Update on Anesthetic Induction Techniques

Lesley J. Smith DVM, DACVAA

Clinical Professor of Anesthesiology

School of Veterinary Medicine, University of Wisconsin

This lecture will focus on practical and physiologic/pharmacokinetic aspects of modern injectable anesthetics. Discussion will focus on the clinical use of alfaxalone in dogs and cats, a comparison of alfaxalone *vs*. propofol, and best practices for using either induction drug. In addition, the lecture will cover pros and cons of ketamine/benzodiazepine (or telazol) inductions and the use of "co-induction" drugs to minimize the negative effects of any of the common injectable anesthetics.

Learning Objectives will include:

- Become familiar with the clinical use of alfaxalone
- Understand the pharmacokinetics of alfaxalone
- Learn the versatility of alfaxalone's use
- Understand the subtle differences between alfaxalone and propofol
- Understand when a ketamine (dissociative) based induction protocol is contra-indicated (or not)
- Learn about ways to minimize induction anesthetic doses with the use of "co-induction" drugs

Alfaxalone is a relatively new injectable anesthetic that was licensed for IV use for canine patients in the USA in 2021. While there is no market for alfaxalone in human medicine, the FDA insisted that it be a DEA schedule 4 drug, requiring record keeping of its use. Alfaxalone is a neurosteroid anesthetic that is very closely related to progesterone in terms of chemical structure. Prior to the current market, alfaxalone was available in Canada and the European countries as a steroidal injectable anesthetic marketed as "Saffan". Saffan was a combined formulation of alfaxalone and alfadione, with a preservative of cremafor. There were many anaphylactic reactions to cremafor and Saffan was taken off the market. Alfaxalone was reformulated with the preservative cyclodextrin and marketed heavily in Australia before becoming available in the US veterinary market.

Alfaxalone, in its current formulation, is basically clear propofol. Its pharmacodynamic properties are very similar to propofol with a few notable exceptions. Induction characteristics and time to intubation are similar, both drugs provide great muscle relaxation when given IV, and cardiovascular and respiratory parameters after induction are similar. Interestingly, alfaxalone, unlike propofol, can be given IM for chemical restraint/sedation. This is covered in the feline anesthesia lecture but can also be applied to fractious dogs. For IM chemical restraint of either dogs or cats, a dose of 1-2 mg/kg IM can be given in addition to an alpha-2 agonist,

benzodiazepine, and/or opioid. Administration of alfaxalone alone for chemical restraint in either dogs or cats is not recommended as muscle rigidity and twitching will result.

Notable differences between alfaxalone and propofol for IV induction of anesthesia:

- Propofol is cleared via extra-hepatic metabolism whereas alfaxalone depends on hepatic clearance
- Alfaxalone duration will be prolonged in patients that are hypotensive (e.g. after acepromazine) due to delayed hepatic clearance; however, this is probably not clinically significant
- There is some (weak) evidence in the literature that alfaxalone is more sparing on cardiovascular function
- Currently, alfaxalone is more expensive than propofol and requires DEA coverage and storage
- Alfaxalone has a longer shelf life than propofol
- Propofol stings on IV injection, alfaxalone does not appear to do so

Other than these few minor differences, both drugs are very similar with respect to IV anesthetic induction. Both can cause transient apnea; both will decrease blood pressure for a few minutes. Both drugs will decrease intra-cranial and intra-ocular pressure, which may be beneficial in a patient with a suspected intra-cranial mass, hydrocephalus, or seizures of unknown etiology, as well as a patient with glaucoma or a descemetocele where rupture of the globe is of concern.

With respect to dosages, alfaxalone given at 2 mg/kg IV to an unpremedicated healthy dog will have a duration of ~ 5 minutes. Cats given a dose of 5 mg/kg IV of alfaxalone will have a longer duration of anesthesia of ~ 20 minutes due to their inability to metabolize alfaxalone to the glucuronide metabolite. That said, we always recommend premedication for dogs and cats with any combination of opioid and sedative (hydromorphone, butorphanol, methadone, buprenorphine, morphine) and (acepromazine, midazolam, dexmedetomidine). With these types of premedications on board, administer alfaxalone at the lowest possible dose needed for intubation (e.g. 0.5 – 2 mg/kg).

When not to use Ketamine/Benzodiazapine Inductions!?

Ketamine is a dissociative anesthetic that stimulates release of catecholamines from the adrenal medulla. As such, it tends to increase heart rate, blood pressure, and cardiac work. Ketamine inductions should be avoided in patients that have been premedicated with an alpha-2 agonist, i.e. dexmedetomidine. Why? Because the increase in afterload caused by the alpha-2 makes the heart work harder. Adding ketamine to that mixture makes the heart rate and contractility increase as well, further increasing cardiac work. Myocardial oxygen consumption increases against an increase in afterload. Moreover, coronary arterial perfusion, supplying oxygen to the myocardium, occurs during diastole. With higher heart rates, the diastolic time is shortened so oxygen deprivation of the myocardium could be a concern.

That said, ketamine is a useful chemical restraint drug for cats when considering premedications. Combine ketamine at 5-10 mg/kg with a sedative and opioid (e.g. dexmedetomindine ~ 5- 10 mcg/kg with the opioid of your choice). Just do not follow up with more ketamine for induction!

Anesthetic Co-Induction Protocols:

It is very helpful to reduce the requirement of any anesthetic induction drug with co-induction (balanced anesthesia) approaches. This will reduce the risk of hypotension, apnea, gagging and increased intracranial pressure, and ease the transition to inhalant anesthetics. Common co-induction protocols involve the use of lidocaine, ketamine, midazolam, and opioids.

- Lidocaine given at 2 mg/kg (DOGS ONLY) will reduce the required dose of induction agent by ~ 10-20%. It is most useful in dogs where increased intracranial or intraocular pressures are of concern because lidocaine given IV decreases the gag reflex.
- Ketamine at 0.5 mg/kg to dogs and cats will decrease the amount of induction drug required by 25-50%. In addition, ketamine provides great somatic analgesia for procedures such as dental prophylaxis and extractions. This low dose of ketamine is not of huge concern in patients with cardiac disease or those premedicated with dexmedetomidine.
- Midazolam will aid in muscle relaxation and intubation and provides a small reduction in induction drug dose requirement. A dose of 0.1-0.2 mg/kg IV can be administered just prior to the induction drug. If you wait too long the patient may become excitable! So have that induction drug ready to go.
- Common opioids that may be used as co-induction drugs include hydromorphone, methadone, fentanyl, and butorphanol. The onset of action of IV buprenorphine renders is useless as a co-induction opioid. Any of these opioids given prior to induction of anesthesia will reduce the requirement for induction anesthetics. Common IV doses for each include:
    - Hydromorphone 0.05 mg/kg IV
    - Methadone 0.1 -0.3 mg/kg IV
    - Fentanyl 2-5 mcg/kg IV
    - Butorphanol 0.1-0.5 mg/kg IV

Remember that the most important part of anesthetic induction is monitoring! Secure the ETT first, leak check, then palpate pulses and assist or ensure that the animal is ventilating. There are no safe anesthetics, just safe anesthetists!