Veterinary Anesthesia and Analgesia: Can You Teach an Old Dog New Tricks?

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ANESTHESIA

Many of the currently used induction agents for dogs and cats have been approved for use in human medicine for decades, but have only recently become popular in veterinary medicine. This seminar will review the induction agents available in USA and discuss some of the newer techniques associated with them.

Induction of anesthesia is the passing from a conscious state to an unconscious state.

INDUCTION AGENTS

Barbiturates

Barbiturates have been used in veterinary practice for decades. Unfortunately, barbiturates are not currently available in the USA, so this seminar will not discuss them further.

Propofol

Propofol is now widely used in veterinary practice.

Mechanism of Action

Propofol works by binding to the GABA receptor (the primary inhibitory neurotransmitter binding site)

CNS Effects

Propofol produces CNS depression and unconsciousness. Propofol is considered "cerebral-friendly" because it decreases cerebral oxygen consumption, decreases cerebral blood flow (CBF), lowers intra-cranial pressure and quiets the electroencephalogram (EEG). Additionally, there is evidence that propofol may increase cerebral autoregulation and may therefore be the drug of choice of patients with CNS disease.

CV Effects

Propofol causes myocardial depression and vasodilation similar to the barbiturates. Unlike the barbiturates there is not a compensatory increase in HR to maintain cardiac output. Propofol does not sensitize the myocardium to arrhythmias.

Respiratory Effects

Propofol causes significant respiratory depression. The majority of the respiratory depression is RATE related. Therefore, if given slowly, most animals will continue to

breathe spontaneously. Not having the **ability** to intubate and ventilate a patient after propofol induction is in the author's opinion malpractice.

Analgesic Effects
Propofol provides no analgesia.

Metabolism
Propofol undergoes significant hepatic metabolism, but also undergoes extra-hepatic metabolism as metabolism is faster than hepatic blood flow. In patients with end stage liver disease, or in pigs during liver transplants, the metabolism rates for propofol are virtually unchanged. Therefore propofol is often a good choice for patients with altered liver metabolism.

Muscular Effects
Propofol produces good muscle relaxation. Isolated muscle myoclonus can be seen. Myoclonus is self limiting and not pathologic.

Miscellaneous
Propofol should be administered IV only. Extravascular administration does NOT result in skin sloughing (compared to the barbiturates), but will not result in anesthesia. Most propofol formulations have no preservative and are a great culture medium. Aseptic technique and strict sterility must be used. The remainder of the bottle should be used within 12 hr of opening bottle. Putting the remainder in the refrigerator only makes YOU feel better.
Prolonged (CRI) or repeated dosing of propofol in cats has resulted in Heinz body formation. Single induction doses have not been associated with any problems in cats.

What's new with propofol?

PropoFlo-28 is a recently marketed formulation that contains the preservative benzyl alcohol. It is labeled for a 28 day shelf live. It is only approved for DOGS. According to the product literature, the concentrations of benzyl alcohol used in this formation may be toxic to cats.

Administration of other GABA agonists (e.g. benzodiazepines (diazepam/ midazolam)) immediately before propofol can decrease the amount of propofol needed by almost 50%. Administering a potent opioid (e.g. fentanyl) can reduce the dose of propofol up to 75%). This is cost saving, and also decreases the cardiovascular and respiratory depression seen with bigger doses of propofol.

Dissociative Anesthetics (Ketamine/ Tiletamine)
Ketamine and tiletamine (part of the combination Telazol) are anesthetics known as "dissociatives", because they dissociate the thalamo-cortical and limbic systems. These drugs produce an altered consciousness, or catalepsy, where patients either may not

know or do not care what is happening to them. Furthermore, the dissociatives produce amnesia and provide analgesia.

Mechanism of Action

Dissociatives are **NMDA (N-methyl-D-aspartate) antagonists**. Since NMDA receptors are excitatory, they work by inhibiting (antagonizing) an excitatory receptor. Most other induction agents work through stimulation of the GABA receptors which thus stimulates an inhibitory receptor.

CNS Effects

Ketamine produces unconsciousness by blocking the excitatory neurotransmitter, glutamate. Ketamine is an unusual anesthetic agent because it increases intracranial pressure, (caution with head injury/ space occupying lesions), increases intra-ocular pressure (caution with glaucoma and penetrating foreign bodies), increases cerebral oxygen demands, increases cerebral blood flow and lowers the seizure threshold which may precipitate seizures. Ketamine should be used with caution with patients with CNS disease.

CV Effects

Also unlike other induction agents, NMDA antagonist increase sympathetic tone (norepinephrine (NE) release). This results in an increase in heart rate, increase in blood pressure and an increase in cardiac output (which is often favorable). Caution should be used with animals with any cardiomyopathy or when they already have increased sympathetic tone (e.g. hyperthyroidism, pheochromocytoma).

Respiratory Effects

Ketamine often causes **apneustic** breathing (apneustic breathing is characterized by rapid breaths followed by breath-holding on inspiration). Ketamine also causes bronchodilation, which is favorable for example in asthmatic cats.

Metabolism

In dogs, ketamine is metabolized to active metabolite, nor-ketamine. Nor-ketamine has 10-30% activity of the ketamine and is excreted through kidney. In cats, ketamine is excreted mostly UNCHANGED through the kidney. Patients with decreased renal excretion may have prolonged drug effects.

Telazol is the trade name of the combination of tiletamine (dissociative anesthetic) + zolazepam (benzodiazepine); thus is similar to valium + ketamine combinations. Telazol is useful because it is a small volume to be delivered; which is useful for darting animals**.** Telazol should not be used in New Zealand White Rabbits as it causes renal necrosis. The premixed combination is convenient, but the metabolism of each drug can be different in different species.

For example in cats:

T1/2 tiletamine = 2.5 hr

T1/2 zolazepam = 4.5 hr

Cats wake up with benzodiazepine effects (slow, smooth)

For example in dogs:

T1/2 tiletamine = 2.5 hr

T1/2 zolazepam = 1.5 hr

Dogs wake up with ketamine effect (quicker, but more agitated, excited)

What's new with NMDA antagonists?

Ketamine is analgesic with somatic analgesia is probably better than visceral analgesia. NMDA antagonists also interact with opioid receptors (the previously designated "sigma" opioid receptors have been reclassified as NMDA receptors) and can be used to prevent and disrupt windup of pain in dorsal horn. Analgesia is produced as subanesthetic doses so minimal behavior effects are seen when used at analgesic doses. In humans, ~ 24hr of constant rate infusion are needed to "break" the windup cycle. It is unclear how long dogs/cats will need to be treated, but at least 24 hr is currently recommended.

Etomidate

Etomidate was first introduced into human anesthesia practice in 1972. At the time it was considered the "ideal anesthetic" due to; its ability to maintain hemodynamic stability and minimally depress the respiratory centers. Etomidate is a non controlled, non barbiturate compound suitable for rapid intravenous anesthetic induction. Etomidate is supplied as a 2% solution in 35% propylene glycol at a pH of 6.9 and has an osmolarity of ~4620 mOsmole/L (normal plasma osmolarity is ~300 mOsmole/L).

Mechanism of Action

Etomidate is an agonist at the GABA-receptor ($GABA_A$) producing hypnosis and CNS depression by enhancing the effects of the inhibitory neurotransmitter GABA. The binding of etomidate to the $GABA_A$ receptor increases chloride conduction producing hyperpolarization of postsynaptic cell membrane and making the postsynaptic neuron more resistant to excitation. Since $GABA_A$ receptors occur almost exclusively on postsynaptic nerve endings in the CNS there are few peripheral effects (e.g. cardiovascular or respiratory).

Cardiovascular System

Etomidate is unique amongst most intravenous injectable anesthetics in that is causes minimal hemodynamic changes and thus maintains cardiovascular function. Administration should not result in change to heart rate, blood pressure or contractility. Furthermore, the baroreceptor and sympathetic nervous system reflexes remain intact. Etomidate is not arrhythmogenic; does not sensitize the heart to catecholamine, and it does not cause histamine release.

CNS Effects

Etomidate is considered cerebral-friendly because it results in decreased intracranial pressure (ICP), decreased cerebral blood flow (CBF), and decreased cerebral metabolic rate for O_2 ($CMRO_2$). Since the mean arterial pressure (MAP) is essentially unchanged, this results in a favorable metabolic state for the CNS; the cerebral perfusion pressure is

increased as is the cerebral oxygen supply: demand ratio. The EEG quiets (similar to propofol, but there can be increased EEG activity at epileptogenic foci).

Respiratory Effects
Etomidate has mild respiratory effects. Induction doses can result in brief periods of apnea, but generally carbon dioxide ($PaCO_2$) is only slightly increased if affected at all. Since etomidate has limited effect on muscle relaxation, airway reflexes are generally maintained.

Endocrine Effects
Etomidate causes a reversible inhibition of the enzyme 11-beta-hydroxylase which is an integral part of the pathway that converts cholesterol to glucocorticoids and mineralocorticoids. The resultant decrease in cortisol, corticosterone and aldosterone production raises concern for patients' ability to respond to stress. Following induction with etomidate, suppression of the adrenal-cortical axis is depressed for up to 6 hours in dogs and 3 hours in cats. Single induction doses do not cause clinical problems associated with steroid production, but care should be taken with patients with pre-existing adrenal-cortical diseases (e.g. hypoadrenocorticism). Use as a constant rate infusion (CRI) is not recommended.

Muscular Effects
Etomidate does not produce significant muscle relaxation. Extensive muscle rigidity and myoclonus can be seen at and following induction, but is not associated with seizure-like EEG activity. The use of muscle relaxants (e.g. benzodiazepines) can minimize the incidence and intensity of the muscle movements.

Analgesic Effects
Etomidate does not provide any analgesia. If patients are anesthetized to facilitate surgery or painful procedures, separate analgesics should be administered.

Metabolism
In humans, etomidate is 98% metabolized by liver (2% excreted unchanged in urine) by hydrolysis or glucuronidation via plasma esterases and hepatic microsomal enzymes. Metabolites are inactive and excreted in the urine (85%) and bile and feces (15%).

Propylene Glycol
Other adverse effects of etomidate arise from the propylene glycol vehicle. The intravenous injection of propylene glycol can be painful. Pain can be minimized by administering etomidate through a running IV line. Furthermore propylene glycol causes the solution to be hyperosmotic (~4620 mOsm) compared to plasma (~300 mOsm), and thus large doses of etomidate have been associated with intravascular hemolysis.

Dose
Etomidate has wide safety margin, due to a large therapeutic index is 16 (i.e. lethal dose is 16x the hypnotic dose) compared to the therapeutic indexes for propofol and

thiopental (3 and 5, respectively). Etomidate should be titrated intravenously "to-effect". This is a benefit since it can decrease the amount of etomidate needed, and thus decrease the costs. ***Etomidate should be administered with a muscle relaxant (e.g. midazolam)***. Duration of anesthesia is directly related to dose. Constant rate infusions (CRIs) are not recommended due to the potential for adrenocortical suppression and hemolysis (see above).

Dogs: 0.5-4.0 mg/kg IV Cats: 0.5-4.0 mg/kg IV

What's New with Etomidate?

Etomidate has a long shelf life (in propylene glycol), is not a controlled drug, and is available in 10 ml vials. This makes it possible to keep etomidate in the private practice setting for the CV unstable patient.

INHALANTS

Isoflurane is the most commonly used gas anesthetic in veterinary medicine. It is relatively inexpensive, and has a good safety margin.

What's New with Inhalants?

Sevoflurane is a newer gas anesthetic that has some advantages over isoflurane.
Sevoflurane is less soluble than isoflurane, so it should take effect more quickly and be removed from the body more quickly. The time differences are real, but not likely clinically relevant and they are even less relevant if other CNS depressants are used (IV induction agents, opioids, sedative, etc).
Sevoflurane is not safer cardiovascularly than isoflurane.
For mask inductions, sevoflurane does provide 2 benefits. The first benefit is that sevoflurane is not irritating to mucous membranes and airways. The second is that the small difference in onset of action can become clinically relevant with a mask induction. The combination of the 2 advantages makes sevoflurane the better choice for mask inductions.
Sevoflurane is approximately 4x more expensive when compared with isoflurane on a cost/ml basis.

ANALGESIA

Medical and surgical advancements in veterinary medicine coupled with higher owner expectations have resulted in veterinarians being confronted with treating more patients in pain. Providing adequate analgesia is more than just being humane (which it is) or providing the type of care clients overwhelmingly want. Based on what we know from humans and laboratory animals, proper pain management decreases morbidity and mortality and allows patients to return to function more quickly.

Review of the Pain Pathway

According to the IASP (International Association for the Study of Pain) pain is "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage." The IASP further states that "The inability to communicate verbally does not negate the possibility that an individual is experiencing pain and is in need of appropriate pain-relieving treatment."[1] Nociception is the detection of a noxious stimulus (that in humans results in "pain"). Nociceptors are free (naked) nerve endings that encode mechanical, chemical, thermal energy into electrical impulses.

Fibers of primary sensory neurons
Aβ fibers: large myelinated low threshold fibers that transduce pressure and innocuous sensations.
Aδ fibers*:* small myelinated, high threshold fibers that transduce sharp well localized pain.
C fibers**:** small unmyelinated (slow), high threshold fibers that transmit slow, burning, diffuse pain.

Aδ and C fibers have a variable distribution and density.
Somatic nociceptors are both deep and superficial in the skin, subcutaneous tissues, muscles, tendons, joint capsules, periosteum, subchondral bone, and fascia.
Visceral nociceptors are located in the peritoneum, pleura, internal organs, blood vessels. They are mostly silent nociceptors (c-fiber) and respond to distention, spasm, ischemia, and inflammation. Interestingly, visceral nociceptors (vs somatic nociceptors) are not always activated in life threatening disease not always painful (i.e. perforation).

Classic pain pathway is divided into 4 parts.

1. Transduction: stimuli from periphery to neural pathway
1st order neurons are naked nerve endings in periphery with cell bodies in dorsal horn ganglia. They encode mechanical, chemical, thermal or electrical stimulus that is "transduced" to afferent action potentials on Aδ or C fibers. The action potentials are propagated by Na^+ channels. 1^{st} order neurons synapse with neurons in dorsal horn (2^{nd} order neurons).
2. Transmission: rostral movement of action potentials within pain pathway
Transmission of action potential occurs via ascending spinal tracts within the spinal cord. The spinothalamic tract (STT) is most prominent nociceptive pathway although many alternative routes are present. The transmission of 2^{nd} order neurons terminates in the thalamus.
3. Modulation: inhibition or enhancement of signal
Inhibition of nociceptive signal can occur peripherally via local effects at the nociceptor: local anesthetics, opioids, and NSAIDs can act those peripheral sites. More centrally inhibition can occur at the dorsal horn of the spinal cord; opioids, serotonin, α-2 agonists, and NMDA-antagonists can decrease pain transmission. Enhancement of nociceptive signal can occur peripherally due to primary hyperalgesia from allogens

(pain producing substances) from the tissues (e.g. histamine). Central enhancement can occur due to secondary hyperalgesia and windup.
4. Perception: conscious perception of noxious stimuli is generally considered pain. 3rd order neurons transmit information from the thalamus to higher (cortical) brain centers. If a patient is anesthetized with a general anesthetic and a toe is clamped, the entire pain pathway is activated up to the cerebral cortex (which is asleep). Without the conscious perception the patient does not "feel" pain. However, if the general anesthetic removed (turned off); the brain is now awake while the entire pain pathway is activated.

Wind-up/ central sensitization
Central sensitization occurs due to changes in dorsal horn neuron excitability. Briefly, there is a summation of potentials, which causes seconds of nociceptive activation to produce minutes of post-synaptic depolarization ("wind-up"). Furthermore there is a decrease in threshold, so that lower threshold stimuli can be perceived as pain (e.g. Aβ fibers). Thus windup can result in an increased responsiveness and a zone of secondary hyperalgesia (increased sensitivity in neighboring areas).

TYPES OF PAIN
Acute pain facilitates tissue repair. The pain response is proportional to the injury and generally responds well to most analgesics such as opioids and NSAIDs.
Chronic Pain
Chronic pain is long lasting (in humans it is longer than 3-6 month duration) and often is not proportional to the stimulus. The neuroendocrine response attenuated and there is poor response to conventional analgesics.
Neuropathic Pain is produced as a result of nerve damage (compression, transection, inflammation, chemical, radiation, surgery, tumor). There is an altered sensory processing of stimuli or ectopic activity (discharge) from axons, neuroma, or cell bodies. Pain is often described as burning or shooting.
Referred Pain is usually associated with visceral pain.

PHYSIOLOGIC RESPONSE TO PAIN
Animals in pain have varied physiologic responses. There is overall a generalized increase sympathetic tone (↑ NE). Increased sympathetic tone results increased; myocardial work, increased minute volume (respiratory work) and a decrease in intestinal and urinary motility. The hormonal response to stress increases catabolic hormones and decreased anabolic hormones, which contributes to slower healing times. Pain/stress produces a leukocytosis with lymphopenia. Depression of the reticuloendothelial system can lead to infection. Most humans respond to pain with anxiety and sleep loss. Prolonged pain is associated with depression and/or anger. Animals in pain have a **greater morbidity and mortality**. Animals in pain have longer hospitalization, more complications, and die more often.

Preemptive Analgesia has been shown to attenuate central sensitization. For prevention of central sensitization, analgesic must be given before or very soon after

pain.[1] Human patients with pre-op and post-op analgesia had lower pain scores than those just receiving post-op analgesia[2]. Patients with pre-op and post-op analgesia had smaller production of inflammatory cytokines.[2] Preemptive analgesia helps prevent/ attenuate neuropathic and chronic pain states.[3]

Multimodal Analgesia

Attenuation of painful information can be accomplished at differing sites along the pain pathway. The modulation of pain is synergistic when treated by more than one pathway. Both the extent and duration of effect is enhanced when multimodal analgesic techniques are used. An example of multimodal analgesia includes the use of NSAIDs with opioids or local blocks with an alpha-2 agonist.

ANALGESICS

Opioids

At least three opioid receptors have been identified; mu, kappa, and delta, however only mu, and kappa receptor are routinely manipulated to provide analgesia. Opioid receptors are present in peripheral tissues, including joint capsule, in the dorsal horn of the spinal cord, and in high density in the brain. Binding of the opioid agonists increases K^+ conductance which causes hyperpolarization and decreases neurotransmitters such as; acetylcholine, substance P, dopamine, and norepinephrine. Side effects associated with opioids include respiratory depression, bradycardia, decreased GI motility and nausea.

Pure mu-opioid agonists commonly available are morphine, hydromorphone, oxymorphone and fentanyl. Pure agonists have a dose dependant effect.
Buprenorphine is a partial mu-agonist and as such will have a ceiling effect, such that increased dosing will not increase the effect.
Butorphanol is a kappa-opioid agonist (with mu opioid antagonist activity). In general, the kappa agonists provide less intense analgesia, but also cause fewer side effects.

Since all opioids decrease ventilation, they should be used cautiously in patients that are in respiratory dysfunction or who are hypoxemic.

What's new for opioids??

Fentanyl patches have become quite popular for treating pain in a variety species. The ability to provide fairly steady state analgesia for days and while at home is advantageous. Cats in particular can have a positive behavior change while the patch is being used. After placement, therapeutic levels are reached in the cat in ~6hrs and ~12 hr in the dog. Patches are designed to last ~3 days, but differences can occur with

differences in uptake; warm skin facilitates uptake whereas cold skin decreases uptake. Patches should NOT be cut. Fentanyl has a large human abuse risk.

Transmucosal buprenorphine Buprenorphine is a partial mu agonist, which means it has a ceiling effect (i.e. after a certain dose, giving more does not result in more analgesia). Buprenorphine can be administered trans-mucosally (not orally) at 0.02mg/kg (20ug/kg). Research has shown that transmucosal administration is as effective and IV administration in cats[4].

Tramadol
Tramadol is classified as an opioid agonist and has a mild mu opioid action, but its metabolite (M1) has 200x the opioid binding affinity of the parent compound. Additionally, some if not most of tramadol analgesic properties are due to inhibition of reuptake of norepinephrine and serotonin (5HT).
Tramadol is well absorbed orally, but cats in particular dislike the taste.
Tramadol should be used with caution for patients taking other serotonin uptake inhibitors; (e.g. selegiline hydrochloride (Anipryl®) or fluoxetine (Prozac®). Elevated serotonin levels can lead to "*Serotonin Syndrome"* which can be expressed as drowsiness, restlessness, altered mentation, muscle twitching, high body temperature, shivering, diarrhea, unconsciousness and death.
High doses may cause anorexia.

Alpha-2 Agonists
Alpha-2 agonists (e.g. dexmedetomidine) produce profound sedation and profound analgesia by binding to pre-synaptic alpha-2 receptors at; the locus ceruleus in brain, the dorsal horn of spinal cord, and at sympathetic nerve endings. Binding of these presynaptic receptors causes a decrease in norepinephrine release which results in decreased pain conduction, decreased in arousal, and increased parasympathetic tone (vagal). Alpha-2 receptors also bind postsynaptically to alpha receptors in the peripheral vasculature causing intense vasoconstriction. The vasoconstriction can lead to a reflex bradycardia and reduction in cardiac output. Almost all drugs in this category; at almost any dose will decrease cardiac output ~50%. Alpha-2 agonists should be used with caution in patients with cardiovascular instability or who are dehydrated or hypovolemic.

What's new with alpha-2 agonists?
Micro-doses (0.5-2ug/kg dexmedetomidine) of these drugs are quite effective for analgesia with less sedation. Micro-dose constant rate infusions (CRI) can provide rescue analgesia for hours to days. I commonly use these drugs for analgesia for painful patients regardless of their need for sedation.

Local Anesthetics
Local anesthetics decrease neuronal conduction by inhibiting sodium influx and thereby stopping propagation of the action potential. The use of local anesthetics are likely the least expensive and most effect analgesic adjuncts.
Lidocaine and bupivacaine are the most commonly used injected local anesthetics.

What's new in local anesthetics?
Prilocaine in conjunction with lidocaine is available as a topical cream (EMLA®). EMLA cream is quite effective, but needs to be applied for ~30 minutes before effective. The author has used EMLA cream on radiation burns and terminal soft tissue pain.

Lidocaine patches (Lidoderm®) have been shown to work transdermally, but do not completely desensitize the area it covers. The patches appear to be effective for musculoskeletal, inflammatory and neurologic pain. Patches can be cut. Almost no systemic levels were detected in dogs[5]; so it is unlikely to see any toxicity.

The surgical placement of "soaker-catheters", which are small fenestrated catheters that are left in a surgical site are becoming more popular. By leaving the catheter at the sight of the wound or injury, local anesthetics can administered at a consistent time frame with less discomfort to the patient .

Gabapentin
Gabapentin has been used in humans to treat many pain states. Gabapentin was designed as a structural analog of GABA, an inhibitory neurotransmitter, however the analgesic effects appears to be mediated via voltage-dependent calcium ion channels (VDCC). Many of these channels in the dorsal root ganglia and spinal cord are upregulated after peripheral nerve injury.
Gabapentin has been successfully used by the author in both dogs and cats. Cats prefer administration of gabapentin to tramadol (taste wise). There is a HUGE range to the dose. I start patients at the lower end and gradually work up the dose. Somnolence is possible with high doses at first, but rarely seen if gradually increased. If gabapentin is discontinued in a patient; they should be weaned off over 2-3 weeks to prevent seizures (reported in humans) and a rebound pain phenomenon.

NMDA antagonists as analgesics
Ketamine/ Amantadine
Ketamine (injectable) and amantadine (oral) are NMDA receptor antagonists. NMDA receptor antagonists prevent and/or attenuate central sensitization (wind-up) at the dorsal horn of the spinal cord and thus may also prevent neuroma or phantom limb pain following amputations. These drugs are used at sub-anesthetic doses, so behavioral side effects should not be seen.

Amantadine is often be given with other drugs and may take days to weeks to reach full effect. Ketamine is generally administered as CRI for at least 12 hr and usually 24hs. The ketamine dose is sub-anesthetic and should not produce any behavioral changes.

NSAIDs (Non steroidal antiinflammatory drugs)
NSAIDs are drugs that have antiinflammatory, antipyretic and analgesic properties. Some of the analgesia is due to central analgesic effects, while the majority of analgesia comes from the drugs ability to attenuate the inflammatory response. Most NSAIDs are inhibitors of the enzymes cyclooxygenase (COX) which catalyzes the formation of

prostaglandins and thromboxane. COX occurs as isoenzymes, COX-1 and COX-2 which have varied effects in the body. The specificity for inhibiting COX-1 or COX-2 is drug dependant. NSAIDs are contraindicated in hypovolemic or hypotensive patients, and should be used with caution in patients with renal or gastrointestinal disease.

Carprofen (Rimadyl) is a commonly used NSAID in veterinary medicine that is approved for dogs. Meloxicam is the only NSAID in the USA approved for use in cats.

Acepromazine
Acepromazine (ACP) is a phenothiazine, major tranquilizer that causes sedation by antagonizing dopamine receptors (D2). The major side effect of acepromazine is a peripheral alpha-1 blockade that causes vasodilation. When administered alone, acepromazine provides sedation only and no analgesia. However, when administered with an opioid agonist, acepromazine potentiates the analgesic effects of the opioid.

Acepromazine is contraindicated in patients where vasodilation is an unwanted side effect, such as cardiac insufficiency, hypovolemia, or hypotension. Acepromazine should also be avoided in patients with liver dysfunction.

Bisphosphonates are drugs that restrict the action of the osteoclasts (the cells that destroy bone). They reduce the breakdown of the bone, and can be used to reduce the risk of fracture and reduce discomfort of skeletal neoplasia. They have a wide safety margin (are approved for use for 20 years in humans), however side effects can include hypocalcemia and renal toxicity. Pamidronate is an IV bisphosphonate that has been shown to provide pain relief in ~50% of dogs with skeletal neoplasia. Dose: pamidronate IV, at 1-2 mg/kg over 2 hours q 21 to 28 days. Anecdotal success has been reported in dogs with both Boniva® & Fosamax®.

Palliative Radiation is a useful adjunct for non-treatable neoplasia.

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