 MANAGEMENT OF INTRA-OPERATIVE HYPOTENSION  
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**Key Points**
- Intra-operative hypotension is common even in healthy patients
- Significant hypotension can lead to increases in anesthetic-related morbidity and mortality
- Treatment of hypotension is directed towards the underlying cause, which can be disease related or due to anesthetic drugs and/or inadequate fluid therapy
- Use of inotropes and vasopressors are reserved for refractory hypotension

**Why treat hypotension?**
Mean arterial pressure (MAP) is the driving force for blood flow (perfusion) through capillaries that supply oxygen to organs and tissue beds of the body. Thus, when speaking of hypotension it is most important to focus on the MAP. In small animals, MAP < 60 mm of Hg results in compromised perfusion of visceral organs and peripheral tissues, potentially leading to whole organ or regional ischemia. In large animals perfusion of skeletal muscle (especially skeletal muscle in recumbent areas of the body) is compromised at MAP < 70 mm of Hg. In all species, MAP < 40 mm of Hg is associated with inadequate perfusion of vessel-rich organs such as the heart, lungs, and CNS. Clinically significant hypotension (i.e. MAP less than 60 mm of Hg) can lead to renal failure, reduced hepatic metabolism of drugs, worsening of ventilation/perfusion mismatch and hypoxemia, delayed recovery from anesthesia, neuromuscular complications during recovery (especially large animals), and CNS abnormalities including blindness after anesthesia that may or may not resolve with time. Pre-existing compromised organ function, particularly of the kidney or liver, makes the patient more susceptible to organ failure due to hypotension. Prolonged and severe hypotension can lead to cardiac and respiratory arrest.

**Estimation of MAP**
Mean arterial pressure = diastolic pressure + 1/3(systolic pressure - diastolic pressure). Most indirect blood pressure monitors provide data for systolic pressure (e.g. doppler method) or systolic, diastolic, and mean arterial pressure (e.g. oscillometric devices). Roughly, the mean arterial pressure is 20 - 30 mm of Hg less than the measured systolic pressure on a doppler in most species. Thus, a doppler reading of 80 to 90 mm of Hg correlates with a mean arterial pressure that would be considered hypotensive. The exception to this rule is cats < 4 - 5 kg (and likely other small mammals) in which the doppler reading correlates approximately half way between the systolic and mean arterial pressure. Direct measurement of blood pressure via arterial catheterization and a transducer is the most accurate method, but requires technical skill and poses some risks (infection, hemorrhage from the catheter, inadvertent arterial drug administration).

**What determines blood pressure?**
Mean arterial pressure = cardiac output x systemic vascular resistance. In thinking about causes of hypotension, it is useful to break this equation down into its various components and then assess the effects of anesthetic drugs or the animal’s physiologic state on each component.
Cardiac output = heart rate x stroke volume. For example, a drug that reduces contractility (e.g. isoflurane) will lower stroke volume and can then contribute to a lower cardiac output, which may result in low mean arterial pressure if systemic vascular resistance has not increased. As a general rule of thumb, cardiac output decreases to ~ 50% of awake values in healthy animals at surgical planes of inhalant anesthesia. This decrease in cardiac output is due to decreases in contractility and decreases in systemic vascular resistance.

Systemic Vascular Resistance:
A reduction in systemic vascular resistance (SVR) will decrease mean arterial pressure. Many of the drugs commonly used for anesthesia will reduce systemic vascular resistance. These drugs include: acepromazine, propofol, and, importantly, all inhalants. All of these drugs decrease systemic vascular resistance in a dose-dependent fashion. Preexisting physiologic factors such as dehydration/hypovolemia from any cause, or events that may occur as a result of surgical intervention (e.g. blood loss), will also decrease SVR. When possible, preexisting causes of reduced SVR should be corrected prior to general anesthesia. Examples include: hemorrhage, inadequate volume administration or replacement, dehydration, endotoxemic shock, overwhelming sepsis, cardiogenic shock, neurogenic shock, anaphylaxis, histamine release, severe hypercapnia, significant hyperthermia.

Heart Rate:
A reduction in heart rate may or may not affect mean arterial pressure. If heart rate is low in the face of good contractility, then often the increase in end-diastolic ventricular volume (and associated increase in ejected stroke volume) will help to maintain cardiac output and Map may be normal. If contractility is poor, as is often the case in patients receiving inhalant anesthetics or in patients with underlying cardiac disease, then stroke volume may not increase in response to a longer diastolic filling time and MAP will be reduced. The following is a list of drugs or pre-existing conditions that may reduce heart rate: physiologic (athletic) bradycardia, hypothermia, increased vagal tone, high cervical cord compression, intracranial disease, electrolyte imbalances, opioids, alpha-2 agonists, acetylcholinesterase inhibitors, anticholinesterases (transient, paradoxical; increase in heart rate usually follows; e.g. glycopyrrolate).

Preload:
Factors that reduce preload (end diastolic ventricular volume) and thus indirectly reduce stroke volume include: reduction in venous blood volume from blood loss, dehydration, inadequate fluid replacement, vasodilation, relative hypovolemia from peripheral vascular pooling (e.g. inhalant anesthesia), physical occlusion of venous return (e.g. GDV). A common cause of reduced preload in anesthetized animals is positive pressure ventilation. During the inspiratory phase of positive pressure ventilation, peak airway pressure is reflected as peak intrathoracic pressure which may be high enough to transiently compress the cranial and caudal vena cavae as they enter the thorax. This results in reduced right atrial and ventricular filling during inspiration and will lead to lower stroke volume on the subsequent ventricular systole.

Contractility:
Reduced contractility is one of the most common causes of hypotension in anesthetized patients. This is because the inhalants are potent negative inotropes, yet are a necessary (almost always) component of general anesthesia. Physiologic factors that reduce contractility should be
corrected, if possible, prior to administration of anesthetic drugs. The following is a list of peri-anesthetic factors that impair contractility: inhalants (isoflurane=sevoflurane>desflurane), propofol, alpha-2 agonists, intrinsic cardiac disease (e.g. dilated cardiomyopathy), pericardial disease, severe sepsis or endotoxemia, electrolyte imbalances, severe acidemia, beta blocking drugs (e.g. propranolol, esmolol), profound hypothermia. Drug related reductions in contractility are dose-dependent. Among the commonly administered anesthetic drugs, inhalants probably have the most profound effect on contractility, with reductions of up to 50% at surgical planes of anesthesia.

In summary, the major players in hypotension are reductions in SVR, heart rate, stroke volume, and contractility. Thus, when developing treatment approaches for hypotension one should consider these 4 major players and rule in/out factors that affect them in the anesthetized animal.

Treatment of Hypotension

Low systemic vascular resistance (SVR):
Almost by definition an animal anesthetized with inhalants will have reduced SVR. Premedication with acepromazine further reduces SVR. One approach is to “fill the space” with aggressive administration of IV crystalloids. Before doing this, however, one must assess the animal’s anesthetic depth, since reducing the administered dose of inhalant will help to increase SVR. In inhalant-anesthetized patients with normal cardiac and renal function a standard crystalloid administration rate before hypotension develops is 5 - 20 ml/kg/hour. This allows for filling of the increased vascular volume caused by inhalant-mediated vasodilation. If further increases in vascular volume are deemed necessary, and the patient has normal cardiac and renal function, one can increase the crystalloid rate to 50 - 70 ml/kg/hr (cats) and 70 - 90 ml/kg/hr (dogs) for 15 minutes and then assess the response to treatment. In other words, run a shock dose of crystalloids for 15 minutes so that the animal receives ¼ of an hour’s worth of shock fluids. This can safely be done 2-3 times unless the animal is at risk for pulmonary edema (e.g. mitral valve insufficiency) or is anemic or hypoproteinemic (dilutional effect). If mean arterial pressure has not increased at this point then one should return to the algorithm. When administering aggressive fluid therapy, it is advisable to monitor PCV/TP, electrolyte status, acid-base balance, and auscult lung sounds in order to recognize and prevent pulmonary edema.

Crystalloid administration alone may be insufficient to increase SVR, partly because crystalloids remain in the vascular space for only ~ 20 minutes. Low oncotic pressure (e.g. hypoalbuminemia) or blood loss may also make a positive response to crystalloid administration less likely. Oncotic agents, i.e. colloids, will help to maintain vascular volume by reducing leakage of water into the interstitial spaces. Oncotic agents commonly used include fresh whole blood, plasma, and synthetic starches. Starches are practical and less expensive than plasma or fresh whole blood. They should not, with rare exceptions, be used exclusively for volume replacement, but rather as an adjunct to crystalloids to enhance total blood volume. A good place to start with colloid administration is to give a bolus of starch (5 ml/kg) over 15 minutes and assess the change in blood pressure. Vetstarch can be infused to a total volume of 50 ml/kg/day. Some clinicians are more cautious with hetastarch and recommend a maximum of 20 ml/kg/day. Caution should be exercised in animals with myocardial or valvular disease and those with coagulopathies (dilutional and direct effect on the coagulation cascade).
It is rarely necessary to increase SVR with drugs. Usually, in hypotensive patients that do not respond to fluid therapy, the cause can be found in stroke volume or, less often, heart rate. Some anesthesiologists recommend phenylephrine at 0.001 – 0.01 mg/kg IV as a slow bolus. Phenylephrine directly activates alpha-1 receptors to cause vasoconstriction. Profound bradycardia may result as a reflex to the sudden increase in vascular tone, not unlike what can be seen with the alpha-2 agonist dexmedetomidine. A caution regarding the use of pressor drugs to increase blood pressure is that you may get better numbers on your monitor, but the vasoconstricting effects of these drugs may be profound enough to compromise organ blood flow. Fluid therapy should always be your first line of defense in increasing SVR!

Bradycardia:
Bradycardia can be friend or foe when dealing with hypotension. On the one hand, a slow heart rate allows for generous right atrial and ventricular filling, which in turn provides optimal diastolic filling and stroke volume on the subsequent systole. Since coronary blood flow and myocardial oxygenation occur during diastole, bradycardia and a long diastolic period help to optimize myocardial oxygen delivery. However, if bradycardia is coupled with less than optimal contractility (either from anesthetic drugs or disease) it is sometimes necessary to increase the heart rate in order to treat hypotension.

Bradycardia is common in anesthetized patients, especially when systemic opioids are used concurrently for analgesia. The first approach to treating bradycardia is to reduce the inhalant, if possible. One can also consider reversal of systemic opioids with naloxone or butorphanol. Since opioids were likely given to provide analgesia, however, reversal may not be desirable for patient comfort and recovery. One should also ensure that the patient is normothermic, as bradycardia 2o to hypothermia will not respond to pharmacologic intervention. Finally, one should address electrolyte or acid-base abnormalities that may be contributing to bradycardia. If bradycardia is secondary to prior administration of alpha-2 agonist drugs (e.g. dexmedetomidine) then one should not attempt to increase the heart rate pharmacologically, but rather consider reversal with atipamezole. This is because alpha-2 agonists increase afterload and the bradycardia is a physiologic response to the increase in afterload. Falsely raising the heart rate with alpha-2 agonists “on board” will dramatically increase myocardial work.

Anticholinergics such as atropine or glycopyrrolate will increase heart rate in most species. Atropine is more potent than glycopyrrolate, and as such is more likely to cause undesirable tachycardia. For this reason, atropine is more often used for life-threatening bradycardia. Both drugs can be given IV or IM. The dose for atropine is 0.02 - 0.04 mg/kg; glycopyrrolate is 0.005 - 0.01 mg/kg. Paradoxic bradycardia and AV block are occasionally seen soon after drug administration, especially with glycopyrrolate. This effect is usually overridden as the plasma concentration of glycopyrrolate reaches therapeutic levels. Administration of anticholinergics can result in tachycardia. Severe tachycardia may worsen hypotension, since diastolic filling and stroke volume are compromised. However, if tachycardia develops after anticholinergic administration it usually resolves within 10 - 20 minutes. Other side effects of anticholinergic administration include ileus (especially in large animals), decreased salivation (which may or may not be desirable in a given patient), mydriasis, bronchodilation, and reduced mucociliary transport in the trachea.
Reduced Preload:

Reduced preload should be addressed first by eliminating factors that might mechanically cause it, such as positive pressure ventilation at high airway pressures, abdominal distension, etc. If positive pressure ventilation is causing reduced preload, this can often be seen by watching the arterial pressure wave or pulse oximeter wave a beat or two after the ventilator fired. Diminished pulse size indicates that peak airway pressure on the ventilator should be decreased, and normocapnia achieved by increasing the respiratory rate with a lower tidal volume. Preload can be increased by following the same steps that were recommended for increasing SVR.

Contractility:

If poor contractility is suspected, one should first address, if possible, physiologic and pathologic causes as discussed above. For example, if the animal is severely acidemic that should be corrected prior to other manipulations to increase contractility. As mentioned previously, inhalants are the most common causes of poor contractility in anesthetized animals. Thus, a logical approach to improving contractility is to reduce or eliminate the inhalant. However, eliminating the inhalant entirely is rarely feasible. One option is to reduce the required inhalant dose by supplementing with systemic opioids. For example, a patient anesthetized with isoflurane or sevoflurane can be given intermittent boluses of IV opioids such as oxymorphone or hydromorphone in order to reduce the delivered inhalant concentration while maintaining surgical anesthetic depth. Recommended doses for oxymorphone are 0.025 - 0.1 mg/kg; for hydromorphone 0.05 - 0.2 mg/kg; either drug can be given in this dosage range as needed to reduce the inhalant and thereby improve contractility. A “fine tuned” alternative is to deliver constant rate infusions of other analgesics, such as fentanyl (2.5 - 20 mcg/kg/hour [note units]), lidocaine (25-50 mcg/kg/min) or ketamine (2 – 10 mcg/kg/min). This can be accomplished using a syringe pump or buretrol. Constant rate infusions allow one to titrate the drug up or down to maintain adequate depth. With fentanyl doses of 10-20 mcg/kg/hour, especially in sick patients, anesthetic inhalant requirement maybe reduced by 100%. In other words, the MAC of isoflurane in a patient receiving fentanyl can be as low as 0.5%.

Inotropes such as dopamine and dobutamine can be given to increase contractility. However, these drugs should not be used without attention to ensuring adequate vascular volume as well. Additionally, before administration of an inotrope, one should seek to minimize inhalant doses as described above. Dopamine and dobutamine stimulate beta-1 receptors in the myocardium, thus enhancing myofilament shortening and ventricular contractility. These drugs are given as infusions, at a dose range of 1 - 10 mcg/kg/min. Individual animal sensitivity varies greatly, so one should always start with the lowest recommended dose. The half life of these drugs is short (3 - 5 minutes) so their effect is short-lived once the infusion is discontinued. Do not bolus these drugs!

Dobutamine is a synthetic catecholamine, while dopamine is a precursor to epinephrine and norepinephrine. As such, these drugs exert effects similar to endogenous catecholamines. The most common side effect noticed in anesthetized animals are tachycardia (especially with dopamine) and occasionally atrial and ventricular arrhythmias. Because the half-life of these drugs is short, termination of the infusion or reduction of the dose usually resolves these complications.
When all else fails!:

Vasopressin, or ADH, is a potent, short-acting vasoconstrictor that works via the ADH-renin-angiotensin cascade. Its effects are dramatic and immediate. Due to a short half-life, vasopressin should be administered as a constant rate infusion, starting at the low end of the dose range. Profound reflex bradycardia may be immediately apparent. Recommended doses in dogs and cats are 0.1 – 0.4 mU/kg/min IV.

Preventing Hypotension

Plan ahead! Assess the patient’s risk for hypotension prior to anesthesia. Ensure adequate volume status, correct underlying acid-base and electrolyte abnormalities, correct underlying pathologic states if possible, use the lowest possible dose required of acepromazine or alpha-2 agonists, or eliminate them altogether, premedicate with agonist opioids for preemptive analgesia and reduction of inhalant requirement, reduce induction drug requirements with IV benzodiazepines and opioids immediately prior to induction, consider supplemental opioids during anesthetic maintenance, as needed, look for alternative methods to provide analgesia and inhalant reduction for surgery, such as epidurals, local blocks etc., give IV crystalloids to all patients receiving inhalant anesthetics. Finally, monitor blood pressure! The best way to prevent hypotension is to detect reductions in blood pressure as soon as they occur!