ANESTHETIC DRUGS – A REVIEW FOR THE VETERINARY TECHNICIAN

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Veterinary technicians are asked to administer drugs and induce anesthesia on a daily basis. Although we are not prescribing the drugs, veterinary technicians should understand why certain drugs are used, how they affect the patient, what side-effects could occur, how long the drugs take to become effective and when they should be administered post-operatively for pain. Being knowledgeable about anesthetic drugs gives you the power to provide better patient care!

PRE-MEDICATIONS

What are the goals of premedication and sedation? Why are pre-medications so important? Providing patients with pre-medications can make catheter placement and anesthetic induction less stressful for both the technician and the patient. Pre-medicating the patient can also help facilitate handling and restraint that in turn increases safety. Lastly, many pre-medications not only provide analgesia, but they also contribute to a multimodal or "balanced" technique that reduces the overall amount of drugs needed for anesthetic induction and maintenance.

Ideal properties of premedication and sedation drugs should include the following:

- Produce reliable sedation and anxiolysis
- Have minimal effects of the cardiovascular system, liver, and kidneys
- Cause minimal respiratory depression
- Produce analgesia
- Have the ability to reverse the drug
- Affordable

Unfortunately there is not one single drug that possesses all of these characteristics, therefore we must carefully choose a combination of drugs to obtain the desired effects. When appropriate combinations of drugs are used in conjunction with each other, it often allows for overall lower doses to be administered. Many drug combinations work synergistically with each other. Common drug combinations include alpha$_2$-agonists given with opioids and phenothiazines such as acepromazine given with opioids (neuroleptanalgesia).

COMMON DRUGS USED FOR SEDATION AND/OR ANALGESIA

Phenothiazines

Acepromazine is the most commonly used phenothiazine administered in veterinary medicine today. Phenothiazines are not controlled, do not cause significant respiratory or cardiac depression and have a wide margin of safety in healthy patients when given at appropriate doses. Acepromazine can cause profound sedation that at higher doses can last up to 24 hours. It also has an antiemetic effect and may prevent animals from vomiting when given several minutes prior to opioid administration. Phenothiazines can prevent histamine release and therefore help reduce allergic reactions. The downside of phenothiazines include peripheral vasodilation which can lead to heat loss and hypotension, the inability to reverse the drug, and lack of analgesia.

Alpha$_2$-agonists

Dexmedetomidine is the most commonly used alpha$_2$-agonist administered in small animal medicine. Alpha$_2$-agonsits are not controlled, provide some analgesia, and are reversible. Alpha$_2$-agonists are potent sedatives that can be used alone or in combination with other drugs such as opioids or tranquilizers. When these drugs are used in combination with opioids or tranquillizers, they have a synergistic or additive effect. Dexmedetomidine works great when given at micro doses intravenously for patients experiencing a rough recovery from anesthesia and due to its shorter duration of action, it is often preferred over acepromazine in many cases.

Alpha$_2$-agonits can have significant cardiovascular side effects. These drugs should only be given to healthy patients and are generally avoided in geriatric, diabetic, pregnant, pediatric, or sick animals. Common adverse effects include profound hypertension, bradycardia and reduced cardiac output. Administration of an anticholinergic to treat bradycardia is contraindicated. Administration of an anticholinergic is not always effective and can actually increase the workload and exacerbate hypertension. It is often better to reverse the drug rather than treat the bradycardia. Dexmedetomidine is usually reversed with atipamezole.

Dexmedetomidine has a biphasic effect on blood pressure. After administration, vasoconstriction occurs leading to an increase in blood pressure and a decrease in the heart rate. After about 20 minutes, the vasoconstriction decreases and blood pressure returns to normal or slightly below normal. The heart rate generally remains low throughout both phases. Dexmedetomidine is reversed using atipamezole.

Benzodiazepines
Diazepam and midazolam and the two most commonly used benzodiazepines in veterinary medicine today. The mechanism of action is believed to be via the activation of the GABA receptor complex. Benzodiazepines cause skeletal muscle relaxation, have anticonvulsant properties, are very safe to use on sick and geriatric patients, and have an antianxiety or calming effect on most patients. Benzodiazepines are best used in combination (working synergistically) with other drugs such as ketamine and opioids. Benzodiazepines can be used as both pre-medications and induction agents, but they are not often effective when used alone or in young, healthy animals. In rare cases, excitation can be caused rather than tranquilization. Benzodiazepines can be reversed with flumazenil. Due to the solubility of diazepam, it should only be given IV. The uptake of diazepam is variable when given IM or SQ. Midazolam is safe and effective when given IV, IM, or SQ.

Opioids
Opioids are commonly used as part of balanced pre-medication regime. Different intensities of analgesia are obtained based on the type of opioid chosen. There are few negative effects associated with the administration of opioids and they are generally safe to use in pediatric, geriatric, and sick or critical patients. Respiratory depression can occur, but is generally only seen when higher doses of opioids are administered.

Full mu opioids include hydromorphone, morphine, oxymorphone, fentanyl, remifentanil, and methadone. These drugs can be used for mild, moderate, or severe pain. Full mu opioids are generally dosed every four hours as needed for pain control (not true for fentanyl or remifentanil as these are ultra-short acting full mu opioids).

Buprenorphine is a partial agonist opioid and should only be used for mild to moderate pain control. Buprenorphine is long lasting and is generally dosed every 6 to 8 hours as needed for pain control. Buprenorphine has a long on-set of action. It takes about 15 minutes to become effective when given IV and about 40 minutes when given IM. Buprenorphine should not be given subcutaneously due to variable uptake and an extremely long on-set of action. Buprenorphine can also be given via a trans-mucosal route in cats. This is a great option for owners who find it hard to give injections to their cats.

Buprenorphine has a high affinity for the mu receptor. It binds to the mu receptor and stays until the drug has been metabolized. Full mu opioids are generally rendered ineffective in the presence of buprenorphine. This is not ideal in patients that require analgesia for severe pain. Buprenorphine provides pain relief for mild to moderate pain.

Butorphanol is an agonist/antagonist opioid that is best used for sedation or mildly painful procedures. It is very short acting lasting only about an hour or so. Butorphanol can also be used to help reverse full mu opioids if naloxone is not available.

Cyclohaxamines
Ketamine can be used as both a pre-medication, nduction agent (often used in combination with a benzodiazepine) and as a constant rate infusion. Ketamine produces a trancelike anesthesia often termed dissociative anesthesia or catalepsy. Common responses after administration include strong palpebral reflexes, increased muscle and jaw tone, central eye position, and an apneustic breathing pattern (patient holding breath for several seconds between a short and quick breath). Unlike most anesthetic drugs, ketamine does not decrease heart rate or depress myocardial function. Most animals will exhibit tachycardia and vasoconstriction that in turn, increases blood pressure. Ketamine should be used with caution in patients with cardiac arrhythmias or some preexisting cardiac disease (hyperthyroidism or cardiomyopathy). Ketamine increases myocardial oxygen consumption.

Ketamine provides good analgesia for skin and limb pain, but is a poor analgesic for visceral pain. Ketamine may increase CSF pressure and is often contraindicated in patients with brain trauma, intracranial tumors, or inflammatory disease of the CNS. Ketamine can also increase intraocular pressure and is contraindicated with some ocular procedures or patients with glaucoma.

Telazol is another cyclohexamine that combines tiletamine with zolazepam (benzodiazepine). Telzol can be used as part of a pre-medication regime or as an induction agent. It is a very helpful drug to use on aggressive, hard to handle patients. In

some cases, patients will be sedated enough to intubate after pre-medication with telazol and an opioid. This drug can be given IV, IM, or SQ.

Anticholinergics
Atropine and glycopyrrolate are commonly used in veterinary practice to treat (or pre-treat) bradycardia in anesthetized patients. It is a controversial subject to give or not give an anticholinergic as part of a pre-medication combination. We currently administer an anticholinergic when an opioid is given as a premedication. Atropine has a quicker onset compared to glycopyrrolate and is shorter acting. Both drugs can be given IV, IM, or SQ. IV drugs are quicker acting and generally require a lower dose compared to the IM and/or SQ routes. It is important to note that anticholinergics may not work well if the patient is hypothermic.

COMMON INDUCTION DRUGS
Propofol is a hypnotic phenol that is highly lipid soluble. Propofol is a popular IV induction agent that can be used alone or in conjunction with a benzodiazepine. Use with a benzodiazepine significantly reduces the overall induction dose needed to achieve anesthetic induction. If propofol is going to be used alone, it should be given in ¼ dose increments over about 2 minutes. If it is used with a benzodiazepine, the propofol should be injected first with a ¼ dose given over about 30 seconds. Half the benzodiazepine dose is then administered. If additional propofol and benzodiazepine are necessary, the steps are repeated. The entire calculated dose of propofol is rarely needed when given at the correct speed. It is important to remember that propofol can cause profound periods of apnea and hypotension so it is essential to give is slow and preoxygenate. Propofol has a rapid onset and a short duration of action (about 10 minutes) when given as a single dose. In canine patients, repeated doses of propofol or CRIs are well tolerated and do not affect the overall recovery. Feline patients are different in that repeated doses or CRIs can contribute to a prolonged recovery. Propofol is a poor analgesic, therefore analgesic drugs need to be administered if a painful procedure is being performed.

Etomidate is an imidazole drug used for induction of anesthesia in small animals. Etomidate is short acting and produces minimal cardiovascular changes (heart rate, rhythm, cardiac output, and blood pressure). It is therefore a good drug for patients that have cardiovascular compromise. Etomidate is a poor analgesic, therefore analgesic drugs need to be administered if a painful procedure is being performed. It is advised to give etomidate with a benzodiazepine. Etomidate is administered in a similar manner to propofol. Etomidate should not be used without administering premedications due to the high incidence of myoclonus and pain on injection. Etomidate can cause depression of adrenal cortical function and should not be given to animals with Addison's disease.

Ketamine used in conjunction with a benzodiazepine is one of the most common induction agents used in practice today. See section above.

Opioid inductions are generally used in debilitated patients including those with cardiac compromise. Fentanyl is commonly used as an induction agent, but other opioids such as hydromorphone or oxymorphone can be use as well. A benzodiazepine should be used in conjunction with an IV opioid and the combination is administered in the same manner as propofol. The immediate area should be kept quiet during an opioid induction because patients are not usually fully anesthetized and can be difficult to intubate even when the full calculated dose is administered. Placing a small amount of lidocaine onto the glottis can help facilitate endotracheal intubation.

Alfaxalone is a progesterone derivative neuroactive steroid. This drug produces hypnosis and muscle relaxation by enhancing the inhibitory effect of GABA in the brain. Alfaxalone can be given IM or IV. As an IM injection heavy sedation is often achieved after about 5-10 minutes. As an IV induction agent, relaxation and anesthesia is rapidly achieved. Alfaxalone is generally used with a benzodiazepine when given IV. This drug combination is given slowly to effect in the same manner as propofol and benzodiazepine. Apnea is a potential side effect therefore caution should be used when given to patients with a difficult airway. Alfaxalone is a good alternative to a propofol CRI in cats. Recovery is slow in cats given a CRI and twitching may be present on recovery.

MAINTENANCE ANESTHESIA
Most general anesthesia is maintained via an inhalant such as isoflurane or sevoflurane in oxygen. Isoflurane and sevoflurane are potent vasodilators and can have a dose dependent effect on hypotension. These inhalants act rapidly and are only minimally metabolized by the liver. Changes in anesthetic depth can be changed rapidly. Minimum alveolar concentration (MAC) is the concentration in the alveoli required to prevent 50% of a group of animals from responding to a painful stimulus. The MAC for isoflurane and sevoflurane for dogs and cats are 1.28/1.63% and 2.35/2.58% respectively.

Many factors affect MAC including patient status, pregnancy, age, hypothermia, anemia, and pre-anesthetic drugs. Iso and sevoflurane do not provide analgesia therefore an analgesic drug must be used if performing a painful procedure.

Nitrous Oxide
Nitrous Oxide is gas inhalant that can be used in conjunction with other gas inhalants such as isoflurane or sevoflurane. The use of nitrous oxide provides analgesia, but it cannot be used to induce animals because the MAC is close to 200% or higher depending on species. Nitrous oxide is a great adjunct anesthetic because it reduces MAC of other inhalants by 20 to 30%. Nitrous oxide has little effect on the cardiovascular, respiratory, hepatic, or urinary systems and when used correctly, has a wide margin of safety. Using nitrous oxide reduces the amount of oxygen available to the patient. It is therefore important to use an oxygen monitor. Nitrous oxide is usually delivered at a percentage of 60% to 66% with the remaining percentage of gas being oxygen (up to 100%). Oxygen should generally not drop below 33%. Nitrous oxide should be discontinued at least 5 minutes prior to turning off isoflurane or sevoflurane and a high fresh oxygen gas flow should be administered. This will help prevent diffusion hypoxia.

CONSTANT RATE INFUSIONS
CRIs are commonly used as an adjunct to general anesthesia. Analgesic CRIs include ketamine, lidocaine, fentanyl, dexmedetomidine, and MLK (morphine, lidocaine, and ketamine together). Using an analgesic CRI provides a balanced or "multimodal" approach to maintaining anesthesia. The use of these drugs often reduces MAC and provides an additional source of pain management.

Propofol or alfaxalone can be used for total intravenous anesthesia (TIVA). Even though gas inhalants are not used during TIVA, you should still intubate, provide oxygen and if needed intermittent positive pressure ventilation (IPPV). Propofol and alfaxalone CRIs are useful for surgeries or procedures involving the trachea. It is also useful for patients with ICP.

POST-OPERATIVE MEDICATIONS
Post-operative medications should be given when a painful procedure was performed. Common post-operative drugs include full mu opioids, buprenorphine, butorphanol, tramadol, and NSAIDS. NSAIDS used in conjunction with opioid administration help provide multimodal analgesia and should be used in healthy patients not concurrently receiving steroids or those with increased renal and/or hepatic values.

DRUG COSTS
It is important to consider the cost of anesthetic drugs in most clinical settings. While it is ideal to carry every anesthetic drugs on the market, it is often not practical. All drugs have a specific use and can really be beneficial for certain surgical or medical procedures. The caseload of the clinic should be taken into consideration when purchasing drugs. If a clinic had to choose between opioids, I would suggest morphine, methadone, butorphanol and buprenorphine. Morphine is cheap, excellent for sedation and analgesia, but causes vomiting in almost all patients. Methadone is expensive, has variable sedation but does not cause vomiting. Butorphanol is great for sedation, mild pain relief and is very short acting. Buprenorphine is expensive but is long lasting, easy to send home with owners, can be given trans-mucosal in cats, but is only good for mild to moderate pain. As you can see, there are pros and cons to all drugs. Below is a table listing estimated costs of common anesthetic drugs.

CONCLUSION
Although we as technicians cannot prescribe drug protocols, we are often the staff inducing, maintaining, and recovering patients from anesthesia. In order to provide excellent patient care, we must understand what drugs we are administering, why we are administering them, what effects they may have on the specific patient, and what options are available if the desired effects are not reached. Educated technicians can make a huge difference in patient outcome and overall care.

SUGGESTED READING
Bryant, S. (2010). Anesthesia for Veterinary Technicians. Wiley and Sons.

Seymour, C. & Duke-Novakovski, T. (2007) BSAVA Manual of Canine and Feline anaesthesia and Analgesia. 2nd ed. British Small Animal Veterinary Association.