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Anaesthesia for Nurses Mini Series

Session Three: Commonly Used Anaesthetic Medications

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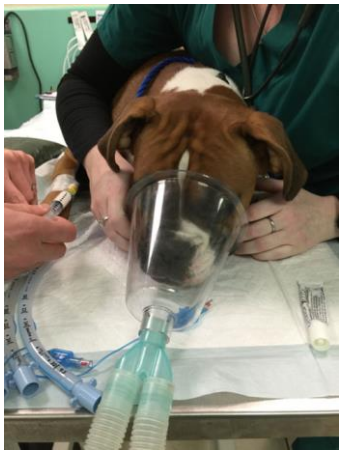

Anesthesia for Nurses: Week 3

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Commonly Used Drugs in Anaesthesia

Premedication and Sedation

Sedatives agents, or premedicants, are used for a number of reasons as part of an anaesthesia protocol. The use of premedication has several benefits for patients, and staff! Some agents may be sufficient when used alone, or in combination with other drugs, to sedate or immobilize an animal sufficiently to allow a minor procedure to be performed, e.g. ultrasonography or radiography. They can decrease stress before and during induction of anaesthesia, which may make for safer and easier handling of the patient for a procedure, and contribute to a smooth and quiet recovery. Importantly they contribute towards a balanced anaesthetic technique, thereby reducing the dose of other anaesthetic agents required for induction and maintenance of anaesthesia, along with providing a role in multimodal analgesia techniques.

Phenothiazines

Acepromazine is a common premedication used within veterinary practice and has excellent effects as a tranquilizer in small animals. They are dopamine (01 and 02) receptor antagonists, having calming, anti-psychotic, mood- altering effects. It does however have some downsides, it is a potent alpha-1 adrenergic receptor antagonist, therefore will lead to peripheral vasodilation and hypotension, and so must be used with caution in patients with cardiac disease or haemodynamically unstable patients. Stable patients with non-clinical disease may be able to compensate for the vasodilatory effects, but it is worth carefully considering its use at all, or the dosage in patients with moderate to severe cardiac disease. Hypotension may lead to a compensatory increase in heart rate, which can increase myocardial oxygen consumption. Acepromazine will protect the myocardium from epinephrine and barbiturate-induced arrhythmias. However, this benefit must be weighed against the negative hypotensive effects. Finally acepromazine is associated with a decrease in body temperature due to a resetting of thermoregulatory mechanisms, combined with increased heat loss from the periphery due to peripheral vasodilation.

Anticholinergics

Atropine and glycopyrrolate are parasympatholytic anticholinergic agents used to treat vagal-mediated sinus bradycardia and AV block by increasing the heart rate. Atropine has a faster onset time (~1–2 min IV), shorter duration of action (~20–30 min IV), and is more likely to incite tachyarrhythmias. Glycopyrrolate has a longer onset time (~2–4 min IV), longer duration of action (~1 h IV), and may be less likely to cause tachyarrhythmias. Low doses of atropine and glycopyrrolate can initially precipitate second-degree AV block, which may require additional doses of anticholinergic for treatment. Anticholinergics were once commonly used as part of a premedication protocol, but are only generally now considered for specific cases, e.g. paediatric patients where a decrease in heart rate would have detrimental effects.

Benzodiazepines

The benzodiazepines, midazolam and diazepam, exert a sedative effect via enhancement of the endogenous inhibitory neurotransmitter, gamma amino butyric
acid (GABA). Their cardiovascular effects are mild, and they are well tolerated in patients with many disease states, including cardiac and renal disease. They have minimal to no effects on heart rate, contractility, or vasomotor tone and do not lead to hypotension across a wide range of doses (0.5–2.5 mg kg−1 IV).

Although respiratory rate decreases, arterial blood gas values do not change appreciably. The major disadvantage of benzodiazepines is that they are inconsistent sedatives in dogs and may be poor sedatives in cats. For example, intravenous (IV) premedication doses can lead to dysphoria, excitement, ataxia, arousal, and, potentially, violent aggression. Although benzodiazepines decrease inhaled anesthetic requirements, this benefit can be achieved when they are combined with induction agents during the induction protocol as opposed to risking excitement when
used as premedicants.

Alpha-2 adrenergic receptor agonists

Alpha-2 adrenoreceptor agonists are potent sedative and analgesic drugs. Medetomidine is an equal mixture of two optical enantiomers, dexmedetomidine and levomedetomidine. Proposed advantages of dexmedetomidine over medetomidine include improved analgesia and a reduced requirement for drug metabolism because only active enantiomer is presented to the liver for metabolism.

Medetomidine produces a biphasic effect on blood pressure (initial increase followed by a return to normal or slightly below normal values). Heart rate is decreased throughout the period of alpha-2 agonist administration, and normal expected heart rates are 45-60 and 100-115 beats per minute for dogs and cats, respectively.

Alpha-2 adrenergic receptor agonists (dexmedetomidine, medetomidine, etc.) are usually contraindicated in patients with cardiac disease. Alpha-2 agonists cause intense peripheral vasoconstriction and decrease sympathetic outflow from the central nervous system. The severe increase in systemic vascular resistance leads to a marked increase in blood pressure, a significant increase in myocardial afterload, and a baroreceptor-mediated reflex bradycardia. Some patients may demonstrate a period of vasodilation and arterial hypotension after the initial hypertension. The initial baroreceptor-mediated bradycardia is exacerbated by a decrease in centrally mediated descending sympathetic tone. Alpha-2 adrenergic agonists can also produce AV blockade and ventricular escape cardiac rhythms. At
sedative doses, these mechanisms will decrease cardiac output (CO) by ~50–60%; dexmedetomidine at ≥5 mg/kg1 IV will decrease CO by 50–60%, and medetomidine at 20 mcg/kg−1 IV will decrease CO by at least 60%. The increase in afterload from vasoconstriction, increase in left atrial pressure from centralization of blood volume,
and decrease in CO are all mechanisms that can be detrimental to the function of a heart with underlying disease. Although alpha-2 adrenergic agonists are extremely reliable sedatives, the cardiovascular side effects are so profound that the depth of sedation may be better sacrificed in the interest of cardiovascular safety.

Minimal effects on the respiratory system are seen in healthy animals and arterial oxygen and carbon dioxide tensions (concentrations) remain within normal limits. Profound sedation after medetomidine can lead to upper airway obstruction in brachycephalic dogs.

Anaesthesia Induction agents

Anaesthesia induction involves administering a major cardiocerebropulmonary depressant to a patient in order to render them momentarily unconscious and subdue their motor, sensory, and sympathetic reflexes yet preserve their body functions enough to sustain life. It is a time of major responsibility and liability during anaesthesia of our patients. Induction can be accomplished through a variety of agents discussed below. As induction is basically a means of causing a quantified and calculated “shock” in our patients, emergency drugs and means of intubation should always be available; baseline vital parameters and IV catheter patency should be established pre induction process regardless of agent.

A smooth, stress fee induction is important. Stress and struggling increases oxygen demand and increases heart rate, and releases catecholamines, which can cause arrhythmias. Pre-oxygenation is recommended in all patients that have a reduced functional residual capacity (FRC), have respiratory or upper respiratory tract disease or anaemia.

Functional residual capacity is the amount of air left in the lungs after a normal expiration. It is important because this air left in the lungs is what provides oxygen for gaseous exchange to continue to occur during the expiratory pause when the patient is not inhaling oxygen. Pre-oxygenating the patient increases the percentage of oxygen in the FRC (room air is only 21% oxygen) therefore delaying the onset of hypoxaemia during endotracheal intubation. This is particularly important in case where intubation may be difficult or prolonged (brachycephalic patients) when the patient may become apnoeic due to the respiratory depressive effects of induction agents. It takes about 90 seconds for a patient that has not been pre-oxygenated to become hypoxaemic in the event of an airway obstruction compared to 3-4 minutes in a pre-oxygenated patient. Ideally pre-oxygenation is performed for 5 minutes using a tight fitting mask. Often a patient will not tolerate a mask and forcing them would be detrimental, in the cases, using a 'flow by' technique is probably better than nothing. Whilst pre-oxygenation is highly recommended it is important that if the patient is stressed by pre-oxygenation it should be discontinued or another technique tried.

Prepare all your equipment required for induction and maintenance prior to induction, work in a logical manner and discuss with the vet any anticipated problems or complications so you can be prepared for all eventualities.

Nearly all anesthetic induction agents are negative inotropes to some degree, and will reduce contractility dose-dependently, this is something which should be considered for every patient, and the dose altered according to the patients presenting signs, physical examination, clinical history, age, temperament etc.

Induction drugs

Many of the induction agents we use in veterinary practice act by potentiating or facilitating the effects of the inhibitory neurotransmitter gamma aminobutyric acid (GABA), by their actions at $GABA_A$ receptors (chloride channels), in the central nervous system (CNS). These agents may also inhibit L-type calcium channels and other ion channels. All general anaesthetics appear to stabilize the desensitized conformational state of the neuronal nicotinic acetylcholine receptor.

Propofol

Propofol is a phenol based induction agent, licensed for use in dogs and cats. It is probably currently the most commonly used induction agent. Until recently it was only supplied as an emulsion containing soyabean oil, egg lecithin and glycerol with no preservative, meaning it strongly supports bacterial growth so once the vial is opened it needs to be discarded or used within 8 hours. However recently a new formulation has been produced for the veterinary market (with benzyl alcohol as a preservative), which lasts up to 28 days once open and is not an emulsion. Propofol causes dose related respiratory and cardiovascular depression, which can cause apnoea immediately after induction and hypotension mainly due to vasodilation. Propofol can also cause hypotension due to a blunting of the baroreceptor reflex. These signs are particularly noted if the drug is administered quickly and in large doses. Propofol has a quick onset and smooth, rapid recovery, due to redistribution and rapid metabolism. Although propofol does undergo some hepatic metabolic, there is also evidence that extrahepatic metabolism occurs, probably in the lungs, but possibly in other sites such as the gut and the kidneys, making it a useful choice in patients with portosystemic shunts or liver disease. Feline red blood cells can be damaged following repeated propofol exposure (injections over several consecutive days) resulting in Heinz body formation, delayed recovery, anorexia, diarrhoea, general malaise, however recent reports dispute this. Cats have a reduced ability to metabolise phenolic compounds, including propofol. This leads to accumulation and a slow recovery when used as a continuous infusion. Propofol reduces intracranial pressure (by causing intracranial vasoconstriction) and does not affect cerebral blood flow-metabolism coupling making it a suitable choice for head trauma patients. Although it will not cause sloughing when administered extravascularly, it can be painful to receive (human patients explain of a burning sensation in their arms) especially in veins that are irritated (e.g., aged IV catheters, vasculitis).

Alfaxalone
Alfaxalone is a neurosteroid, which, is licensed in both cats and dogs. It is a progesterone analog that produces unconsciousness via interaction with the GABA receptor complex. Unlike Saffan (alfaxalone and alfadalone), which was solubilised in Cremaphor El, alfaxalone (Alfaxan) is solubilised in cyclodextrins therefore does not cause histamine release. Alfaxalone has similar cardiovascular effects as propofol although it has been suggested that the heart rate increases to minimise hypotension and anecdotally there may be less apnoea on induction. It is becoming increasingly popular as an induction agent and may appear to be useful in critically ill patients. As with propofol alfaxalone provides no analgesia. Peer-reviewed safety studies in dogs and cats have reported Alfaxan® to have a high therapeutic index, a rapid onset of action resulting in prompt, smooth recoveries from anaesthesia. Dose-dependent cardiorespiratory depression was noted but this was minimal at lower dose rates. No evidence of the allergic type reactions previously cited with the Saffan® formulation has been reported.

Ketamine
Is a dissociative anaesthetic, which is commonly used to as part of the 'triple combination' in cats but is often overlooked as an IV induction agent. It Increases muscle tone so should be combined with drugs that produce muscle relaxation. It provides cardiovascular stability and is unique in that it actually stimulates the sympathetic nervous system therefore, increasing blood pressure, heart rate & cardiac output. Ketamine maintains laryngeal & ocular reflexes so ocular lubricant should be used. Due to reports of hyperexcitable recoveries it is recommended that patients are recovered in a quiet calm environment and that it is used in combination with sedatives. Ketamine increases intraocular and intracranial pressure so should be avoided in head trauma patients and those with fragile eyes. Due to the increased sympathetic stimulation stimulating the cardiovascular system there is increased myocardial work and increased oxygen consumption so Ketamine should be avoided in patients with cardiac disease. Ketamine may be useful in critically ill patients to maintain blood pressure and respiration, however there is an argument that some critical cases may already be at maximal sympathetic tone to maintain perfusion to vital organs, so they are unable to further stimulate the sympathetic nervous system further to increase heart rate. Ketamine can be combined with an opioid and benzodiazepine is a standby for induction of both low and high-risk patients. Ketamine is a versatile drug and can be administered to provide general anaesthesia IV, IM and also as a continuous infusion at sub-anaesthetic doses to provide intra and post-operative analgesia. This has the added advantage of decreasing the amount of inhalational agent required.

Etomidate

Etomidate is an imidazole derivative induction agent used in people. It is a hypnotic non-controlled induction agent that also appears to act via activity at the GABA-A receptor. It is not licensed for use in animals and is relatively expensive. Etomidate is solubilized in 35% propylene glycol that renders it hyperosmolar, somewhat painful to receive in human subjects. Hemolysis of red blood cells following administration is attributed to the hyperosmolar nature of the compound. These effects can be minimized by concurrent administration of IV fluids with etomidate. The main advantage of etomidate over other induction agents is that it is extremely cardiostable and has virtually no effect on the cardiovascular system. This means it has virtually no effect on cardiac output, heart rate or blood pressure, and therefore is very useful in patients with cardiac disease or cardiovascular instability. The main disadvantage of etomidate is that it inhibits adrenal steroid production meaning that the patient is unable to mount an adequate stress response to anaesthesia and surgery, and may develop an addisonian crisis. However this appears to be of more concern after continuous infusions of the drug (so therefore is no longer used in this way) and does not seem to be significant after a single induction dose. Other undesirable side effects include; excitement on induction and (for the propylene glycol formulation) pain and thrombophlebitis on induction. Premedication is highly recommended prior to etomidate administration in order to reduce the incidence of side effects (e.g., myoclonus, vomiting), seen more commonly than with other agents.

Benzodiazepines/opioid combination

The benzodiazepines, midazolam and diazepam, exert a sedative effect via enhancement of the endogenous inhibitory neurotransmitter, gamma amino butyric
acid (GABA). Their cardiovascular effects are mild, and they are well tolerated in patients with many disease states, including renal disease. Although use of benzodiazepines is generally recommended, caution must be exercised in using these agents in animals that may demonstrate paradoxical excitement on administration, such as juvenile patients and young cats. The sole administration of benzodiazepines to most veterinary patients is generally not suggested for this reason, and, to improve sedation, co-administration with an opioid or other sedative is advised.

Neuroleptanalgesic combinations such as diazepam or midazolam (0.2–0.5 mg/kg IV) and fentanyl (0.005–0.02 mg/kg IV) administered to effect, produce minimal cardiovascular effects and are appropriate for anesthetic induction in dogs with unstable cardiovascular function. When using this combination, the anaesthetists should ensure opioid-associated bradycardias (and respiratory depression) are controlled and the patient is sufficiently sedated beforehand or is quite compromised. Alternatively, some patients may require additional induction with propofol despite the risk of dose-dependent vasodilation and hypotension. In these situations, reducing the dose of propofol with pre-induction sedation and/or combining propofol with one (i.e. midazolam) or two (i.e. midazolam/fentanyl) additional induction drugs can minimize propofol doses.

Inhalant inductions

Inhalant inductions are no longer recommended, even for aggressive or hard to handle cat and dog patients, given the great variety of premedication agents and induction agents, combinations of which can be administered through a variety of means (transmucosal, parenteral). Inhalant mask or tank inductions not only constitute health and safety/waste anaesthetic gas violations but provide an uncontrolled, stressful, and often broncho-irritating (dependent on agent) entrance into unconsciousness, the complete opposite of what we want to achieve with a low stress induction!

Generalizations regarding induction regardless of agent utilized include:
a. Always have the ability to intubate (appropriate size ET tube, laryngoscope, oxygen source) close by regardless of whether intubation is performed as part of the anesthesia procedure or not.
b. Check all intravenous catheters prior to induction to ensure patency and venous vs. subcutaneous access.
c. Take vital parameters, particularly pulse rate, pre-induction to help determine speed of administration of agent, and timeliness of intubation, if performed.
d. Pay careful attention to not open the mouth as wide as possible on all patients (due to the possibility of reducing cerebral circulation and cranial nerve function in certain species like the cat) and not extend the tongue as much (avoid hyoid apparatus damage).
e. Always be prepared with reversal and emergent agents, (calculations and immediate accessibility), but particularly around the time of using an induction agent.
f. The more critical the patient, the more the induction should be titrated to effect.

Differences between Isoflurane and Sevoflurane

	Isoflurane	**Sevoflurane**
General Information	Clinical use in 1981 Halogenated methyl ethyl ether Isomer to enflurane	Synthesized in the 1970's
Blood/Gas Partition Coefficient	1.46	0.68
Vapour Pressure at 20°C	240	160
MAC	Dog: 1.28, 1.39, 1.30 Cat: 1.63, 1.61	Dog: 2.36, 2.10 Cat: 2.58
Apnoeic Index (apnoeic concentration ÷ MAC)	Dog: 2.51, 2.61 Cat: 2.40	Dog: 3.45
Biotransformation	< 0.2% metabolized Carbon monoxide formation more likely than sevoflurane if CO_2 absorbent is dry or becomes excessively hot	3% metabolized Degraded in presence of sodalime and Baralyme to CF3 (Compound A) Compound A formation is greater in desiccated CO_2 absorbents Defluorination is about the same as methoxyflurane but serum fluoride level is much less than methoxyflurane
Odour	Pungent	Pleasant-smelling
Induction	Dogs: Time to intubation with mask induction 8.6 +/- 2.6 min Cats: No difference in quality or speed of chamber induction vs. sevo No difference in quality of mask induction vs. Sevo Time to mask induction 264 +/- 75 sec (significantly longer than sevoflurane) Time to mask intubation 292 +/- 73 sec (significantly longer than sevoflurane)	Dogs: Time to intubation with mask induction 5.7 +/- 1.6 min Faster and smoother mask induction vs. Iso Milder reflex inhibition of breathing compared to iso when administered nasally Cats: Time to mask induction 210 +/- 57 sec (significantly shorter than isoflurane) Time to mask intubation 236 +/- 60 sec (significantly shorter than isoflurane)
Recovery	No difference in recovery time or quality in dogs vs. sevo	No difference in recovery time or quality in dogs vs. iso
CNS	Maintains autoregulation of cerebral vasculature to changes in $PaCO_2$ Drug-induced anticonvulsant effects Does not induce epileptic activity at any depth	Maintains autoregulation of cerebral vasculature to changes in $PaCO_2$ Drug-induced anticonvulsant effects May predispose the brain to convulsive activity at deep levels or in pre-existing convulsive conditions
Cardiovascular	Depresses CV system in dose related fashion Decreased SV, CO, and SVR Fewer dysrhythmias and heart rate changes compared to halothane	Similar CV changes to isoflurane In cats, sevoflurane seems to allow a higher BP compared to isoflurane at deep levels of anaesthesia In cats, sevo produces does dependent CV depression, mostly

	Isoflurane may maintain more stable hemodynamic conditions vs. sevo during hypovolaemia	due to myocardial depression
Respiratory	Dose and time related respiratory depression, less than or equal to halothane As effective of a bronchodilator as halothane	Dose-related respiratory depression, similar to isoflurane In unpremedicated dogs, sevo caused less respiratory depression at higher equipotent doses compared to iso In cats at two times MAC, respiratory depression more profound than halothane As effective or better bronchodilator vs. halothane
Liver	No evidence of liver injury Liver enzyme induction similar to isoflurane Less alteration in blood flow than halothane	No evidence of liver injury Liver enzyme induction similar to isoflurane
Kidney	No significant changes in renal blood flow	No significant changes in renal blood flow Compound A formation can cause renal injury, therefore > 2L/min flow rate is manufacturers recommendation to reduce Compound A formation In low-flow systems, concentrations of compound A in dogs were below that reported to cause nephrotoxicity in rats
Skeletal muscle	Enhances neuromuscular blockade Can trigger malignant hyperthermia	Enhances neuromuscular blockade Can trigger malignant hyperthermia

Looking at the available research in dogs and cats, there are advantages to both isoflurane and sevoflurane depending on the circumstances. For example, isoflurane may be advantageous if cost is an issue, in circumstances of hypovolaemia, or if there is renal impairment. Sevoflurane may be advantageous if mask inductions are necessary or if the anaesthetist needs to be able to quickly change the depth of anaesthesia. However, when truly scrutinizing the two inhalation agents side by side, there really aren't that many major differences and one could easily justify using either one in most anaesthetic circumstances.

Understanding Pain Pathways

Pain is defined as an unpleasant sensory or emotional experience associated with actual or potential tissue damage. When a painful stimuli occurs pain receptors (nociceptors) are stimulated, this painful stimuli can be mechanical injury, ischaemia, heat or chemicals, e.g. prostaglandins and cytokines, and this creates an action potential. Action potentials are then transmitted via pain fibres (A-delta and C fibres) through the spinal cord pathways to the thalamus and higher centres of the brain, where perception of the pain occurs. Therefore, an animal needs to be conscious in order to perceive, or feel, pain. The animal will respond to this painful stimuli with various physiological responses including an increase in sympathetic nervous system activity (autonomic response), with an increase in heart rate, blood pressure, and respiratory rate. Motor activity may also increase.

Overview of pain physiology

The first stage of the pain pathway is called nociception and involves the initial trauma be it surgical or from an injury activating nociceptors in the periphery. Nociceptors are specialised sensory nerve endings that are activated by various noxious stimuli and act to convert the stimulus to an ionic impulse by the process of transduction. The second stage is transmission and involves the channeling of the noxious stimulus by a peripheral nerve into the central nervous system. The first connection or synapse in occurs in the spinal cord in the dorsal horn. There are two types of nerve fibre commonly associated with pain transmission, A fibres which transmit sharp, stabbing-like stimuli and C fibres which transmit dull, aching pain. From this first synapse the neuro-impulse may follow one of several pathways. It is channeled up to the brain in the spinothalmic tract and then the thalamocortical projections. Only when it reaches the level of the cortex will it be perceived as pain. The thalamus and cortex are responsible for pain perception. Modulation of this neuro-impulse may take place within the spinal cord itself by neuro-modulators such as endogenous opiates and also by descending inhibition from higher centres within the brain itself. This process is important, as it may be a protective mechanism to allow an injured animal to escape from a predator.
It is important to note that the pain pathway is therefore not a one-way system and both descending and ascending inhibition and activation may occur. This is an important concept when considering the changes that occur within the nervous system during the development of chronic pain.

Sensitization

Because the pain pathway has plasticity (i.e. it is flexible), rather than being rigid, once the pain pathway has been stimulated it can change the way it responds to further painful stimuli.

Peripheral sensitization

After a tissue is damaged by a noxious stimulus, inflammation occurs. The damaged tissue releases many different chemicals and inflammatory mediators, such as prostaglandins and histamine. This ‘inflammatory soup’ stimulates more nociceptors in the area, widening the painful area, but it also lowers the nociceptor threshold. This results in the pain pathway responding more violently to a noxious stimulus, so previously non-painful stimulus becomes painful as it now reaches the new lower nociceptor threshold (allodynia) and a painful stimulus provokes greater and more prolonged pain (hyperalgesis).

Central sensitization

A bombardment of painful impulses causes changes in the dorsal horn neurons in the spinal cord. This causes the neurons to become excitable and exaggerate further pain impulses. The neurons start to process non-painful inputs as pain signals. Central sensitization also results in secondary peripheral hyperalgesia where further nociceptors are recruited in undamaged tissue causing a more intense and more prolonged pain response. The result is a larger area that feels pain and a massive intensification of pain, which is very difficult to control.

Activation and upregulation of the N-methyl-D-aspartate (NMDA) receptor in the spinal cord is an important event in central sensitization. The NMDA receptor contributes to the transmission of noxious input from the periphery to the CNS following repeated input of noxious stimuli. It is not activated initially, but after repeated noxious stimulus activation occurs and there may be a sudden increase in the amount of noxious input to the spinal cord and on to the brain where it is perceived as pain.

Pain management in practice

Incorporating good pain management into practice involves an understanding of basic pain physiology and also some of the concepts of analgesia. The important concepts that are of benefit when producing a “pain plan” for a patient are multi-modal analgesia, preventive analgesia and pain assessment.

Due to the complexity of the pain pathways and the numerous neurotransmitters, the use of multiple drugs (a balanced or multimodal approach to analgesics) is preferred, in order to provide the most effective pain control. Additionally, the use of multiple analgesic drugs allows for decreasing the dose of any single drug, and thereby decreasing the side effects encountered. The aim should be to administer analgesics prior to tissue damage occurring, i.e. preemptive analgesia, when again will reduce the volume and frequency of analgesics required.

Pain assessment is a useful tool to allow identification of a patient in pain and therefore to provide appropriate analgesia at an appropriate time. There are a number of pain assessment tools available in small animal practice, for both dogs and cats. It is important to always use your clinical experience though and if you consider an animal to be in pain, analgesia should be administered regardless of the “pain score”. There are a number of simple scales such as a visual analogue scale or a numerical rating scale, which may be used. The most commonly used assessment tool in the dog is a composite descriptive scale, the short form of the Glasgow composite pain scale. They have several categories on which the patient is scored, each with a list of descriptors. Each descriptor is assigned a score and the total the dog’s pain score. The Glasgow composite pain scale has more recently been validated for use in cats. The Colorado State University feline acute pain scale is a similar system that has been developed for the cat.

It is important to be aware of the fact that removing an animal from its normal environment may alter its behaviour. This should be taken into consideration when assessing patients in the clinic setting. Using your own judgement and experience is the most important factor when assessing a patient.

Classes of analgesic drugs

As we previously discussed the analgesic drugs we use in practice act at different parts of the pain pathway. The three main classes of analgesics used in veterinary practice are the opioids, the non-steroidal anti-inflammatory drugs (NSAIDs) and the local anaesthetics. There use should be considered in all patients in pain whenever appropriate. As we discuss these analgesic drugs we will highlight their potential side effects and when their use may not be appropriate. Alongside the main classes of analgesics used we will also consider some of the other adjunct analgesics that have an important place in providing excellent analgesia.

Opioids

Opioids should be considered as the first line analgesics in all patients in pain. Morphine is considered the gold standard and all other opioids are compared to it. Opioids act at receptors in the central nervous system at the level of the spinal cord and the brain and may also act peripherally for example in the joints. There are a number of opioid receptors now recognised, mu, kappa and delta receptors are the most studied and a number of subtypes are also described. The mu receptor is considered the most important in providing analgesia. Opioids modulate transmission and alter perception of pain, but importantly do not block the stimulus completely.

In the UK methadone, buprenorphine, butorphanol and pethidine are currently licensed for veterinary use. Methadone, morphine and buprenorphine are widely used to provide excellent analgesia. Since methadone became licensed in the dog and cat is has increased in popularity and has some advantages over morphine. One study has shown methadone to provide better analgesia in the dog compared to buprenorphine. The same has not been currently documented in the cat, although buprenorphine has been shown to provide equal or better analgesia than morphine.

Methadone and morphine are both full mu agonists and produce excellent analgesia. Methadone does not cause vomiting or histamine release though and also acts at NMDA receptors. Both have duration of action of around four hours.

Buprenorphine is a partial mu agonist and probably still the most commonly used opioid in small animal practice in the UK. It is unable to produce as good analgesia as morphine or methadone but it has a higher affinity for the mu receptor so a longer duration of action of around 6 to 8 hours. It may be used by the oral transmucosal (OTM) route in the cat and has been shown to be as effective as IV administration provided it is not swallowed.

Pethidine is also a full mu agonist providing excellent analgesia. It has a much shorter duration of action of around 60 to 90 minutes and cannot be given IV due to significant histamine release.

Butorphanol is a useful sedative in combination with acepromazine or the alpha-2 adrenoreceptor agonists such as medetomidine. It does not really have a place to play in the provision of excellent analgesia.

Fentanyl is a full mu agonist, therefore it provides good analgesia but of very short duration. It is more commonly used as a continuous rate infusion, although is available as transdermal patches and recently was licensed in the dog as a slow release transdermal solution (see later for more information).

Unwanted effects

The side effects of opioids are respiratory and cardiovascular depression and reduced gastrointestinal motility. Respiratory depression is rarely of significance in clinical practice, but does vary with the opioid used. High dose fentanyl IV administration is the main use where it may require intervention. Cardiovascular depression is usually observed as bradycardia and again depends on the opioid, its route of administration and dose. If a bradycardia is induced which affects the blood pressure than treatment with an anticholinergic is indicated or a lower dose of opioid used.

NSAIDs

NSAIDs are the most commonly utilised treatment for a painful condition on presentation. Most NSAIDs are available in an injectable form and have duration of action of around 24 hours. They act to reduce the signs of inflammation and with that to treat the associated pain. There are many injectable forms licensed and available in small animal medicine. Their main site of action is in the periphery where they decrease inflammatory mediator production, although they are also recognised to have a central effect. Tissue damage results in disruption to the cell membrane, which releases phospholipids. Cell membrane phospholipids may be degraded by certain enzymes; of particular importance are the cyclooxygenase (COX) enzymes to produce inflammatory mediators such as the prostaglandins, prostacyclin and thromboxane A_2. It is the inflammatory mediators that act on the peripheral nociceptors and initiate them to fire and convey an action potential. NSAIDs inhibit the COX enzymes and therefore prevent the production of these inflammatory mediators. NSAIDs should be considered the first line of analgesic where possible and appropriate.

When should I avoid using a NSAID?

NSAIDs are generally safe in the healthy patient with careful and considered use but their side effects are related to their mechanism of action. Their inhibition of prostaglandin production is probably the most important mechanism related to this. Prostaglandins are important for maintenance of renal blood and gastrointestinal mucosa blood flow. NSAIDs should therefore be avoided in patients with renal disease gastrointestinal disease and those with bleeding disorders. Other conditions where their use should be avoided include hypoproteinaemia, the trauma patient, concurrent corticosteroid use, the vomiting/diarrhoea patient, the dehydrated patient and concurrent ACE inhibitor use. Where a patient has been noted to have had a previous reaction to an NSAID it is often sufficient to change to a different drug to avoid this.

Local anaesthetics

Local anaesthetics act by blocking sodium channels, which are found on neuronal cell membranes as well as within other excitable cells such as the myocardium. Transmission of an action potential (AP) along a nerve requires depolarisation of the neuronal membrane as the AP travels. Depolarisation of the membrane involves movement of charged ions across it, of which sodium movement is the most important. Local anaesthetics act by blocking the sodium channels and preventing the action potential propagation. The clinical effect of a local anaesthetic depends on the dose, volume and route of administration. It is for this reason that local anaesthetics are the only true analgesics. There are four local anaesthetics commonly used in the UK are lidocaine, bupivacaine, levobupivacaine and ropivacaine. Only lidocaine is currently licensed in small animal medicine.

As well as blocking sodium channels on neuronal cell membranes local anaesthetics may also block other sodium channels within the body. The presence of sodium channels within myocardial and other neuronal cells gives rise to the concern regarding toxicity of local anaesthetics. Lidocaine is the least toxic and is the only local anaesthetic that may be administered by the IV route. Bupivacaine is the most toxic, with levobupivacaine and ropivacaine in the middle. In the conscious patient signs of toxicity will initially manifest with neurological signs and progress to cardiac signs if local anaesthetic concentrations continue to increase. Neurological signs are not usually seen in the anaesthetised patient and cardiac rhythm and ECG changes will be the first indication of toxicity. To reduce the risk of toxicity careful dosing to bodyweight and assessing to ensure local anaesthetic is not inadvertently injected into a blood vessel. For example, care should be taken when performing a local block in a cat following use of lidocaine topically prior to endotracheal intubation, as the two doses used are cumulative and both must therefore be taken into account.

Locoregional anaesthesia

This is the technique of performing nerve blocks using local anaesthetic drugs, most commonly alone but also in combination with other drugs to manipulate their onset, duration or add to their effect. The term loco-regional anaesthesia is now used to describe this technique and is appropriate for describing both local anaesthesia and neuraxial (epidural and spinal) anaesthesia. The objective of loco-regional anaesthesia being to prevent or reduce perception of a painful stimulus (nociception).
Loco-regional anaesthesia is used extensively in human medicine for the provision of intra and post-operative analgesia. The techniques utilised in veterinary medicine have largely been adapted from those described in human medicine but relevant species differences in regional anatomy are required for successful block performance. With clinical and cadaver studies now being carried out on a regular basis, it has allowed for a greater understanding of the most applicable techniques for our veterinary patients.
Local anaesthetic techniques are relatively easy to perform with a good knowledge of anatomy and require very little in terms of drugs and equipment. With careful practice they can form an important part of a patient's anaesthetic management. Perhaps most importantly local anaesthetic techniques are the only part of the anaesthetic protocol that completely blocks peripheral nociceptor input, thereby aiding in reducing the development of altered or chronic pain states.

Local anaesthesia can reduce intra-operative inhalational anaesthetic requirements; therefore reducing the adverse effects associated with this class of drugs, in particular vasodilation and subsequent hypotension. They can aid in providing a stable level of general anaesthesia and reduce the number of alterations that may be required to the vapouriser setting. They are therefore particularly useful in patients were avoidance of significant hypotension and reduced cardiac contractility are desired. This may be for example in patients with cardiac, renal or hepatic disease.

NMDA receptor antagonists

The NMDA receptor is responsible for the process of central sensitisation and the development of chronic pain. It is located within the dorsal horn of the spinal cord and is up regulated and activated by intense synaptic transmission from peripheral nociceptors. Ketamine is a well-known drug that is an NMDA receptor antagonist. Commonly used as an anaesthetic agent, it also has analgesic properties at sub-anaesthetic doses. At doses of 0.5mg/kg IV and 1.0mg/kg IM it may be used for 'pre-emptive' or 'preventive' analgesia. It has been documented to improve post-op analgesia in ovariohysterectomy cases when administered prior to surgery and is of benefit when traction is applied to the ovarian ligament. Ketamine may also be used as a constant rate infusion (CRI) at doses of 5-20mcg/kg/min.

Alpha-2 adrenoreceptor agonists

Alpha-2 adrenoreceptors are widely located throughout the body and have a number of functions. Activation of the alpha-2 receptor inhibits neurotransmitter release from primary afferent neurons and affects pre and post-synaptic modulation of nociceptive signals in the dorsal horn. They are also important in controlling descending and ascending modulation of nociceptive pathways between the higher centres of the brain and the spinal cord. Analgesia is mediated by alpha-2 receptors both spinally and supraspinally. Care should be taken when using the alpha-2 agonist drugs such as medetomidine or dexmedetomidine because sedation associated with their administration may make pain assessment difficult. Important points regarding alpha-2 agonist use:

- Intensity and duration of analgesia is dose dependent
- Synergism is present with activation of opioid receptors
- Cardiovascular depressant effects may limit their use in certain patients
- Cardiovascular effects are dose dependent

Paracetamol
Paracetamol is only to be used in dogs and may be a suitable alternative when a patient becomes intolerant to NSAIDs or a NSAID cannot be administered for various reasons. It has no anti-inflammatory effects and no renal or gastric injury has been reported at clinically used doses. Its site of action is most likely as a COX enzyme inhibitor, but due to its clinical effects this is likely to be specific to within the CNS. Its analgesia and anti-pyretic effects are both thought to be centrally mediated. It may also have some serotonergic effects acting at 5-HT receptors. It is dosed at 10mg/kg IV or PO every 8 to 12 hours and may be administered in conjunction with corticosteroids or NSAIDs if necessary. The licensed veterinary product also contains codeine and is licensed in dogs for 5 days only.

As veterinary nurses, pain management is a vitally important aspect of patient care for a variety of reasons:

- The most obvious reason is because our patients cannot talk, therefore it is up to us to read and interpret their body language.
- This is not always an easy task and required knowledge of different species, breeds, and ideally of individual patients too.
- Sometimes they may be trying to tell us they are in pan, and we need to interpret the signs they are giving and their body language. Equally, they may be trying to hide their suffering from us – something some species have evolved over thousands of years to do.

- Another reason is that it is part of our duty of care, and part of our responsibility as nurses. We owe it to our patients to look after them as a whole, not just a series of body parts and systems – this is where the holistic approach comes into its own and is what makes a good nurse.
- Treating pain makes patients more co-operative and less aggressive and facilitates procedures such as intravenous catheter placement and radiography.