Alfaxan anesthesia - reflecting on the past year

Alfaxan has been available to Canadian veterinarians for over a year now and I would like to share with you some of my observations about this interesting transition period.

Small animal clinicians I have consulted with seem to fall into one of three camps: The members of the first group love Alfaxan and have embraced it fully as a go-to induction agent. The second group dislike it intensely. The third group have a bottle of Alfaxan on their hospital shelves and have been looking at it warily. But they have not yet taken the plunge and administered it to any of their patients.

To some extent, practitioners' experiences with and opinions about Alfaxan have been influenced by the anesthesia protocols they've transitioned from in order to address the sudden and drastic injectable drug shortage imposed by Sandoz. Members of the Alfaxan fan-club have witnessed and appreciated the rapid, predictable transition to unconsciousness along with the rapid awakening with minimal hangover that Alfaxan brings to the veterinary anesthesia landscape. Generally, these practitioners have made the transition from propofol induction protocols and so the magnitude of the change has been minimal.

The not-so-crazy-about-Alfaxan clinicians have complained about poor recoveries and patients "waking up" in the middle of a procedure. These clinicians can't wait for diazepam to become available once again so that they can return to their ketamine/diazepam induction protocols.

The third group may be struggling with the issues surrounding making changes to their anesthesia protocols because they simply don't like change. They may also be hesitant and dismayed by the lack of information about Alfaxan anesthesia if they are relying on American sources for their information. This is because Alfaxan has not yet been released for use in the United States. However, it has been in clinical use in the UK and "Down Under" for many years.

I fall into the fan club category, though like many of you, I experienced some trepidation when I made my first forays into uncharted Alfaxan waters. Who can blame us? We manage anesthetic risk in part by minimizing the unknowns we have to deal with, since we can't always predict how our patients will respond to the anesthetic drugs we choose. So we use the same basic anesthetic drug protocol on all our patients. Not a bad strategy as long as the protocol we rely on has at least some built in flexibility.

One of the reasons for the very different levels of enthusiasm about Alfaxan is the contribution that ketamine induction makes to the whole anesthesia process. Ketamine is analgesic. It also is cleared from the circulation more slowly than either Alfaxan or propofol. Thus, it provides background intra operative analgesia and contributes to unconsciousness along with the inhalant anesthetic that is used for maintenance. If you take ketamine induction out of the equation and replace it with Alfaxan, then you may have problems with pain control that result in rough recoveries. Alfaxan will be pretty much cleared from circulation in 20 minutes or so (depending on the dose you administer) and at that point, you are left with anesthetic gas along with your premedication drugs to keep your patient asleep and comfortable. Sometimes that may not be

enough unless you adjust your inhalant anesthetic levels upward before the patient's plane of anesthesia becomes too light.

If you do not make adjustments to your anesthetic protocols to address the absence of ketamine, you will become frustrated by the problems that pop up. However, the adjustments that need to be made are small and manageable. Practitioners who transitioned to propofol based inductions have already been through this adjustment process which is why the introduction of Alfaxan into their anesthesia protocols has been relatively smooth without any real noticeable difference. They have observed a few improvements with Alfaxan substitution for propofol in that there is less respiratory depression and apnea at induction making the transition to inhalant anesthetic gas maintenance more seamless. Practitioners have also noticed less hypotension with Alfaxan induction compared to propofol induction.

I have some advice for clinicians who have struggled with Alfaxan use and yet remain open to ketamine and diazepam induction alternatives:

1. Consider "ketofol" for anesthetic induction. Ketofol is a term coined in human anesthesia and refers to the combination of ketamine and propofol together for induction. Because less total propofol is needed to achieve good intubation conditions, ketofol reduces the severity and the incidence of respiratory depression and hypotension associated with propofol administration. So, it results in a smooth transition to inhalant maintenance. In addition it establishes a ketamine analgesia background to supplement the poor to absent analgesia provided by inhalant agents. For brief procedures this ketamine analgesia is sufficient to reduce pain in recovery. For longer procedures, this ketamine analgesia background can be sustained by its continued administration as a constant rate infusion (CRI) intra-operatively and even post operatively if required.

2. Add local/regional blocks to your anesthesia protocols. Just about every surgical procedure brings with it an opportunity to provide analgesia through the process of numbing the surgical site prior to or immediately after surgery. This is a different approach to peri operative analgesia by ketamine CRI. But it accomplishes the same goal of patient comfort in recovery and makes for very smooth awakening. One difference between the use of regional analgesia and the use of CRI analgesia is that the patients with regional analgesia wake up with less "hangover", are clear headed quickly after extubation and show an interest in food early on in recovery.

3. Revisit how anesthetic depth is being assessed. I suspect that patients undergoing induction of anesthesia with Alfaxan may be manifesting signs of a lighter plane of anesthesia that are being missed by anesthetists so that they seem to "suddenly wake up" when they are not supposed to. Two key signs of anesthetic depth are jaw tone and palpebral reflex. If your anesthetist assesses these two vital signs every 5 minutes intra-operatively he/she will detect the subtle tightening of the jaw muscles and the return of a brisk palpebral reflex that announce a lightening of the anesthetic plane. At that point, upward adjustments to inhalant anesthetic gas delivery can be made in time and awakening can be avoided. Of course, this approach to anesthesia monitoring

requires an actual anesthetist instead of someone who floats by and checks blood pressure every once in a while on their way to accomplishing other tasks. Generally, patients do not “suddenly wake up” though it may seem that way.

Why not simply go back to ketamine based induction protocols once this annoying drugs shortage is over? Well you certainly can do that. But you would be wise to consider familiarizing yourself with at lest one non-ketamine dependent induction drug protocol since some of your patients may present for anesthesia with underlying disease that is intolerant of high doses of ketamine. The doses of ketamine in “ketofol” are relatively low compared to the amount of ketamine that is administered in combination with diazepam or midazolam. So ketofol may be acceptable for this patient population. In some situations it may be wise to omit ketamine completely from the induction protocol.

The hiccups encountered during the injectable anesthetic drug shortage and the introduction of Alfaxan on the Canadian veterinary scene have certainly provided opportunities for insight into what effective anesthesia. They have also forced us to evaluate how we manage change in our practices. Alfaxan is not the last anesthetic drug that we will be introduced to in our careers. I suggest that we try to remember how anesthesia protocols are composed of component elements which influence each other. The earlier in the anesthesia delivery process that we introduce a new step or a new drug, the greater it’s influence and potential to dramatically change the way in which anesthesia unfolds - for better or for worse. Start planning for how you will deal with introducing the next “big thing” in anesthesia since it is only a matter of time before that happens.

Here is an except about Alfaxan from my anesthesia recipe book:

Alfaxalone (alphaxalone) - brand name Alfaxan

Steroid with anesthetic properties (but no steroid effects)

Beneficial qualities:

- Minimal hypotension.
- Minimal changes in heart rate.
- Minimal respiratory depression.
- No tissue irritation if administered peri vascularly.
- Suitable as an intramuscular sedative.
- Excellent muscle relaxation providing ease of endotracheal intubation.

Undesirable characteristics:

- Calculated volume may be impractical for sedation of larger patients (dogs).
- No preservative - contents of opened bottle should be discarded after initial use.

Indications:

- Induction of anesthesia.
- Chemical restraint/sedation for non painful manipulations such as diagnostic imaging, IV

catheter placement.

Dose recommendations:

- 2 mg/kg IM for chemical restraint or anesthetic premedication.
- 1 to 3 mg/kg IV for induction of anesthesia.

How I administer Alfaxan:

Always premedicate before administering Alfaxan for anesthetic induction.

If you are administering Alfaxan IM to cats, also administer glycopyrrolate 0.01 mg/kg IM either at the same time or soon after.

Draw up 3 mg/kg as an induction dose for both cats and dogs. I usually end up administering 2 mg/kg but I like to have some extra leftover to top up as needed during the procedure.

Administer 0.5 mg/kg IV every 30 seconds until the patient fails to pull its foot back on toe pinch (or pulls back weakly).

As soon as the patient tolerates a face mask, deliver oxygen supplementation for the duration of the induction process.

You will likely administer about 1 to 3 mg/kg total dose although a higher dose is safe and acceptable if needed. The dose will vary as a result of differences in premedication drugs/doses, the presence of acute illness or advanced age.

If the patient has a pronounced cough at intubation, administer an additional 0.5 mg/kg Alfaxan to help smooth the transition to inhalant.

Respiratory depression is always possible so be vigilant about monitoring your patient.

Inducing Anesthesia with IV “ketofol”

1. Draw up 5 mg/kg of propofol and 5 mg/kg ketamine into the same syringe.
2. Administer 0.1 ml/kg/kg of the above mixture IV as a bolus.
3. As soon as possible place a face mask (with diaphragm removed) over the patient’s mouth and deliver supplemental oxygen. If the patient resists face mask placement, do not force it. The patient will likely readily accept the mask after receiving about 1 to 2 boluses of the ketamine and propofol mixture.
4. Wait 30 seconds and administer a further similar sized bolus.
5. Continue steps 2 and 4 until the patient’s head is down and resting quietly in a face mask. This will probably require between 2 and 5 bolus injections depending on the level of pre-anesthesia sedation, age and overall health status of the patient.

Concurrent use of ketamine along with propofol during induction reduces the necessary dose of propofol while providing a brief period of supplemental analgesia.

It also acts as a loading dose of ketamine prior to ketamine by CRI as long as infusion begins immediately after induction.

The contraindications to ketamine administration should be considered to apply to this

combination of propofol and ketamine.

Because the stability of this mixture of two drugs has not been tested, do not store any remainder of the ketamine/propofol combination.