Rabbit Nursing: Anaesthesia and Critical Care Mini Series

Session Two: Anaesthesia- drugs and monitoring

Molly Varga BVetMed DZooMed MRCVS
RCVS Recognised Specialist in Zoo and Wildlife Medicine

Rabbit Nursing 2- Anaesthesia

Learning objectives
•The attendee will be familiar with drugs commonly used in rabbit anaesthetics
•The attendee will become familiar with the changes to clinical parameters caused by common anaesthetic drugs
•The attendee will understand the limitations of the monitoring equipment
•The attendee will understand when intervention is required during an anaesthetic when clinical parameters vary from what is expected

Sedation VS General anaesthesia
•Anaesthesia is defined as insensitivity to pain, especially as artificially induced by the administration of gases or the injection of drugs before surgical operations (from the Greek an- without + aisthesis sensation)
•Sedation is defined as the act of administering a sedative drug to produce a state of calm or sleep (from the Latin *sedare* to settle)
•Balanced anaesthetic is a combination of loss of consciousness, loss of sensation with minimal side effects usually produced by using low doses of two or more drugs, to minimise side effects

Pre-anaesthetic assessment RECAP
•When should this occur? Morning of surgery, or a certain time prior?
•TPR: how and when? How valuable is this?
•In hospital acclimatisation
•Pre-anaesthetic screening: what is useful and what isn't?
•Pre-emptive analgesia and premedication
•Provision of fluid therapy
•Pre-oxygenation

Anaesthetic agents and the cascade
•What is licensed?
•'Hypnorm'- a combination of fentanyl (pure mu agonist opiate) and fluanisone (butyrophenone) combine to provide neuroleptanalgesia
•'Alfaxan'- Alfaxalone- steroid anaesthetic agent- recently authorised for both intravenous and intramuscular use
•'Anaestamine'- one of the formulations of ketamine- a dissociative sedative.
•All other agents are used under the cascade- therefore you need a specific clinical justification for their use. Which means you need to understand the differences in what each drug achieves.

Benzodiazepines
•Diazepam, midazolam or zolazepam.
•These compounds potentiate the effects of GABA the primary inhibitory neurotransmitter by binding to specific receptors and preventing GABA reuptake, leading to sedation.
•Benzodiazpines can be used alone for their anxiolytic properties or in combination with ketamine (to produce sedation) or opioids (mild sedation).
•They may be used as a premedicant prior to administration of alpha-2 agonist combinations.

Diazepam
•Diazepam is very lipid soluble and is best used intravenously or orally,
•It is irritant to tissues when used intramuscularly. Uptake from this route can be unpredictable
•Produces anterograde (retrospective) amnesia
•Good muscle relaxation
•Anti-convulsant

Midazolam
•Midazolam in comparison is less irritant to tissues, is water soluble and has a faster onset and shorter duration than diazepam, and is more potent.
•Produces anterograde amnesia also
•Good muscle relaxation
•Anti-convulsant action

Alpha-2 agonists
•Medetomidine or dexmedetomidine (active enantiomer of medetomidine).
•These drugs act on peripheral and central alpha adrenoreceptors to produce dose dependent sedation, muscle relaxation and analgesia.
•There is minimal respiratory depression associated with these drugs.
•They are commonly used with ketamine, and opioids as part of a sedation or anaesthetic protocol.
Hepatic metabolism but urinary excretion
•These drugs cause cardiovascular effects including a peripheral vasoconstriction (will affect monitoring parameters) that leads to a spike in blood pressure and a compensatory bradycardia, that can last for around 20 minutes.
Even when the blood pressure returns towards normal, the heart rate can remain slow, due to the drugs central sympatholytic effects, resulting in reduced cardiac output, and a shunting of blood away from peripheral tissues towards the central organs

Ketamine
•Antagonises glutamate (excitatory neurotransmitter) at the NMDA receptors in the central nervous system.
•Also antagonises opioid mu receptors, whilst being agonistic with kappa and delta receptors.
•Used to provide sedation or dissociative anaesthesia. Also confers significant visceral and somatic analgesia.
•It is associated with mild increases in cardiac output and blood pressure, mild respiratory depression and retention of cranial nerve reflexes.
•Muscle relaxation is poor.
•Cardiac depression and arrhythmias may occur in animals with increased sympathetic tone eg shock or cardiac disease.
•Commonly used with either benzodiazepines or alpha-2 agonists.

Opioids
•Drugs that act on opioid receptors (mu, kappa, delta) in the nervous system that modify perception of pain
•Depending on the individual drugs affinity for certain types of receptor varying effects are achieved- eg analgesia or sedation.
•Opioids are generally used in combination with other agents such as alpha-2 agonists and ketamine, or as a premedicant for propofol or alfaxone.
•Opioids may help with shortness of breath in advanced diseases such as COPD or neoplasia

Pure mu agonists
•Morphine, fentanyl and methadone
•Fentanyl is a pure mu agonist and combined with fluanisone in ‘Hypnorm’ is the one (of two!) injectable sedative/anaesthetic agent licensed for rabbits.
•Methadone and morphine are increasingly used in premedication protocols for rabbits scheduled to undergo surgery perceived to be very painful eg orthopaedic procedures

Partial Mu Agonists
•Buprenorphine is a partial mu agonist and provides both sedation and a degree of analgesia.
•Commonly used as part of a combination where pain levels are not expected to be severe.

Mu Antagonists
•Butorphanol- sedative and antitussive
•Butorphanol produces analgesia via its affinity with kappa receptors. It partially antagonises mu receptors- may be used to antagonise effects of pure mu agonists

Propofol
•Propofol is thought to work by the modulation of the inhibitory activity of GABA at the GABA preceptors.
•It is used to induce and sometimes maintain anaesthesia. IV injection results in a rapid loss of consciousness and redistribution and rapid metabolism in the liver contribute to its short duration of action.
•It should be used with caution in animals with cardiac, renal or hepatic compromise.
•Apnoea post-induction can limit the ease of intubation using blind techniques.

Alfaxalone
•is a neurosteroid anaesthetic that works agonistically at the GABA receptors inhibiting action potential propagation and decreased activation of pathways associated with activation and arousal. It is used either intravenously or intramuscularly for sedation or induction of anaesthesia.
•Alfaxalone has minimal cardiovascular side effects but at higher doses it may cause a reduction in mean arterial pressure and a reflex tachycardia.
•No inherent analgesia.
•Alfaxalone should be used with caution in patients with hepatic compromise
•Is now authorised for use in rabbits in the UK

Gas Anaesthetics
•Volatile anaesthetic agents, the mechanism of action of which is poorly understood.
•Sevofluorane and isofluorane are the most commonly used gaseous agents in the UK.
•With few exceptions, these agents should NOT be used for induction of anaesthesia in rabbits. This procedure is distressing and potentially harmful to the rabbit and can prove fatal if the individual refuses to breathe and collapses.
•Both of these agents can safely be used for maintenance of anaesthesia ideally through an endotracheal tube, supraglottic device (V-gel) or face mask.
•Isofluorane causes dose dependent hypotension(vasodilation) as well as dose dependent respiratory depression. Whilst safer than older agents, isofluorane can still sensitize the myocardium to the effects of adrenaline leading to arrhythmia.
•Sevofluorane has a less pungent smell than isofluorane and is better accepted by rabbits. It has a rapid onset and cessation of action, and does not sensitise the myocardium to adrenaline. Similar to isofluorane, sevoflurane causes dose dependent hypotension and respiratory depression.

Less Commonly used drugs
•Acepromazine: used to be used regularly as a drug of choice for mild sedation or premedication. Is anxiolytic. Causes vasodilation via alpha-1 adrenoceptor blockade. Highly protein bound.
•Etomidate: short acting hypnotic imidazole derivative non-barbiturate induction agent, generally used with benzodiazpines to improve muscle relaxation and avoid seizure activity. Minimal cardiovascular or respiratory side effects, however significant hepatic metabolism therefore use with care in patients with hepatic function compromise. Also can cause short term adrenal suppression, with reversible inhibition of corticosteroid synthesis. Very irritant so IV only. Can result in myoclonus or seizures therefore ideally use with benzodiazepines

Antagonists
•Atipamezole: antagonises alpha-2 adrenergic agonists- reverses both the sedative, as well as cardiovascular and respiratory effects of these agents. Acts by preventing binding of alpha-2 agonists to receptors. Where metabolism of drugs is impaired, may get recycling because the half life of atipamezole is less than that of medetomidine.
•Flumazenil: antagonises benzodiazepines by competitive inhibition at the benzodiazepine binding site on the GABA receptor. Anxiety, restlessness and lowered seizure threshold can all occur when benzodiazepines are reversed.
•Naloxone: antagonises opiate drugs by competitive antagonism at the opioid receptors. Onset of action rapid, but half-life is very short. Repeat doses may be required, if the original opioid is not metabolised by the time naloxone wears off. NB reversing the opioid also reverses/removes analgesia and can leave a patient in acute pain.

Drug Combinations
•Giving combinations can reduce the dose of each drug, thereby reducing potential side effects
•Allows us to balance the pros and cons of each medication
•Increased likelihood of balanced anaesthesia (amnesia, unconsciousness and analgesia)

Alpha-2+ketamine+opiate +/- gas
•Classic ‘triple combination’
•Alpha-2 and ketamine both provide analgesia as well as sedation
•Opiate provides varying degrees of analgesia and sedation
•Opiates can depress respiration
•Ketamine increases blood pressure and cardiac output but can depress respiration
•Alpha-2 causes a blood pressure spike and compensatory bradycardia

•Alpha-2 and opiate can be antagonised is necessary but NB this antagonises the analgesia also

Ketamine+midazolam +/- alfaxalone or propofol + gas
•Ketamine- good analgesia but poor muscle relaxation
•Midazolam- good muscle relaxation and sedation
•The combination has minimal respiratory depression although can result in increased blood pressure and cardiac output
•May be used as a premedicant for propofol as an induction agent
•Inhalation anaesthesia can then be used for maintenance

Fentanyl/fluanisone +/- benzodiazepine or propofol +/- gas
•Neuroleptanalgesic authorised for use in rabbits in the UK
•Provides sedation, immobilisation and analgesia
•Suitable alone for minor procedures where muscle relaxation is not required
•Adding a benzodiazepine provides muscle relaxation.
•Lasts 20-40 minutes.
•Propofol (off license combination) or alfaxalone can then be used at reduced doses for induction of deeper level of anaesthesia and to allow for intubation
Opiate + Alfaxalone + gas
•Opiate is used for analgesic properties as well as sedation- premedicant in this combination.
•Alfaxalone is used to induce unconsciousness and allow for airway security and inhalational agent for maintenance
•Alfaxalone must be give by slow IV over 1 minute, and has no inherent analgesia.
•Some practitioners will use alfaxalone initially intramuscularly to achieve initial sedation, then a reduced dose IV for final induction.
•The opiate chosen must provide sufficient analgesia for the proposed procedure.

Securing the Airway
•Why?
•Rabbits often have both upper and lower airway infection
•Lung fields are small in comparison to other species- inflation is crucial
•Lung inflation dependent on diaphragm and therefore intra-abdominal pressure
•Allows for ventilation when indicated
•Allows for finer control of the anaesthetic
Intubation Techniques

Blind Technique
•NB rabbits have complete tracheal rings- there is no stretch
•Tracheal diameter is smaller compared to more familiar species
•Tube fit should be snug but not tight, and cuff inflation should be avoided (risk of stricture)
•Once rabbit is asleep enough, a suitable size tube is lubricated and introduced into the back of the mouth and directed towards the larynx Local anaesthetic can be trickled down the inside of the tube to provide reduced sensitivity to touch here.
•Listen to the breath sounds and gently advance the tube into the trachea when the glottis is open during inspiration. Placement can be confirmed visually or by capnography
Endoscopic guided
•As above but placing the endoscope within the lumen of the ET tube allows visualisation of the larynx.
•Endoscopes that are small enough are VERY expensive- the rabbit MUST be sufficiently asleep to make certain it doesn't try to bite the tube/endoscope. A mouth gag may be safest

Otoscopic guided
•As above, but an otoscope is used to visualise the larynx
•A bitch urinary catheter is used as a guide- threaded down the otoscope into the trachea, and then the otoscope can be withdrawn and the ET tube threaded down the catheter and into the trachea. The guide is then withdrawn.
•Alternatively the ET tube can be introduced into the glottis by passing it down the side of the otoscope, so there is a degree of visualisation- this is technically more difficult

Supraglottic Airway Devices
•Supraglottic airway devices are the gold standard in human anaesthesia
•The device is advanced directly through the mouth and the end-piece forms a seal with the glottis
•Placement must be confirmed with capnography ideally
•Seal is tight enough to facilitate ventilation
•Can be sensitive to movement of the head
•Slightly tight devices can occlude the blood vessels at the base of the tongue leading to tongue cyanosis in the face of adequate oxygenation elsewhere

Assessing Depth of Anaesthesia
•Loss of righting reflex
•Reduction in jaw tone
•Tail or toe pinch
•Loss of swallow reflex
•Loss of palpebral reflex
•Loss of corneal reflex
•Reduction in anal tone

Monitoring Options
•Nurse with a stethoscope- checking heart rate, pulse rate, capillary refill and respiratory rate and depth
•Pulse oximetry
•Capnography
•Real time ECG
Audible heart monitor/Doppler probe blood pressure

Pulse Oximetry
•Measures the degree of oxygenation of the blood.
•Give an indirect indication of the efficiency of ventilation
•Pigmentation, small size and high heart rates can all affect how accurate the instrumentation is
•Can be used on the tongue, ear, occasionally vulva.
•NB be VERY cautious about clipping hair off feet to use for pulse oximetry- this hair often doesn't grow back readily.
Capnography
•Indicator of respiratory/ventilation efficiency and cardiac output
•Measure % CO2 exhaled by the patient
•Specific adaptors can be used to reduce dead space
•In-line capnography- direct immediate measurement of exhaled CO2
•Side-line capnography- measurement of remote from circuit with a slight time delay

Real-Time ECG
•Gives instantaneous data regarding cardiac function and output
•Normal values are available and validated
Audible Heart Monitor/Doppler Probe
•Using the Doppler probe from a blood pressure monitor allows hands free audible cardiac monitoring.
•Probe can be placed over either a relatively central or a peripheral artery
•Using probe over a peripheral artery also allows blood pressure to be monitored periodically as well
•Gives an idea of both cardiac output and efficiency

Ventilation
•Artificial ventilation is becoming the standard of care for many veterinary patients
•Means that the lung inflation is controlled and that oxygenation can indirectly be controlled
•No longer requires muscle relaxants- controlling the rate and depth of respiration gently at the beginning of an anaesthetic removes the respiratory drive
•Long and deep will keep them asleep

Volume Cycling
•Relies on knowing the tidal volume of the species in question
•Approximately 6ml/kg in rabbits

•The ventilator can then be set to an appropriate volume which is then expected to adequately inflate the lungs
•The ventilator applies the set volume only, regardless of the pressure achieved. This could mean that there is under or over inflation

Pressure Cycling
•Relies on knowing what is a safe pressure to inflate the lungs up to
•Approximately 10-15mgHg is usually safe
•The ventilator will continue to inflate until the required pressure is reached
•Requires a snug fitting cuff to the ET tube or the pressure will never be achieved
•Volume required for ventilation will vary

Approach to a Routine Anaesthetic Intervention
•Make certain you are happy the patient is normal
•Reduce stress in the environment
•Premedication and pre-oxygenation are sensible
•Place IV catheter
•Calculate and draw up appropriate drug doses
•These patients should be amenable to most anaesthetic protocols, as long as the monitoring is excellent
•Elective anaesthesia must have a good outcome
•Remember good analgesia is anaesthetic sparing- make certain your analgesic protocol is multimodal and appropriate

How to Approach Difficult Cases
•Define and address the abnormalities present- in particular with respect to gut motility (if appropriate) and fluid balance.
•Consider issues with the individual that will impact induction, maintenance and clearance of anaesthetic. Stabilisation and pre-oxygenation are beneficial
•Plan a protocol, usually a multi drug/low dose protocol that will have minimal impact on cardiac, respiratory and fluid balance reserve capacities. Consider how these drugs will affect monitoring parameters
•Have emergency drugs/antagonist drugs drawn up. Discuss a worst-case scenario plan
•Consider the use of a ventilator

Tachycardia
•Heart rates >300-350 are tachycardic for most rabbits
•Check efficiency of perfusion (CRT and peripheral pulses)
•Consider whether the drugs used would increase heart rate
•Consider antagonist if appropriate
•Consider analgesia- improve this if inadequate
•Consider atropine/glycopyrrolate to reduce heart rate medically
•NB many rabbits have atropinase so atropine may not work
•Re-assess regularly

Bradycardia
•Heart rates below 120-150 are bradycardic for most rabbits
•Check peripheral perfusion
•Consider whether the drugs used could cause this
•Antagonise drugs if appropriate
•Reduce the amount of anaesthetic being provided if on gas
•Re-assess regularly

Hypertension
•Suggests inadequate analgesia and and anaesthesia
•Check both of these, as well as heart rate
•Consider whether the drugs used could be the cause
•Antagonise these if indicated

Hypotension
•Suggests either overdose of anaesthetic or blood/fluid loss
•Can result in poor organ perfusion and ongoing issues
•Check anaesthetic levels and doses
•Consider whether the drugs used could be the cause of the change noted
•Antagonise drugs if indicated
•Provide suitable fluid therapy ie fluid volume replacement as well as ongoing losses and maintenance requirements

Respiratory Arrest
•Anaesthetic depth too deep
•Issues with dead space
•Animal losing respiratory drive due to concurrent issues- Check anaesthetic depth and provision

Hypothermia
•Excessive heat loss due to body surface area
•Can significantly affect recovery from anaesthesia
•Active warming- heat pads, warmed fluids, hot hands, Bair Hugger
•NB beware of causing skin damage/thermal burns

Hyperthermia
•Malignant hyperthermia- can be an individual response to anaesthetic agents
•Actual fever- this requires fluid therapy and potentially NSAIDs- should be aware of this prior to GA
•Over-warming
•Check warming methods- remove/stop
•Check for burns
•Cooled fluids, application of cooled water to extremities etc

Causes of Anaesthetic Mortality
•Cardiac pump failure
•Vascular collapse
•Cardiac arrhythmia associated with increased circulating catecholamines
•Pre-existing cardiac pathology
•Anaesthetic overdose
•Poor airway maintenance
•Inadequate ventilation
•Aspiration of gastric contents, shock, multi-organ failure, sepsis, thromboembolism, anaphylaxis
•Human error
•50-60% of deaths occur in the post-operative period

Factors Affecting Mortality
•ASA grading
•Familiarity with the anaesthetic
•Staffing levels
•Monitoring equipment available
•Length of procedure
•Provision of fluids
•Intubation/mask
•Lack of appropriate analgesia
•Post-operative monitoring

Considerations for high risk patients
Paediatric Patients
•Small weight, so accurate weighing is essential particularly if injectable drugs are to be used
•High surface area to volume ratio, so heat loss is a real threat
•Stress can lead to hyperglycaemia, but not eating can lead to hypoglycaemia
•Mouth and trachea size not amenable to intubation. For very small animals airway control is not easily possible
•Small size can make intravenous access challenging as well- consider intra-osseous access
•Very juvenile patients may have reduced or limited ability to metabolise anaesthetic drugs

•Little option of drug redistribution to fat or muscle so prolonged recoveries
•Most body systems are immature
•Cardiovascular system: BP lower; HR, CO and CVP are higher than adults. Circulating volume also higher. Sympathetic and parasympathetic innervation to heart mature at different times
•Respiratory: Increased O2 demand cf adults, and lungs are more compliant so sensitive to pressure damage
•Hepato-renal: hepatic enzyme systems for biotransformation are not mature, albumin levels are low, renal concentrating ability is less than adults, glomerular filtration is not mature and fluid requirements are increased due to poor urine concentrating ability.
•Metabolic: fasting results in rapid use of hepatic glycogen stores so glucose levels reliant on gluconeogenesis rapidly. Hypoglycaemia made worse by chilling and septicaemia.
•Thermoregulation: body size and reduced ability to thermoregulate result in hypothermia, which can lead to bradycardia, prolonged drug metabolism and prolonged recovery

Patients with Gastrointestinal Stasis or Blockage
•Gastro-intestinal stasis or blockage can be associated with a cascade of effects on electrolyte balance within the body.
•Physical size of the gut can impede respiration and affect venous return to the heart.
•Potassium in particular can be affected (potassium in secreted in saliva, but reabsorbed in caecum and colon), causing cardiac side effects
•Can see hyper- or hypoglycaemia
•Secondary issues with fluid balance also occur that can be made worse if blood pressure is affected. Make certain fluid balance is addressed, fluid choice can be critical
•At minimum check the animals electrolyte status. In cases of gut stasis avoid anaesthesia until the animal is stable. In cases of blockage, make yourself aware of the animals status and plan a protocol that will mitigate the risks.
•Make certain there is appropriate analgesia- consider use of CRI
•Horses having GI surgery have double the risk of dying compared to other equine surgeries

Conclusions
•Assess the patient properly- case selection is key
•Record baseline clinical parameters when the patient is at rest and not stressed
•Use a protocol that you are familiar with and works for you- it will generally be more predictable
•Make certain that the pre- and post-operative periods are carefully monitored Try to ensure a low stress environment and make certain that the animal is either eating or being assist fed and passing droppings, that it is maintaining its fluid balance or receiving parenteral fluids. Make certain analgesia is sufficient for the expected level of pain