal tube and circle breathing system. Oxygen flow rate during anesthetic induction and maintenance was set at 1 L/min. The patient was instrumented with an electrocardiograph, pulse oximeter, capnometer, and oscillometric blood pressure monitor. The cuff for the oscillometric blood pressure monitor was placed over the metatarsal region; the width of the cuff was approximately 40% of the limb circumference. The patient’s body temperature was monitored with a rectal thermometer and maintained between 36.7°C and 37.4°C (98.1°F and 99.3°F) throughout the procedure with a convective air warming system. Lactated Ringer’s solution was administered at a rate of 10 mL/kg/h (4.5 mL/lb/h), IV.

The dog was mechanically ventilated at a rate of 13 breaths/min, and end-tidal partial pressure of CO₂ was maintained between 45 and 50 mm Hg. Heart rate remained within a clinically acceptable range during anesthetic maintenance (Figure 1) and was similar to rates reported for dogs anesthetized with isoflurane and a constant rate infusion of morphine. Systolic arterial pressure, measured indirectly with the oscillometric blood pressure monitor, ranged from 79 to 92 mm Hg, diastolic arterial pressure ranged from 25 to 35 mm Hg, and mean arterial pressure ranged from 43 to 55 mm Hg. These values were of concern because direct systolic arterial pressures < 60 mm Hg represent hypotension and are assumed to result in inadequate organ perfusion. In addition, in anesthetized dogs with hypotension, oscillometric methods for measuring arterial blood pressure may only approximate or underestimate the true mean arterial pressure. To obtain more accurate measurements of arterial blood pressure, a catheter was placed in the dorsal pedal artery, and arterial blood pressure was measured directly with a balanced transducer. At this time, hypotension was confirmed because mean arterial pressure measured directly was < 60 mm Hg. Stimulation of the oral cavity by the attending dentist did not increase arterial blood pressure measurements. The attending dentist performed an infraorbital block with bupivacaine (1 mg) to provide adjunctive analgesia during the dental procedure.

Question
What is an appropriate plan to treat the hypotension in this dog?

Answer
Systemic arterial pressure depends on a complex set of physiologic processes (Figure 2). In simple terms, however, heart rate and stroke volume determine cardiac output, and cardiac output and peripheral vascular resistance determine systemic arterial pressure. Thus, the most common causes of hypotension in anesthetized dogs include hypovolemia, peripheral vasodilation, and reduced myocardial contractility. As

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a result, treatment of hypotension in dogs anesthetized with inhalant anesthetic agents should focus on identifying pharmacologic agents and physiologic factors adversely affecting stroke volume, heart rate, and peripheral vascular resistance.

Inhalant anesthetic agents have been reported to cause a dose-dependent decrease in mean arterial pressure. For example, administration of isoflurane at 1.5 to 2 times the minimum alveolar concentration (in dogs, the minimum alveolar concentration of isoflurane ranges from approximately 1.3% to 1.8%) decreases systemic vascular resistance and myocardial contractility, thereby decreasing arterial blood pressure. For this reason, the first step in the treatment of hypotension in the dog described in the present report was to decrease the concentration of isoflurane being delivered from 2% to 1.25%. After 15 minutes, however, although neither mean arterial pressure nor heart rate had increased, brisk palpebral and corneal reflexes were evident and the dog had increased limb and jaw tone, indicating a light plane of anesthesia. Consequently, it was determined that the isoflurane concentration could not be decreased any further without the use of adjunctive anesthetic agents.

Agents used for premedication of dogs have also been reported to affect arterial blood pressure, and the dog described in the present report was premedicated with acepromazine and morphine prior to induction of anesthesia. Although opioids such as morphine generally have mild effects on arterial blood pressure in dogs, morphine may increase plasma histamine concentration, potentially resulting in vasodilation and hypotension. Additionally, administration of opioids in combination with acepromazine can decrease arterial blood pressure. Acepromazine is classified as a phenothiazine tranquilizer as well as an α₂-adrenergic antagonist and even when administered systemically at low dosages (eg, 0.025 mg/kg [0.011 mg/lb]) can decrease systemic vascular resistance by causing vasodilation. Although the dose of acepromazine used in the dog described in the present report was only 0.01 mg/kg (0.0045 mg/lb), it is possible that acepromazine was contributing to the hypotension in this dog. Treatment of hypotension caused by α-adrenoceptor antagonists generally requires restoration of circulating volume through administration of isotonic crystalloid or colloid solutions. Both isotonic crystalloid and colloid solutions increase intravascular volume and blood pressure. However, because of osmotic gradients across extracellular membranes, approximately 80% of an isotonic crystalloid solution is filtered into the interstitium within 2 hours, with the result that such solutions have a short-term effect on blood pressure. In contrast, colloid solutions contain high-molecular-weight particles and, thus, maintain intravascular osmotic pressure.

Because the hypotension persisted in the dog described in the present report, the delivered concentration of isoflurane was reduced, a bolus of lactated Ringer’s solution (20 mL/kg [9 mL/lb]), followed by a bolus of 6% hetastarch (10 mL/kg [4.5 mL/lb]), was administered IV over 45 minutes. Nevertheless, the dog’s heart rate did not change and mean arterial pressure increased only slightly, reaching a maximum of 55 mm Hg.

Administration of an anticholinergic drug (eg, atropine sulfate or glycopyrrolate) to increase the heart rate was not warranted in the dog described in the present report because the recorded heart rate was steady and within the range expected for a dog of this size during isoflurane anesthesia. Administration of anticholinergic drugs may result in tachycardia, which can worsen hypotension by decreasing diastolic filling and stroke volume and should typically only be used to treat hypotension in dogs with concurrent bradycardia and decreased cardiac contractility.

Because neither reducing the delivered concentration of isoflurane nor administering fluid therapy had restored arterial blood pressure to the normotensive range in the dog described in the present report, and because isoflurane has been reported to depress myocardial contractility, dobutamine hydrochloride, a sympathomimetic β-adrenoceptor agonist, was administered as a constant rate infusion (2.5 µg/kg/min [1.1 µg/lb/min]) to enhance myocardial contractility. In response, mean arterial pressure increased to 70 mm Hg and heart rate increased to 91 beats/min, allowing the dental procedure to continue. Activation of cardiac β-adrenoceptors by dobutamine increases blood pressure by increasing myocardial contractility, thereby increasing cardiac output.

The procedure continued uneventfully until a small amount of bleeding was seen originating from the pulp canal. The attending dentist dipped a paper point into a dilute solution of epinephrine (1:30,000) and applied it to the pulp cavity in an attempt to vasoconstrict the bleeding vessel. Within 1 minute, the heart rate, which had ranged from 70 and 78 beats/min prior to this time, increased to 155 beats/min and mean arterial pressure decreased to 46 mm Hg.
Question
What caused the abrupt increase in heart rate and decrease in mean arterial pressure in this dog?

Answer
The abrupt increase in heart rate and decrease in mean arterial pressure were most likely a result of systemic absorption of epinephrine resulting in a phenomenon known as “epinephrine reversal.” Epinephrine reversal was first described in 1906 and is defined as conversion of epinephrine’s typicalpressor response to a depressor response in the presence of α-adrenoceptor blockade. On the other hand, stimulation of β1-adrenoceptors causes bronchodilation and peripheral vasodilation. When epinephrine is administered in the absence of other pharmacologic agents, the α- and β1-adrenoceptor agonist effects predominate, enhancing cardiac contractility and heart rate. On the other hand, stimulation of β2-adrenoceptors causes bronchodilation and peripheral vasodilation. When epinephrine is administered in the absence of other pharmacologic agents, the α- and β1-adrenoceptor agonist effects predominate, enhancing cardiac contractility and heart rate. On the other hand, stimulation of β2-adrenoceptors causes bronchodilation and peripheral vasodilation. In this case, the hypotension, therefore, may have resulted, at least in part, in reflex tachycardia lasting longer than epinephrine’s duration of action.

Once epinephrine reversal was identified in the dog described in the present report, the administration rate of lactated Ringer’s solution was increased to 20 mL/kg/h and dobutamine administration was discontinued. The dosage of dobutamine used in this dog was relatively low (2.5 µg/kg/min). However, higher dosages (eg, >10 µg/kg/min) may predispose to tachycardia and cardiac dysrhythmias. Because epinephrine may also cause tachycardia and increases the likelihood of cardiac dysrhythmias by increasing the rate of spontaneous myocardial depolarization, it was thought prudent to discontinue dobutamine administration. Although halogenated anesthetics such as halothane may potentiate the arrhythmogenic effects of epinephrine, newer agents such as isoflurane and sevoflurane are significantly less arrhythmogenic. Therefore, administration of isoflurane was continued. Over the next 60 minutes, the heart rate slowly decreased to 90 beats/min and the mean arterial blood pressure increased to 60 to 65 mm Hg. Although this was longer than the reported duration of epinephrine’s cardiovascular effects when the drug is administered systemically in dogs (<20 minutes), it is possible that prolonged hypotension resulted from withdrawal of inotropic blood pressure support (ie, discontinuation of dobutamine administration) in the continued presence of acepromazine and isoflurane. The hypotension, therefore, may have resulted, at least in part, in reflex tachycardia lasting longer than epinephrine’s duration of action.

Once the dental procedure was completed, the dog was allowed to recover from anesthesia. No complications were reported, and the dog was discharged from the hospital the same day.

Discussion
A common effect of some premedications and inhalant anesthetics is hypotension. This case illustrates the steps used to diagnose and treat hypotension in anesthetized dogs. Most of the methods mentioned (ie, decreasing concentration of the inhalant anesthetic, increasing intravascular volume, and enhancing cardiac contractility through the use of sympathomimetics) can be implemented in private veterinary practices. This case also illustrates that care should be taken when epinephrine is used as a vasoconstricting agent following administration of α-adrenoceptor antagonists because of the possibility of epinephrine reversal.

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