Small Animal Anesthesia: Doing Things Right

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Anesthetic induction techniques in veterinary medicine are one area we continue to fall short. While larger mammalian patients tend to suffer less by the induction box or forced masking techniques, with pre-medication and easier IV access for injectable forms of induction agents, we continue to practice outdated and unsupported methods of anesthesia induction for our rodent and other small animal patients.

Isoflurane is the predominate gas anesthetic used in the veterinary clinic setting. Isoflurane has a lower blood solubility compared to halothane, but greater solubility compared to sevoflurane. While the definite mechanism of actions is still not fully understood, we do suspect isoflurane binds tightly to GABA centers and inhibits NMDA subtypes. Regardless of the type of gas anesthetics we are using, halogenated anesthetics are going to be one of our most cardio-respiratory depressive agents. To alleviate these depressive effects, we strive to use mean alveolar concentration (MAC) sparing drugs in combination or to fully replace gas anesthetics. MAC is understood as the minimum alveolar concentration of the gas anesthetic in the alveoli to keep a majority of a species population at a surgical plane of anesthesia. Isoflurane, along with its close relatives halothane and sevoflurane, have some pretty significant side effects especially at higher concentrations (>2% on the vaporizer), or with repeated chronic use.

Post-operative cognitive (long-term cognitive impairment) and muscle dysfunction are two common side effects described in the literature for both humans and animals. This is a disorder this is temporary but can last hours to weeks depending on the health status of the patient, including age and the duration of use. It is characterized in animals as a general depression or blunted natural behaviors. In studies evaluating post isoflurane exposure, animal models have failed previously taught behaviors, had significantly slower responses, or poorer scores. General weakness is described in humans with post-operative muscle dysfunction and is suspected to be the same in animals.

Isoflurane has been shown to be genotoxic in rats, but not mutagenic in male wild-type flies at lower levels, (<2%). This is damage to DNA structure, usually temporary, but may have lasting effects not currently understood. In healthy animals this damage is typically auto-repaired. Damage to DNA integrity can represent a critical variable in studies using transgenic mice or gene therapy directed goals. Along with some genotoxic effects, researchers have appreciated isoflurane triggered neurodegeneration in the developing mouse pup brain with repeated exposure of concentrations >1% on the vaporizer for certain periods of time.

Anesthetic inhalants can also cause persistent nausea in several animal species, along with ileus. Ileus is a concern in every species when exposed to anesthetic inhalants, most prominently rabbits.

Finally, we must consider the ethical and animal welfare concerns when utilizing anesthetic gas induction. Stress hormone surges, such has cortisol, are well described in the literature for gas induction. High levels of cortisol are immunosuppressive and can delay wound or surgical site healing,

not to mention the changes in behavior or social status in groupings of animals. Continued efforts in reducing stress hormone release fail to find non-pharmacologic means.

We must also consider human safety and exposure to waste anesthetic gas (WAG). Chronic exposure to WAG is well described in human literature. While most gases have a certain odor additive, staff can become desensitized to it and risk further health issues, especially for pregnant females. The cost for large animal models and using higher concentrations of gas and oxygen is relevant from an economic point of view and should also be factored in when considered best practices.

Ehrenwerth and Eisenkraft give the formula: 3 x Fresh gas flow (FGF) (L/min) x volume % = mL liquid used per hour

Behaviors such as circling, pacing, digging and jumping have also been described with inhalant anesthesia induction. This is likely due to the strong odor of isoflurane and its irritating effects to the airway and eyes. These signs illustrate a state of distress to the animal. This distress is similar to that in the ongoing debate over concerns with euthanizing with carbon dioxide.

Solutions to these concerns are varied. With the medications available to us today we have options to do either completely injectable protocols that can offer sedation times from 10-30 minutes with a single injection, or total intravenous anesthesia (TIVA) techniques for animals that have IV access. We also have mixed protocols which would eliminate gas induction altogether and minimize vaporizer percentages having the injectable induction agent(s) on board. Any of the anesthetic options we have available will need to be chosen based on the aim of the study, variables to which the agents can contribute, and the level of invasiveness or pain expected from the procedure. The other benefit of injectable anesthesia protocols is the ability for some of the agents to be fully reversible (dexmedetomidine) or are short acting, such as fentanyl, remifentanil or sufentanil. Many of the combinations with injectable anesthetics are likely to contain one that provides analgesia during and after the procedure, addressing welfare concerns.

Anesthetic Agent	Dose	Effects	Reversible	Analgesic
Dexmedetomidine	0.25-15mcg/kg IV, IM, SQ, TM	Moderate to profound sedation, dose dependent	Yes	Yes
Alfaxalone	1-30mg/kg IV, IM	Moderate to profound sedation, dose dependent	No	No
Ketamine	1-35mg/kg IV, IM, SQ, TM	Moderate sedation when used alone	No	Yes
Telazol	mg/kg	Moderate to profound sedation, dose dependent	Partially	Yes
Midazolam	0.1-0.5mg/kg IV, IM, TM	Slight sedation when used alone	Yes	No

Fentanyl (F), Remifentanil (R), Sufentanil (S, Alfentanil (A)	F = 5-25mcg/kg IV R= S= 1-7.5mcg/kg IV A= 2-15mcg/kg IV	Moderate to profound sedation, dose dependent	Yes, fast acting	Yes
Butorphanol		Slight to moderate sedation when used alone	Yes	Yes, limited to 30-40 minutes in mammals
Buprenorphine	Mammals 0.015-0.05mg/kg IM, SQ, IV, TM	Slight to moderate sedation when used alone	Partially	Yes

Appropriate blood pressure is vital for sustaining healthy cardiovascular, cerebral and internal organ systems. Without healthy blood pressure these systems can suffer, leading to chronic disease processes and death. In veterinary medicine monitoring blood pressure is still relatively new when compared to the human medical field and refining the best techniques in accurate measurement and treatment is under constant research. Nearly every species we deal with has physiologic differences and tolerances when it comes to their blood pressure and how effective various modalities work in each species. The following is a very broad overview of common medications used to treat abnormal blood pressure under anesthesia, with a focus on hypotensive correction.

Treating hypertension or hypotension (MAP <60mmHg for many species) while under anesthesia should never first start with pharmacological agents unless the patient has a pre-diagnosed cardiovascular condition. Treatment for either hyper or hypotension should first start with a carful patient assessment. These are some questions that should run through your head before moving to pharmaceutical intervention. Is the patient too light or painful? Is the gas inhalant or total IV anesthesia rate too high? Is the fluid therapy adequate? Are my monitoring devices (i.e. Doppler or mechanical blood pressure monitors) appropriately placed and do the numbers appear to match with how the animal looks clinically? Does my patient have an underlying cardiac issue? Does my patient have an arrhythmia?

Atropine- Although not typically considered a blood pressure medication, atropine plays an important role in treating certain arrhythmias under anesthesia. Neonates and immature animals are more reliant on heart rate for appropriate cardiac output and thus blood pressure. While atropine has fallen out of favor in the pre-medication plan it is a drug that warrants shelf space in all operating rooms.

Ephedrine- Ephedrine is a safe, yet somewhat expensive option in the first line of pharmaceutical intervention of hypotension. Ephedrine increases cardiac output, heart rate, blood pressure, coronary blood flow, and myocardial oxygen consumption. It reduces the need and time for CRIs of other vasopressors and inotropes with its longer duration of action. Ephedrine is used in human medicine second to phenylephrine for hypotension during pregnancy and fetal surgery. One study found that in dogs a bolus only lasted 5 minutes, and the increases of cardiac output and increased BP were merely transient. Ephedrine also causes stimulation of the respiratory centers and bronchodilation.

Dopamine- This is a highly dose dependent drug. For effective increases in MAP in dogs and cats

research suggests rates starting at 7µg/kg/min to increase the A1-adrenergic agonist effects, taking the lead. The effect will increase systemic and pulmonary vascular resistance, venous return, and possibly PVCs due to splenic contraction. Tachycardia can occur at higher dose rates. When using dopamine, it is recommended to decrease the CRI in a stepwise manner. The receptor effects of dopamine are dose dependent. Dopamine stimulates the release of endogenous norepinephrine from presynaptic storage sites at adrenergic receptors, causing an endogenous sympathomimetic effect. There is some debate on the use of dopamine in felines as they lack the typical distribution of dopamine receptors found in canines.

Dobutamine- Dobutamine is another commonplace inotrope used to treat hypotension related to poor cardiac output. Current thought regarding the medication for treatment of hypotension during inhalation anesthesia is that it lacks good predictable effects, especially in cats. Higher doses ~10mcg/kg/min were needed to produce vascular resistance in dogs and an increase in cardiac output but caused vasodilation in cats. In both studies minimal to no increase in blood pressure was noted.

Phenylephrine- Phenylephrine is a direct-acting sympathomimetic amine with strong Alpha1-adrenergic receptor agonist effects. It is used intravenously during anesthesia to increase systemic vascular resistance therefore increasing blood pressure. Phenylephrine is the first line medication for hypotension during fetal surgery.

Norepinephrine- This medication has largely B-adrenergic receptor mediated effects. At sufficient doses we see an increase in cardiac output, increased SYS, DIA and MAP, along with systemic and pulmonary vascular resistance. Coronary arterial flow is also increased via vasodilation. Tachycardia is less pronounced compared to epinephrine.

Epinephrine 0.01–1 µg/kg/min
Norepinephrine 0.01–0.2 µg/kg/min
Dobutamine 1–20 µg/kg/min
Phenylephrine 0.2–2 µg/kg/min
Dopamine 1–10 µg/kg/min, >10 µg/kg/min Primarily α effects
Ephedrine 0.05–0.5 mg/kg

Airway management:

Traditional endotracheal intubation uses a sterile or thoroughly disinfected endotracheal tube for each patient to prevent the spread of infectious disease. The endotracheal tube should be lubricated with a very thin layer of sterile xylocaine or K-Y jelly. The author also uses an extremely thin layer of sterile non-water-based eye lubricant to avoid the drying out of the lubricant and subsequent traumatizing removal of soft tissue during longer procedures. The is also a commercially available spray for ETTs called SILKOSPRAY by Rusch. Operators should avoid using a lubricant containing benzocaine, as this can lead to a dose-dependent methemoglobinemia (MetHb), which does not bind oxygen; most hospitals are unable to test for MetHb in clinic.

Intubation may stimulate the vagus nerve, increasing parasympathetic tone especially in dogs. This may result in bradycardia, hypotension and cardiac dysrhythmias. If the animal has an underlying cardiovascular disease, cardiac arrest may occur. Atropine or glycopyrrolate can be given as part of the premedication. This is also a consideration when eye surgery is going to be performed or repeated

movement of the head/throat region, to prevent the parasympathetic stimulation.

Operators should not be forceful in the intubation technique as this can damage the larynx, pharynx, or soft palate and lead to tissue edema. Ideally, the tip of the endotracheal tube should be past the larynx and not beyond the thoracic inlet. If the tube is advanced too far, it may enter one bronchus, resulting in ventilation to only one lung. Premeasure the length of the endotracheal tube and the distance between the nose and the thoracic inlet prior to anesthesia. A general rule of thumb is once the cuff of the ETT has passed the arytenoids advance about a centimeter more, then stop. The end of the tube should be at the level of the animal's incisors to eliminate dead space and respiratory resistance.

Laryngeal Mask Airways (LMAs) for the veterinary patient were introduced by Docsinnovent with the v-gel™ for rabbits and felines (soon to have a canine and equine model), which is a modified tube that only covers the supraglottic region. Although ET intubation is the author's preferred method, v-gel™ offers a quick and easy approach when ET intubation proves too difficult. They are not ideal for animals requiring oral surgery as they take up a decent amount of space in the mouth, and there is potential for fluid leakage around the tube if undergoing a dental procedure. The other limiting factor is they require capnography to ensure proper placement. The tubes themselves have a built-in port for sidestream capnography, but also support mainstream capnography with an adaptor that will add to the total dead space. Older sidestream machines may not be ideal for small patients as some machines require taking 50-200 ml/min of the ventilated gasses for sampling.

In the event an animal cannot be intubated, the forced mask ventilation technique may need to be utilized. This technique consists of fitting a patient with a mask that covers the nose and mouth with as few leaks as possible. The head should be placed so that the trachea is fully extended and as straight as possible to allow easier movement of air. There are various pre-manufactured masks, but at times it is necessary to create a homemade mask out of syringe cases, small bottles, or tubing. Taking advantage of the patient's bottom incisors case be useful for masks made from syringe cases. The technique involves using a larger suture or small sized string tied/looped around the top incisors or canines and pulled through the mask. Letting the string hang out the end and pulling taut as the non-rebreathing circuit is connected will ensure a sealed mask. Careful attention should be paid to not create ocular trauma with careful positioning and plenty of eye lubricant. If the forced mask ventilation technique is used, it is important to remember to protect the animal's eyes. Too often a mask is left putting pressure or digging into the inferior eye socket. This technique can also lead to gas in the stomach that may need to be treated postoperatively by tubing or carefully expressing the air out.

If direct visualization of the glottis or a portion of it is not possible, Jane E. Ouandt, DVM., M.S., DACVA describes the following techniques: in the case of a pharyngeal or an oral mass, one method to use is retrograde intubation. A hypodermic needle is passed through the ventral aspect into the skin of the neck and into the trachea at the junction of the second and third tracheal rings. A guide wire, or canine urinary catheter that will pass easily through the needle, is maneuvered through the needle cranially into the larynx, pharynx and oral cavity. It is then used as a guide for the passage of the endotracheal tube. After the tip of the tube is within the larynx, the needle and guide wire can be removed. The endotracheal tube is then advanced into the final position. Subcutaneous emphysema and pneumothorax are possible complications with this technique.

In an emergency situation a tracheostomy can be performed. Indications for a tracheostomy include relieving an upper respiratory tract obstruction, facilitate removal of respiratory secretions, decrease

dead space, provide a route for inhalant anesthesia when oral or facial surgery is complex, reduce resistance to respiration, when you are unable to orally intubate, reduce the risk of closed glottis pressure, or cough, following pulmonary or cranial surgery.

To perform a tracheostomy, make a midline skin incision on the ventral neck equidistant from the larynx and the manubrium. Part the two sternohyoid muscles on the midline and continue blunt dissection down to the tracheal rings. Make an incision transversely between the rings; keep the incision small, only big enough for the tracheostomy tube. Alternatively, make a longitudinal incision to include two or three tracheal rings. Don't place the incision too close to the first tracheal ring, or it could potentially damage the cricoid cartilage and lead to subglottic laryngeal stenosis. Place stay sutures around the tracheal ring adjacent to the incision on either side of the surgical opening. The sutures will aid in placement of the tube and are left in, labeled cranial and caudal, to help when the tube is routinely replaced or cleaned, or if it gets dislodged.

The tube ideally is two-thirds to three-fourths of the tracheal diameter. If a specifically designed tracheostomy tube is not available, an endotracheal tube can be used but may need to be cut so it is short enough that it does not go into one bronchus. Fasten the tube in place by tying it around the neck with umbilical tape or gauze. The soft tissue is loosely closed with sutures and the skin is closed with non-absorbable sutures. It is important to allow any air escaping around the tube to vent to the outside and not accumulate under the skin.

External pharyngotomy is a type of intubation that can be performed for oropharyngeal surgery or orthopedic procedures of the mandible or maxilla. This type of intubation aids in the visualization of the area and allows for normal dental occlusion so that proper reduction of jaw fractures can be achieved. Initially place the endotracheal tube orally. Make a skin incision near the angle of the mandible. Pass hemostats bluntly through the incision into the caudal part of the pharynx. Remove the endotracheal tube adapter, grasp the tube, and pull it through from the pharynx through the subcutaneous tissue and skin incision. Replace the adapter and connect the tube to the breathing circuit. Secure with tape and suture. Extubation is done with the cuff deflated and the tube pulled through the skin incision.

Jet insufflation is a technique similar to the retrograde intubation, except a small oxygen tube is connected to the needle or catheter tip and the air is forcefully pushed into the lungs. It is imperative that the air can escape, otherwise lung injury can result.

Drug	*Drug Class*	*Dose*	*Time to Effects*	*Effects on BP*	*Effects on HR*	*Efficacy in Species*	*Fetal Safety*	*Mechanism of action*	*Notes*
Dopamine ($0.70 per ml)	Adrenergic /Dopaminergic inotrope	10-12 mcg/kg/min (Alpha effects)	2-5 minutes, last 5-10 minutes post cessation	++	+++	C, F, NHP, O, S, B	Most likely safe, but use with caution	Precursor to norepi and indirectly releases norepi causing	2-10 mcg/kg/min, organ and GFR are increased sans

								vasoconstriction	vascular resistance
Dobutamine ($0.40 per ml)	Beta adrenergic inotrope	1-20 mcg/kg/min	2-5 minutes, Peaks at 10 minutes lasts 5-10 minutes post cessation	++ Dose dependent	++ Dose dependent	C, F, NHP, O, S, B, R(High dose)	Most likely safe	Increase myocardial contractility (can increase cardiac O2 demands)	Good for alveolar fluid buildup, patient must be hydrated, liver is primary metabolizer. Can produce ectopic HBs, chest pain, palpitations, nausea and headaches.
Phenylephrine ($7.72 per ml)	Alpha adrenergic agonist Vasopressor	0.5-3 mcg/kg/min in NaCl or D5W	Immediate, lasts 5-10 minutes post cessation	+++	0-+ (report of reflex bradycardia, correct with atropine)	C, F, NHP, O, S, B, R, L	Safe and preferred in humans. Can cause uterine contraction.	Vasoconstriction, slight decrease in cardiac output with increase in coronary flow.	Use in hydrated patients
Ephedrine ($26.50 per ml)	Symp. Bronchodilator/ Vasopressor	0.03-0.25 mg/kg bolus, q 5 min	immediate	+++	+++	C, F, NHP, O, S, B, R, L	Safe for healthy fetus (excret	releases norepi causing vasoconstriction (Can	Do not use in cardiac patients

							ed in milk)	deplete norepi)	
Norepinephrine ($39.00 per ml)	Alpha & Beta Adrenergic Vasopressor Cardiac inotrope	0.01-0.2 mcg/kg/min, max dose of 2 mcg/kg/ min. Add 4mg to 1L 5% Dextrose sol. run at 0.75-1.5 ml/kg/hr	immediate	+++	0-+ (report of reflex bradycardia, correct with atropine)	C, F, NHP, O, S, B, R, L	Do not use if viable pregnancy	Vasoconstriction, coronary artery dilator, slight increase in cardiac contractility	Use in hydrated patients. Good for Septic patients, high doses can lead to poor perfusion
Epinephrine ($6.00 per ml)	Alpha & Beta Adrenergic agonist	0.01-1 mcg/kg/min, START LOW	immediate, lasts 5-10 minutes post cessation	+++	+++	C, F, NHP, O, S, B, R, L	Do no use for viable pregnancy	Vasoconstriction, Increased cardiac contractility, increase in coronary and pulmonary flow	Better for increasing systolic BP, can Decrease Diastolic. Use in hydrated patients only. Can cause poor tissue perfusion at high doses.
Vasopressin ($69.50 per ml)	Hormone	20 pressor U/ml, 1-	Immediate	+++	0-+	C, F, NHP, O,	Do no use if viable	vasoconstriction	Hepatic flow increase

		4mU/kg/min				S, B, R, L	pregnancy		

Pre-Anesthetic Preparedness:
Being prepared is essential for a successful procedure, not to mention hastening induction, anesthetic time and recovery. Everything one will and might need should be at hand or set up prior. Cheat sheets of emergency drugs should be made and, although a bit wasteful, pre drawn in the event of an emergency.

Capnography: Although capnographs are becoming more and more standard on multiparameter monitors, correct or accurately interpreting of the waveforms is still fairly uncommon in veterinary medicine. Typically, the waveforms are looked upon as just breaths. However, each wave is indicative of a breath or lack thereof- so much more that can be gathered from the wave stature and anatomy. Understanding the waveforms better will allow anesthetists to gauge the quality of the breath, possible occlusions or leaks, and perfusion quality of the animal.

Local Anesthetics and Epidurals:
The use of local anesthetics is not extremely advanced but is often underutilized. In any species of mammals, avian, reptile or amphibians literature suggests the use of local anesthetics to reduce doses of systemic anesthesia, bettering the physiological parameters we monitor and strive to keep with normal limits. The general rule of thumb for dosing in all taxonomies is 2mg/kg of lidocaine or bupivacaine. If more volume is needed the local anesthetic can be mixed with 0.9% saline with minimal change to the efficacy of the block.
Epidurals can theoretically be performed in any species with epidural space, which is all vertebrates. Although species specific dosing of epidural medications is still largely extrapolated from small animal dosages, opioid epidurals are typically safe for most species and should be considered.

Venous/Arterial Access: (Arterial, venous, IO, Central lines, sheaths, exotics)
Intravenous catheterization in should be a minimum for any patient undergoing anesthesia. Arterial lines for invasive BP or arterial blood gasses should be consider for ASA3 patients or patients that require closer monitoring.

Induction Methods: We are all familiar with mask/chamber induction, propofol and Ket/Val induction, but what else is there? Tailoring anesthetic medications based on the patient health status can alleviate induction-related complications intra-operatively. Other benefits of tailored induction protocols, depending on the half-life of the medications used, can complement analgesic protocols and have MAC sparing effects.

TIVA and CRIs: Gas anesthesia is not ideal for some protocols or situations; therefore, we are left with IM sedation with more difficult titration depending on the surgical intervention and stimulation, patient pain levels and emergent situations. To ease the less than ideal complications surrounding general sedation using IM medications, total intravenous anesthesia (TIVA) via the venous system should be utilized. TIVA offers the anesthetist the option of titration, emergency analgesia and the ability for multimodal anesthesia. There are numerous protocols that can be used for different species. The author prefers these various mixtures because of their cross-species safety and efficacy: Fentanyl/Midazolam/Lidocaine/Propofol or Alfaxan.

Lung Recruitment is a strategy aimed at re-expanding collapsed lung tissue, and then maintaining high PEEP levels to prevent subsequent 'de-recruitment'. In order to recruit collapsed lung tissue, sufficient and even scary pressure must be imposed to exceed the critical opening pressure of the affected lung. In dependent areas of the lung, the pressures required may exceed 50cm H_2O in human lung recruitment procedures. Such pressures are dangerous for upper lung lobes and alveoli, increasing risk for trauma. A strategy is needed to limit trans-alveolar pressures in the upper lobes and provide sustained high pressures in the lower areas of the lungs sufficient to cause recruitment of collapsed tissue, which is most commonly achieved with special positioning. (This technique should not be done without appropriate training and research).

Percutaneous transtracheal ventilation is a method of placing a large gauge needle directly into the trachea to provide emergent or supplemental oxygen to the lungs. The needle placement is generally midline just under the thyroid cartilage and above the cricoid cartilage. This is a temporary maneuver and should only be performed on anesthetized or sedated patients as risk of injuring the trachea or esophagus and even major vessels increases with movement. Appropriate and inappropriate gas exchange has positive and detrimental effects, but resiliency to hypercarbia can be less appreciable in mammals.

Normothermia will help retain a steady metabolic rate and aid in keeping a normal blood pressure to perfuse our patients' vital organs.

Using warming devices such as warmed surgical tables and circulating warm water blankets work well. *Caution should be taken to not allow direct contact with the patient, in order to avoid thermal burns.

Recently warm water bags have been shown to have an opposite effect and can steal heat from an anesthetized patient as they cool. Warm air blowers are ideal but can be cumbersome with tiny patients. A personal favorite is bubble wrap. Not only is it cheap and disposable, it also offers a lightweight and insulated option in thermoregulation. Tiny knitted socks work well to cover exposed limbs. Humidivents™ are also a good option but can add to dead space and IPPV may be indicated. These devices work by inserting the device between the ETT and the circuit hose. The paper filter keeps warm moist air in the chest cavity. They also help protect the anesthesia machine from aerosolized bacteria the patient may be harboring with expiration. As a last resort, warm water enemas can be used in extremely cold patients, but a cooling evaporation effect can occur if the patient becomes wet during the process.

References available upon request.