ANESTHETIC AGENTS

The following provides a very brief overview of the anesthetic agents most commonly used in HSVMA-RAVS’ small animal protocols. This is NOT a detailed monograph on the listed drugs. Consult additional anesthesia texts or Plumb’s Veterinary Drug Handbook for more detailed information.

PRE-ANESTHETICS AND ANALGESICS

ANTICHOLINERGICS

Atropine
Mode of Action
- Blocks the action of acetylcholine at the terminal ends of the parasympathetic nervous system, thereby reversing parasympathetic effects.

Effects
- Increased heart rate
- Reduced GI activity
- Decreased tear and salivary secretions

Use
- Preferred agent to counteract vagally-induced bradycardia.
- Can be given IV, IM or SQ.
- Duration of effect: 45-90 minutes

Precautions
- Cardiac: Avoid with tachycardia (HR > 140 in K9, 180 in feline) or clinical signs of heart failure; may induce cardiac arrhythmias. Partial dosing can result in paradoxical bradycardia
- GI: Constipation or obstruction
- Can result production of thick mucous in the airways, particularly in cats.

Glycopyrrolate
- Synthetic derivative of atropine with similar effects.
- Onset and duration of effect longer than atropine - not for use in emergency situations.
- May be less likely to cause tachycardia and cardiac arrhythmias than atropine
- Can cause an initial paradoxical bradycardia and AV block when given IV. This effect is usually overcome as plasma levels become therapeutic

Note:
- Hypothermia results in decreased depolarization of cardiac pacemaker cells, causing bradycardia. Since not vagally mediated, this bradycardia can be refractory to anticholinergics.

OPIOIDS

The opioids are a diverse group of naturally occurring and synthetic drugs used primarily for their analgesic activity. Opioids combine reversibly with specific receptors in the central nervous system, altering the transmission and perception of pain.

The clinical effects of opioids vary between the mu opioid receptor agonists (morphine, hydromorphone), partial mu agonists (buprenorphine), and agonist-antagonists (butorphanol), and depend on additional patient factors, including the presence or absence of pain, physical condition of the animal, concurrent drugs administered, and individual sensitivity.

Caution should be used with most opioids in the following cases: Respiratory disease or chest injury; head trauma, increased CSF pressure or other CNS dysfunction; hypothyroidism, severe renal disease or Addison’s disease; geriatric or debilitated patients.
Morphine Sulfate
Mode of Action
- Pure mu agonist

Effects
- Potent analgesia and sedation
- Minimal cardiovascular effects though higher doses can cause bradycardia
- Respiratory depression (usually not clinically-relevant)

Method of Use
- Can be administered IV, IM or SQ
- Duration of effect is 2-6 hours
- Can also be used for epidural analgesia
- Reversible with naloxone
- Schedule II controlled drug

Precautions
- Significant sedative synergism between morphine and acepromazine in the dog – reduce acepromazine dose
- Use with caution in cats if no sedative/tranquilizer is used due to potential excitatory response
- May cause panting (due to resetting of thermoregulatory mechanism)
- Often causes vomiting and defecation when given IM or SQ

Buprenorphine (Buprenex®)
Mode of Action
- Partial mu agonist
- More potent than morphine and of longer duration due to its slow dissociation from receptors

Effects
- Moderate analgesia
- Minimal, if any, sedative effect

Method of Use
- Can be administered IV or IM
- In cats, is also well absorbed via oral mucosa
- Delayed onset – time to peak effect: 20-30 mins IV, 45-60 mins IM
- Duration of effect influenced by dose (4-8 hrs)
- Schedule III controlled drug

Precautions
- Difficult to reverse if undesirable effects occur (uncommon)

Butorphanol (Torbugesic®)
Mode of Action
- Mixed agonist/antagonist (kappa agonist, mu antagonist)

Effects
- Mild to moderate analgesia, moderate-strong sedative

Method of Use
- Can be administered IV, IM or SQ
- Duration of effect is 30-60 mins in dogs and 1-3 hrs in cats
- Reversible with naloxone
- Schedule IV controlled drug

Precautions
- Short duration of action may require additional re-dosing or additional analgesics post-procedure
**PHENOTHIAZINES**

**Acepromazine**

Mode of Action
- Thought to depress portions of the reticular activating system causing sedation.
- Anticholinergic, antihistamine, antispasmodic and alpha-adrenergic blocking effects.

Effects
- Strong sedative
- Antiemetic effect

Method of Use
- Used in healthy adult animals in combination with opioid analgesic as a pre-anesthetic sedative and to help decrease dose of general anesthetic required.
- May be administered PO, SQ, IM or IV (with caution).
- Duration of effect is 6-8 hrs

Precautions
- Increased potency in geriatric animals, neonates and animals with liver dysfunction.
- No analgesic effect—painful patients should be treated with NSAID or opioid instead.
- Can cause significant hypotension.
- Maximum total dose is 3 mg, regardless of body weight

**NSAIDS (Non-Steroidal Anti-Inflammatory Drugs)**

**Ketoprofen**

Mode of Action
- Inhibits inflammatory cascade by blocking cyclooxygenase (COX) enzymes.

Effects
- Antipyretic, analgesic and anti-inflammatory effects via inhibition of cyclooxygenase-2 (COX-2)
- COX-1 inhibition effects platelet function and integrity of gastrointestinal mucosa

Method of Use
- May be administered PO, IM or IV.
- Duration of effect is 12-18 hrs

Precautions
- Avoid in animals with hepatic or renal disease and in dehydrated or hypotensive patients.
- Do not combine with other drugs known to alter hemostasis or cause gastrointestinal erosion (aspirin, corticosteroids, etc)
- Generally avoided for long-term use due to substantial risk of GI side effects with prolonged use.

Notes
- Other drugs in this class occasionally used include carprofen, etodolac, and meloxicam.

**ALPHA-2 AGONISTS**

**Dexmedetomidine (DexDomitor®)**

Mode of Action
- Alpha-2 adrenoreceptor agonists - Stimulation of these receptors causes a decrease in the level of norepinephrine released in the brain resulting in sedation and analgesia.

Effects
- Profound sedation and anxiolytic action. Moderate to profound analgesia
- Peripheral vasoconstriction resulting in increased systemic vascular resistance and increased blood pressure. Heart rate decreases to compensate for the increased blood pressure and maintain cardiac output.
- Lowered respiratory rates and a reduction in body temperature

Method of Use
- May be administered IM or IV.
- Onset of action following IM injection is 5 minutes and 1 minute following IV dose
- Duration of sedation is 30-90 minutes.
- Effects are reversible with atipamezole
- Typically used at doses MUCH lower than the label recommends.

Precautions
- May have the potential to cause severe cardiovascular and respiratory complications. Standard doses of these drugs are given only to young, healthy patients and careful monitoring is essential. Reversal agents are available and can be used if adverse effects are seen.

**ALPHA-2 ANTAGONISTS**

**Atipamezole** (Antisedan®)

**Mode of Action**
- Alpha-2 antagonist used as reversal agent for medetomidine, dexmedetomidine or xylazine

**Method of Use**
- Completely, permanently reverses dexmedetomidine effects
- May be administered IM or IV
- For complete reversal, administer same volume atipamezole as dexmedetomidine
- Can be used at partial dose for partial effect

**Precautions**
- Will reverse all of the effects of dexmedetomidine, including analgesia, thus administration of another analgesic agent may be appropriate at the time of reversal.

**Notes**
- Yohimbine is an alpha-2 antagonist that is less selective for alpha-2 receptors (i.e. it also is effective at alpha-1 receptors). It may occasionally be used in HSVMA-RAVS' clinics.

**INDUCTION**

**DISSOCIATIVES** (Cyclohexamines)

**Ketamine**

**Mode of Action**
- Disrupts pathways within the cerebrum and stimulates the reticular activating center.

**Effects**
- Exaggerated reflex responses and increased muscle tone
- Significant superficial analgesia, but poor visceral analgesia.
- Increased heart rate
- May exhibit apneustic respiration (inspiration followed by prolonged pause and short expiration).

**Method of Use**
- Primarily used as an induction agent or to perform a short procedure with little pain involved.
- Concurrent use of a tranquilizing agent, such as diazepam, acepromazine, or xylazine, helps prevent excessive muscle rigidity, improves ease of intubation, and provides smoother recovery.
- May be given IM or IV or orally (fractious cats).
- Schedule III controlled drug.

**Precautions**
- Positive inotropic effect on the myocardium and increases heart rate, cardiac output, blood pressure, pulmonary artery pressure and central venous pressure.
- May cause increased salivation.
- Increased intracranial and intraocular pressures
- Hyperthermia may occur in dogs during recovery
- Animals recovering from cyclohexamines often show exaggerated response to touch, light or sound and may show seizure-like activity. Avoid unnecessary stimulation during recovery.
- As diazepam is unpredictably absorbed when given IM, ketamine/diazepam mixtures are generally administered only intravenously.
**Tiletamine** *(Telazol®)*

Tiletamine is a cyclohexamine similar to ketamine and sold only in combination with zolazepam which is a benzodiazepine similar to diazepam.

Telazol produces results similar to that of ketamine and diazepam combinations with the following advantages:

- Less pronounced apneustic breathing
- May be administered IM, IV, or SQ
- Smaller volumes are used.
- Because of IM route, particularly useful for chemical restraint of aggressive dogs and cats (can be mixed with butorphanol for added analgesia).
- Can be given orally to dogs

Onset of anesthesia is 2-5 minutes after IM injection, duration of anesthesia is 20-30 minutes. As with ketamine, IM injection may be painful. Recovery may be prolonged with IM injection (up to 5 hours).

**BENZODIAZEPINES**

**Diazepam** *(Valium®)*

Mode of Action

- Hypnotic sedative—probably effects release of endogenous GABA, an inhibitory neurotransmitter.

Effects

- Anti-anxiety and calming effects, and good skeletal muscle relaxation.
- Anticonvulsant activity.
- Minimal adverse cardiovascular and respiratory effects. High margin of safety.

Method of Use

- Can be administered PO or IV
- Generally used for anesthesia in combination with ketamine, an opioid or propofol.
- Not water-soluble - incompatible with most other agents and should not be mixed in a syringe with any agent other than ketamine.
- Reversible with flumazenil
- Schedule IV controlled drug.

Precautions

- Use cautiously in animals with hepatic or renal disease and in debilitated or geriatric patients.
- Propylene glycol base makes diazepam somewhat painful and un-predictably absorbed IM.

**Midazolam** *(Versed®)*

Midazolam is a benzodiazepine similar in action to diazepam but can be administered IM or IV.

**Zolazepam** *(Telazol®)*

Zolazepam is a benzodiazepine similar in action to diazepam. It is manufactured in combination with tiletamine as the product Telazol®. *(see tiletamine above)*

**OTHER INDUCTION / MAINTENANCE AGENTS**

**Propofol**

Mode of Action

- Unique hypnotic agent consisting of a phenol in a hyperlipid emulsion – method of action is unknown but it may affect the GABA system.

Effects

- Very fast acting injectable agent without cumulative effect - rapid induction and recovery.
- No analgesic effects.

Method of Use

- Must be administered IV.
- Can be given as intermittent bolus or CRI for maintenance of anesthesia.
As a bolus carefully titrate to effect, generally administering 25% of calculated dose at a time. Administration with IV diazepam can decrease propofol need by 50%.

Precautions
- Rapid administration can result in respiratory depression/apnea, hypotension and reduced myocardial contractility: use caution in animals with cardiovascular/respiratory disease.
- Hyperlipid emulsion promotes bacterial growth. Once bottle is opened, use within 6-8 hours.

MAINTENANCE

INHALANT ANESTHETICS (isoflurane, halothane, sevoflurane)

Basic inhalation anesthesia:
- Liquid anesthetic in the anesthetic machine is vaporized, mixed with oxygen and delivered to the patient by mask or endotracheal tube. The anesthetic travels to the alveoli of the lungs, where it diffuses into the bloodstream. Because of their relatively high lipid solubility, inhalation agents readily leave the circulation and enter the brain, inducing anesthesia.
- Anesthesia is maintained as long as sufficient quantities of the agent are delivered to the alveoli so that the blood, alveolar and brain concentration are maintained.
- Inhalant anesthetics induce unconsciousness, amnesia, muscle relaxation, blunting of autonomic reflexes and immobility. The mechanism of action is uncharacterized.

Isoflurane
Mode of Action
- Fluorinated hydrocarbon.
- Metabolism=99% respiration (good for neonatal and geriatric patients)

Effects
- Dose-dependent hypotension (can be significant) and decreased cardiac output (due to vasodilation and negative inotropic effects).
- Mild respiratory depression
- Good muscle relaxation, little or no analgesia
- Can cause some increased CSF pressure
- Depression of thermoregulatory centers (use care to avoid hypo-/hyperthermia)

Method of Use
- Administered via mask or endotracheal tube.
- Most commonly used to maintain anesthesia after administration of an injectable induction agent, but can be used to induce anesthesia.
- Return to consciousness with isoflurane alone may occur as rapidly as 1-2 minutes.

Precautions
- May cause significant hypotension and respiratory depression at higher doses.
- Anesthetist must be knowledgeable and familiar with anesthetic equipment used.
- Isoflurane-only induction can take several minutes and can be quite stressful for the animal. This technique is generally reserved for very young patients or aggressive cats (administered via induction chamber).