Cardiovascular Function During Anesthesia

The goals for management of anesthetized animals undergoing surgery include providing sufficient central nervous system depression and muscle relaxation to facilitate surgical conditions, while maintaining adequate perfusion of vital organs with oxygenated blood. Cardiac output (CO), the quantity of blood pumped by one side of the heart per minute, is the amount of blood available for perfusion of organs and tissues. Awake horses have an average CO of approximately 70 ml/kg/min, which decreases by approximately 1/3 to 1/2 during inhalation anesthesia, depending on the agent used, the depth of anesthesia, and the mode of ventilation [1,2]. Cardiac output is related to blood pressure according to the formula:

\[ P = F \times R \]

where P is mean arterial blood pressure (MAP), F is flow or CO, and R is systemic vascular resistance (SVR). Because CO measurement is generally too complicated for routine clinical applications, anesthetists generally rely on measurement of arterial blood pressure to assess adequacy of circulatory function.

Mean arterial blood pressure of awake horses is generally in the range of 105 to 135 mm of Hg, but decreases during inhalation anesthesia [1,2]. In most species, a MAP of 60 to 70 mm of Hg is considered to be the minimum pressure that will result in adequate perfusion of vital organs and tissues such as the brain and kidney [3]. An additional consideration for horses (and other large animals such as cattle) is that anesthetic-induced hypotension and hypoperfusion may lead to inadequate perfusion of their large muscle mass, which may be evidenced in the immediate recovery period as post-anesthetic myopathy. Experimentally, post-anesthetic myopathy has been produced by maintaining horses for 3 1/2 hours at a level of halothane anesthesia deep enough to result in MAP between 55 and 65 mm of Hg and CO between 23 and 29 mL/kg/min [4]. Clinically, it has been noted that the greater the degree of hypotension and the longer the duration of anesthesia, the greater is the incidence of post-anesthetic lameness [5]. In severe cases, muscle damage can prevent the horse from being able to stand after anesthesia, and may even necessitate euthanasia [4].

Although anesthetists tend to focus on results of measurement of blood pressure, it is important to recall that change in blood pressure is not always accurately reflecting change in blood flow (CO) or regional tissue perfusion. In fact, during some conditions, MAP maybe negatively correlated with CO [6]. This is because changes in vascular tone also have important effects on blood pressure. For example, horses with endotoxemia sometimes have very low MAP, presumably from vasodilation, yet may maintain reasonably good CO [7]. In contrast, during surgical stimulation [8,9] or administration of an alpha-adrenergic agonist [10] vasoconstriction frequently causes MAP to increase, while CO may decrease.

Both clinical impression and experimental work indicate that horses are more susceptible to anesthetic-induced cardiovascular depression than are dogs. Mean arterial blood pressure of horses at 1.5 MAC halothane (which approximates a surgical plane of anesthesia) is decreased approximately 38% compared to the awake state, while dogs at the same anesthetic depth have only a 19% decrease in MAP.
Cardiac index (CI) of horses at 1.5 MAC halothane may be decreased 64% below the awake value, whereas in dogs CI is decreased 30% [11]. Therefore it is not surprising that the majority of horses (even young, apparently healthy horses) anesthetized with inhalation agents require therapeutic intervention to maintain a MAP considered to be necessary for adequate tissue perfusion. In a retrospective clinical report published in 1988, 55.4% of halothane-anesthetized horses required treatment for hypotension [12]. A cursory survey of equine anesthesia records from the Veterinary Teaching Hospital at Colorado State University for the month of August 1999 revealed that 91% of horses subjected to halothane, isoflurane, or sevoflurane anesthesia for elective surgical procedures were treated for hypotension. It is apparent that appropriate management of anesthetized horses requires the ability to support the cardiovascular system, by use of fluid therapy, inotropes, and/or vasopressors.

**Fluid Therapy**

In general, a fluid administration rate of 10 ml/kg/hr is adequate for routine, elective inhalation anesthesia procedures. Preexisting dehydration or hypovolemia, and/or anesthetic-induced vasodilation, may contribute to intraoperative hypotension and conditions requiring additional fluid administration. For routine fluid therapy during anesthesia, or for replacement of large-volume deficits, use of lactated Ringer's or one of the commercially-produced balanced electrolyte solutions is recommended, in order to maintain relatively normal serum levels of sodium, potassium, calcium, and chloride. Dextrose (5%) in water may occasionally be indicated for treatment of primary water deficits or hypoglycemia, and normal (0.9%) saline may be preferred for animals with hyperkalemia, hyponatremia, or hypochloremia.

Horses administered lactated Ringers solution, 20 ml/kg, IV, before halothane anesthesia, maintained significantly higher MAP and a nonsignificant trend toward higher CO and central venous pressure, compared to control horses that received no IV fluid therapy [13]. However, because of the depression of myocardial contractility induced by inhalation anesthetics, IV fluids alone may not be sufficient to maintain acceptable CO and blood pressure.

Preanesthetic administration of hypertonic (7.5%) saline, 4 ml/kg, IV, resulted in significantly higher MAP and CO compared to control during halothane anesthesia in horses [13]. Hypertonic saline was associated with improved myocardial contractility and stroke volume [13]. However, clinical use of hypertonic saline is generally reserved for emergency treatment of shock, and requires follow-up treatment with balanced isotonic electrolyte solutions or blood products, in order to avoid depleting intracellular fluids by its osmotic effect. For horses that are hypoproteinemic (serum protein < 3 to 3.5 g/dl, or serum albumin < 1 to 1.5 g/dl), plasma oncotic pressure may be insufficient to retain fluid within the vascular space, and pulmonary edema may result from administration of electrolyte solutions. To increase or maintain plasma oncotic pressure and improve vascular volume, colloids such as dextrans or hetastarch, or blood plasma can be used. For horses that are severely anemic (PCV < 20%), whole blood or packed erythrocytes may be required to restore adequate oxygen-carrying capacity.

**Inotropes**

Positive inotropes are drugs that strengthen the force of myocardial contractions. Vasopressors are drugs that stimulate contraction of the muscular tissue of capillaries, arteries, and/or veins, causing vasoconstriction. The drugs listed in this section are positive inotropes, but some also have vasopressor effects. For a given drug, the relative inotropic and vasopressor effects often vary with dose.

**Calcium** - calcium gluconate administered to awake horses at 0.1, 0.2, and 0.4 mg/kg/min resulted in increased CO, stroke index, and contractility, while MAP was unchanged and HR decreased [14]. Both halothane and isoflurane cause significant decreases in serum ionized and total calcium concentrations in horses [15]. In halothane-anesthetized horses, infusion of calcium gluconate (0.1, 0.2, and 0.4 mg/kg/min) resulted in increased MAP, but HR decreased, and contractility and cardiac index did not improve [15]. In isoflurane-anesthetized horses, calcium gluconate increased contractility and cardiac index as well as MAP, and HR remained decreased only until termination of the infusion [15]. Cardiac arrhythmias associated with calcium infusion were not detected [15]. However, arrhythmias accompanying calcium administration are possible occurrences in some clinical circumstances and vigilance is warranted. The authors concluded that for isoflurane-anesthetized horses, calcium gluconate at the lowest dosage (0.1 mg/kg/min) was effective at augmenting cardiac function, but that the highest dosage (0.4 mg/kg/min) would be required for halothane-anesthetized horses [15]. The effective half-life of calcium solutions is very short; therefore, constant infusion is required to achieve sustained effects.
**Dobutamine** - dobutamine is a synthetic catecholamine with direct agonist activity at β-1, β-2, and α-1 adrenergic receptors [16]. The hemodynamic effects of dobutamine infusion at 3 or 5 µg/kg/min in halothane-anesthetized horses include increases in systolic, mean, and diastolic blood pressures, CO, and left ventricular dP/dt (an index of contractility), whereas SVR remained unchanged and HR decreased [17]. Clinically, an infusion rate of approximately 2 (range, 1.5 to 3.2) µg/kg/min in anesthetized horses is generally effective in restoring MAP > 70 mm of Hg [12]. Bradyarrhythmias, such as sinus bradycardia and/or 2nd degree atrioventricular (A-V) block, are potential sequellae of dobutamine therapy, occurring in about 26% of anesthetized horses [12,17]. A recent study, in which halothane-anesthetized horses were given dobutamine at 4 µg/kg/min, suggested that the effective half-life of dobutamine in anesthetized horses may be longer than traditionally assumed, as peak hemodynamic effects were not achieved within 40 minutes of infusion, and effects of a 60-minute infusion persisted more than 30 minutes after it was discontinued [18]. The clinical significance of these findings is unclear, as dobutamine is generally very reliable in the treatment of low CO and low blood pressure in anesthetized horses, and serious side effects are rare. In addition, dobutamine has been shown to be superior to dopamine, dopexamine, phenylephrine, and saline solution in improving MAP, CO, and intramuscular blood flow in anesthetized ponies [10].

**Dopamine** - dopamine is a naturally-occurring catecholamine with direct agonist activity at β-1, α-1, and α-2 adrenergic receptors, as well as at dopaminergic receptors [17]. Dopamine is also reported to have indirect adrenergic activity through release of endogenous norepinephrine [17]. In one study of anesthetized horses, dopamine infusion at 2.5 or 5 µg/kg/min significantly increased CO, but because of decreased SVR, MAP did not change [19]. In another study, although dopamine infusion at 3 µg/kg/min did not alter any hemodynamic values, an infusion at 5 µg/kg/min increased CO and left ventricular dP/dt. Again, because of decreased SVR, there was no significant change in MAP at that dosage [17]. At an infusion rate of 10 µg/kg/min, both CO and MAP significantly increased, with SVR returning (increasing) to baseline values [17]. Increased HR and 2nd degree A-V block occurred in some horses given the 2 higher infusion rates of dopamine [17]. A more recent study reported the occurrence of premature atrial and ventricular contractions, ventricular tachycardia, and ventricular fibrillation in halothane-anesthetized horses administered a one-hour infusion of dopamine at 10 µg/kg/min [20]. Therefore it appears that, in anesthetized horses, dopamine is a less potent inotrope than dobutamine, is less efficacious at increasing MAP, and is more likely to induce serious cardiac dysrhythmias [17].

**Dopexamine** - dopexamine, a structural analogue of dopamine, is reported to be a potent β-2 adrenergic agonist, a weak dopaminergic (DA-1) agonist, an inhibitor of reuptake of norepinephrine at sympathetic nerve terminals, and has no α- and minimal β-1 adrenergic activity [21]. At stepwise infusion rates of 5, 10, and 15 µg/kg/min in halothane-anesthetized horses, HR, cardiac output, and MAP increased, while SVR decreased, in a dose-dependent manner [21]. However, the side effects of dopexamine, which include tachycardia, tachyarrhythmias, profuse sweating, muscle twitching, and a noticeable lightening of anesthesia depth, limit its usefulness in clinical cases [10].

**Ephedrine** - ephedrine is a non-catecholamine sympathomimetic with both direct and indirect actions at α and β adrenergic receptors. In both lightly and deeply halothane-anesthetized horses, ephedrine (0.06 mg/kg) has been shown to increase CO, stroke volume, and arterial blood pressure. These effects were more pronounced, and SVR was decreased, at the deeper plane of anesthesia [22]. Ephedrine has the advantages of being inexpensive and simple to administer; it can be given as an IV bolus, rather than as a continuous infusion as is required with many inotropic drugs. The same dose of ephedrine can be repeated several times, if hypotension persists or recurs a few minutes after the initial dose. Heart rate may increase or decrease slightly, but changes are usually transient and dysrhythmias are rare. Although experimentally ephedrine has been shown to increase cardiac output in anesthetized horses, clinical impression suggests that ephedrine is not as consistently reliable as dobutamine at increasing blood pressure. Ephedrine may increase the requirement for additional anesthetic agent [23].

**Epinephrine** - epinephrine is a potent inotrope, but its clinical usefulness is limited by its arrhythmogenicity. In halothane-anesthetized horses, infusion of epinephrine produces premature ventricular depolarizations and, in some cases, ventricular fibrillation and death [24]. Hypercapnia, which is common in spontaneously-breathing anesthetized horses, may exacerbate the risk of epinephrine-induced ventricular arrhythmias [25]. Epinephrine is not recommended for routine use in anesthetized horses, but remains a component of cardiopulmonary resuscitation in response to cardiac arrest.
**Vasopressors**

The following drugs are used primarily for their vasopressor effects, although they may also affect CO. **Norepinephrine** - norepinephrine is a naturally occurring endogenous neurotransmitter approximately equal (or slightly less) in potency to epinephrine for stimulation of \(\beta-1\) (cardiac) receptors. It is a potent \(\alpha\)-agonist and produces intense arterial and venous vasoconstriction. A continuous infusion of norepinephrine (0.1-0.2 µg/kg/min, IV) is used in horses to provide short term (e.g., 15 - 30 minutes) treatment of refractive hypotension (Steffey, EP, personal communication). Like dobutamine, but unlike phenylephrine the actions of norepinephrine are short-lived; usually subsiding within 2 - 5 minutes of discontinuing IV infusion. A decrease in HR (due to a pressor induced reflex in vagal tone) commonly accompanies use of norepinephrine. Clinical experience suggests cardiac arrhythmias in horses are less frequent with use of norepinephrine compared to epinephrine. Despite infrequent occurrence of life-threatening ventricular arrhythmias with use of norepinephrine, vigilance is necessary.

**Phenylephrine** - phenylephrine is an \(\alpha\)-1 adrenergic agonist which in conscious horses causes vasoconstriction (increased SVR), resulting in an increase in MAP, while cardiac output is decreased [26]. There is minimal published documentation of its effects in anesthetized horses. In a study of 8 halothane-anesthetized ponies, phenylephrine infusion (0.25 to 2 µg/kg/min) not only failed to improve intramuscular blood flow, but was associated with clinical signs of post-anesthetic myopathy in 2 of the ponies.10 The authors suggested that phenylephrine should be reserved only for situations in which hypotension is refractory to other medications, and not used for routine treatment of halothane-induced hypotension in horses [10]. The use of phenylephrine might be considered an appropriate adjunct to treatment of hypotension associated with large doses of acepromazine, with endotoxemia, or other situations in which vasodilation is profound. Clinical experience suggests that a phenylephrine bolus of 0.002 mg/kg, IV, may be effective at increasing MAP. This dosage may be repeated if needed, or a constant rate infusion can be administered for prolonged effect. Heart rate should also be monitored carefully, since phenylephrine can contribute to bradycardia [26].

**Anticholinergics**

Because blood pressure is directly related to CO, and CO is directly related to HR, prevention of bradycardia by administration of anticholinergics appears to be a logical approach to alleviating intraoperative hypotension. However, if bradycardia in horses is arbitrarily defined as HR < 25 beats/min, only a small minority of anesthetized horses are actually bradycardic. Anesthetic-induced hypotension is more rationally and effectively treated by use of drugs that improve contractility, such as dobutamine or ephedrine. In addition, administration of anticholinergics to horses has been shown to depress gastrointestinal motility and increase the risk of abdominal discomfort or colic [27,28]. For these reasons, it is recommended that the use of anticholinergics be limited to horses that are truly bradycardic as well as hypotensive, that only low dosages be used, and only in horses without predisposition to gastrointestinal problems. **Atropine** - as mentioned previously, atropine is not routinely administered to horses because of concerns about possible detrimental effects on gastrointestinal motility. Clinical signs of abdominal discomfort have been observed following atropine dosages of 0.044 and 0.176 mg/kg, IV, in ponies [27]. However, a smaller dose of atropine (0.006 mg/kg, IV) given at anesthesia induction, 1 hour after detomidine administration, reversed detomidine-induced bradycardia and was associated with higher MAP and reduced need for inotropic support during halothane anesthesia [29]. At that dose of atropine, none of the horses developed cardiac dysrhythmias or signs of colic [29]. Clinical experience suggests that even smaller doses of atropine (0.002 to 0.004 mg/kg, IV) are often effective at correcting intraoperative bradycardia or bradyarrhythmias associated with \(\alpha\)-2 agonists and/or dobutamine administration. However, atropine has been shown to reduce the arrhythmogenic dose of dobutamine in halothane-anesthetized horses [30]. Therefore, if atropine is used to treat intraoperative bradycardia, it is recommended that dobutamine or other inotrope infusions be terminated a few minutes before atropine is given.

**Glycopyrrolate** - in awake horses, glycopyrrolate, 0.005 mg/kg, IV, increased HR but caused some depression in gastrointestinal motility; a dosage of 0.01 mg/kg produced signs of colic [28]. When glycopyrrolate, 0.0025 mg/kg, IV, was used as a premedication for xylazine and ketamine anesthesia, HR, CO, and blood pressure increased for approximately 30 minutes, but gastrointestinal motility was reduced for up to 9 hr, and one horse showed mild signs of colic [31]. In halothane-anesthetized horses, glycopyrrolate at 0.0025 to 0.005 mg/kg, IV, resulted in increased HR and improved blood pressure [32]. One horse out of 17 in the latter study did
develop clinical signs of colic, although it was not clear that glycopyrrolate was a contributing cause [32]. Therefore glycopyrrolate, like atropine, should be used with caution in horses.

References

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