The “Fax” (Facts) About Alfaxalone.
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“A well-spent day brings on happy sleep.”
Leonardo Da Vinci

General Anesthesia (GA) is a chemically induced state resulting in unconsciousness, muscle relaxation, loss of reflexes, and analgesia.

As we prepare for an anesthetic event we recognize the importance of the knowledge and skill required in monitoring and maintaining a metabolically stable patient for a successful outcome. A general understanding of: anesthetics (pharmacology, pharmacokinetics, and pharmacodynamics) and toxicology of these drugs, methods for delivering and assessing drug (anesthetics and antagonists) effects, and the appropriate action required in the event of an anesthetic-related complication/emergency

A complete GA event consists of: pre-anesthetic evaluation/premedication, induction, maintenance, and recovery. Each stage is equally important.
A critical moment in the anesthetic process is the induction period. As we administer anesthetics (most anesthetics cause a degree of respiratory depression) and change the state of the patient from AWAKE to ANESTHETIZED, we appreciate the seriousness of obtaining the patient’s airway (intubation) to insure ventilation and appropriate oxygenation. Our goal is to make this transition – conscious>>unconscious – as smooth as possible.
An ideal induction agent consists of: rapid onset of action, minimal respiratory and cardiovascular effects, and rapid metabolism.

Alfaxalone
Alfaxalone is a neurosteroid anesthetic agent used clinically to induce GA in a variety of species. Even though it is a steroid molecule it is devoid of endocrine activity. It has recently been approved for induction and maintenance of anesthesia in dogs and cats in the United States. Alfaxalone produces muscle relaxation and anesthetic effect through interaction with the GABA\(\alpha\) (Gamma-aminobutyric acid sub-type A) receptors in the CNS. Inhibition of neural impulse transmission occurs due to the modulation of the transport of chloride ions. This effect prevents the development of action potentials and stops impulse transmission producing muscle relaxation and anesthesia.

Alfaxalone is not a new drug. It was previously used in the early 70’s as an anesthetic agent (Saffan) for animals. This “older” formulation was composed of a castor oil surfactant – used to dissolve the alfaxalone - and was responsible for adverse effects (histamine release); eventually it was taken off the market. New formulations contain a cyclodextrin – a non-irritating, non-histamine releasing carrier agent; this carrier is responsible for solubilizing alfaxalone.
Alfaxalone is a preservative free, clear, colorless, non-irritating agent. Because it is lacking in a preservative, it is recommended to discard any unused alfaxalone after 6 hours from initial vial opening. It is considered a class IV controlled substance. Administration of alfaxalone generally produces a rapid, smooth induction with excellent muscle relaxation. It has a short duration of action - i.e. 6-10 mins after a 2.0mg/kg IV dose given to an unpremedicated dog – and typically an uneventful recovery.

Alfaxalone is rapidly metabolized by the liver and has minimal cumulative effect. Alfaxalone produces minimal respiratory and cardiovascular effects. Dose-dependent respiratory depression can occur – slightly less than that of propofol. Cardiovascular function is adequately maintained with little suppression to cardiac output (CO) and blood pressure. Alfaxalone has a wide safety margin (5-10 times overdosing – cats, dogs respectively). Alfaxalone does NOT provide analgesia; it may act synergistically with analgesic agents.

**Administration of Alfaxalone**

Even though alfaxalone is primarily thought of as an induction agent it can be used in all stages of the anesthetic process.

**PREMEDICATION**

The premedication (PM) period is the beginning stage of an anesthetic event. The purpose of the PM period is to provide sedation and analgesia to the patient. The most commonly used route of administration for anesthetics/analgesics during this period is intramuscular (IM).

Alfaxalone is clinically effective when given intramuscularly, although it is not approved for this route of injection in the United States. Alfaxalone can be administered in the premedication (intramuscularly) or subcutaneously (SQ) period to help minimize stress in the anxious feline patient. Alfaxalone in combination with an opioid (oxymorphone, butorphanol, methadone) given IM (10-15 minutes to take effect) can produce mild to heavy sedation in these patients. Usually this premed provides adequate sedation for IV access and quick, simple procedures (radiographs, bandages, blood collection). Recovery times can be anywhere from 30-45 minutes – depending on patient status, dose used, opioid used (may need to be partially or fully reversed). Paddling, agitation, hypersensitivity to stimuli may occur during recovery.

Intramuscular administration is limited due to its large volume for injection. IM administration in the medium/large dog is not recommended for this reason.

The dose for cats - 2.0-5.0mg/kg IM with maximum sedation reached ~20minutes.

My experience: start with 2.0mg/kg (in addition to opioid of choice). Place the patient in a quiet, visible environment and wait 15 minutes. If desired effect is not reached at that; administer another dose of alfaxalone (usually 1.0mg/kg IM) and give the patient another 5-10 minutes.

As with the administration of any premedication resuscitation equipment (endotracheal tube, laryngoscope) and supplemental oxygen should be available in the event of a cardiopulmonary complication.
SQ administration of alfaxalone may take up to 30-45 minutes to reach peak effect.

**INDUCTION**

Induction is a critical moment in the anesthetic process. Anesthetics are administered to the patient until unconsciousness is achieved; the point at which airway management (endotracheal intubation) begins. Intubation should be rapid and smooth.

As with most induction agents, alfaxalone should be administered slowly (over 60 seconds) IV to effect. A slow titration – ¼ of the dose given every 15 seconds to achieve intubation – will allow for less negative cardiovascular and respiratory effects in addition to less amount of the drug needed. Alfaxalone can be given with or without other agents i.e. opioids, benzodiazepines for induction. Adding other agents will further reduce the required anesthetic dose of alfaxalone. An alfaxalone induction is usually smooth though muscle twitching or excitement can be noted.

The recommended dose for an unpremedicated dog is ~ 1.0 - 2.0mg/kg.
The recommended dose of an unpremedicated cat is ~3.0 - 5.0mg/kg.
Always consider using lower doses in older or compromised patients.

Since dose-dependent respiratory depression/apnea may occur, preoxygenation (abort if the patient becomes unwilling and distressed) with 100% oxygen prior to induction is recommended to minimize possible hypoxemia. Airway management equipment (laryngoscope, endotracheal tubes) and supplemental oxygen should be readily available. Even though cardiovascular effects are minimal i.e. increased heart rate, decreased myocardial contractility, decreased systemic vascular resistance - close monitoring is advised to prevent or discourage hypotension which may be further exasperated by the addition of inhalant.

**MAINTENANCE**

During the maintenance period the patient is maintained immobile, insensitive to pain, and metabolically stable. Depth of anesthesia is encouraged by the use of inhalants and injectable anesthetics (bolus, constant rate infusions (CRI), total intravenous anesthesia (TIVA)).

Alfaxalone can be administered (IV bolus) safely and effectively to maintain anesthesia. Suggested dose of alfaxalone: 1.0-2.0mg/kg IV can result in 3 – 10 minutes duration of anesthesia. The dose should be adjusted according to the patient’s needs. Because alfaxalone is rapidly metabolized and has little cumulative effect it can be used as a CRI. Currently CRI doses are not fully established. Doses range from 3.0- 7.0mg/kg/hr – 5.0-10mg/kg/hr – cats and dogs respectively.

**RECOVERY**

The recovery period is the end-stage of the anesthetic process. It is during this period where a staggering number of complications seem to occur – usually due to lack of supervision and minimal attention to the sedate (possibly cardiopulmonary depressed) patient. It is the point at
which administration of anesthetics has ceased and the patient is starting to regain consciousness. Patients are very vulnerable during this period i.e. respiratory depression, hypothermia and should be monitored very closely to promote a smooth, successful return to consciousness. Vitals should be assessed frequently until the patient has returned to near “normal” physiologic function.
The neurologic function of the patient should be assessed (minimizing increased movement, sound, and anxiety) and supported (sedatives) to ensure a safe, uneventful recovery.

Alfaxalone is rapidly eliminated from the body. Recovery from alfaxalone is typically fast and smooth. Duration of effect depends on dose and route of administration (15-45mins). Its effects can be prolonged when used in combination with other drugs or as a CRI. Excitement can occur in patients waking up too quickly.

ADVANTAGES
Alfaxalone is a quick acting induction agent with minimal cardiovascular and respiratory effects that can be used in many exotic species, dogs and cats.
Unlike its “predecessor” (Saffan), alfaxalone is not associated with histamine release.
Alfaxalone can be used safely on puppies and kittens less than 12 weeks of age.
It can be used safely in cesarean sections with minimal negative effects (depression) to the neonates.
Alfaxalone is a suitable anesthetic agent for sighthounds.
Because of its minimal cardiopulmonary effects it can be used in compromised patients minimizing the use of etomidate – a hypnotic, a cardiovascular sparing anesthetic associated with gagging, twitching, regurgitation, vomiting and adrenal suppression.

DISADVANTAGES
The most common negative side effect (similar to propofol) of alfaxalone is dose-dependent respiratory depression. Caution with administration – appropriate dose and speed at which drug is injected – will ensure adequate respiratory function.
Airway management equipment (laryngoscope, endotracheal tubes) and supplemental oxygen should always be readily available – regardless if used for sedation or for GA- in the event that a complication occurs.
Recovery from alfaxalone is usually smooth and rapid. Excitement and agitation can occur in patients that wake up too quickly (no premed or other drugs used).
Some feline patients can wake up paddling and twitching. Alfaxalone used in combination with other drugs (opioids, tranquilizers) has been shown to discourage this type of recovery. Alfaxalone does NOT have any analgesia associated with its use.
The cost of alfaxalone can be considered a deterrent. With this said, it is important to consider that alfaxalone (when compared to propofol) may cost more per patient although the total anesthetic cost may be the same or less (as propofol) with a wider margin of safety.
REFERENCES
9. Nieuwendijk, Hans, Veterinary Anesthesia Support Group; VASG.org

Additional references available upon request