PAIN CONTROL IN SEVERELY SICK AND INJURED PATIENTS

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OVERVIEW

Critically ill dogs and cats often have painful conditions and can present a challenge in balancing pain control, cardiovascular stability (or lack thereof), and ability to perform repeated assessment. It is a common misconception that giving strong pain relievers to unstable patients will cause further deterioration. When used carefully and appropriately pain relievers will not cause further deterioration and will in fact often contribute to resolution of cardiovascular instability. Untreated pain increases sympathetic tone and causes a hormonal cascade that contributes to cardiovascular instability and delays healing. Fortunately, there is a vast array of options that can be safely used in critically ill and injured patients.

Pain is a different experience for every individual - there is not going to be a one-size-fits-all protocol to manage pain. Using a multi-modal approach to address pain at different receptors will allow lower doses of multiple drugs to be used, which can mitigate the side effects of a large dose of a single agent. For example using fentanyl, lidocaine, and ketamine in combination allows a lower dose of fentanyl to be used and may result in less nausea and GI stasis than if fentanyl was used as a single agent pain reliever.

ASSESSMENT

Patients should be assessed frequently to ensure pain is well controlled. Use of a validated pain scoring system such as the Glasgow Composite Measure Pain Scale (GCMPS) allows caregivers to evaluate the need for intervention, and the effect the intervention has on the patient. Because every patient's pain is an individual experience and each patient will respond differently to a particular medication, the animal should be re-evaluated shortly after administering a pain reliever to determine if the dose administered was adequate, too much, or not enough, and additional drugs administered or subsequent doses adjusted accordingly.

Patients with severe trauma (falling from heights, hit by vehicle, severe body wall trauma, etc) are likely to need opioid-based analgesia in the early stages of treatment. The pure mu opioids are the first line drugs for severely traumatized animals - including head injured patients. In fact, untreated pain may result in worse outcomes for head injured patients. Morphine, hydromorphone, fentanyl, and methadone are the most common pure-mu opioids used in veterinary medicine.

When working with very unstable animals with painful diseases or conditions the key to safety with all cardiovascular-altering drugs (sedatives, analgesics, induction agents, etc) is *start low and go slow*. Begin with the low end of the dose range, administer the drug slowly, re-assess the patient in 10-15 minutes (time to peak onset of most of the pure mu opioids when given IV or IM), and if the animal is still uncomfortable administer half of the original dose. Wait another 10-15 minutes and re-evaluate. Repeat that same half-dose again if the patient is still uncomfortable. This technique allows the clinician to slowly and safely ramp up the medications to achieve pain control. Other injectable drugs such as ketamine, lidocaine, and dexmedetomidine can be used in conjunction with opioids to provide very good analgesia and allow low doses of all to be used, minimizing the side effect profile. The technique for using any of these drugs is the same - start low and go slow. When using the start low and go slow

technique setting a timer is important - medical personnel involved in caring for very unstable patients or for multiple patients commonly lose track of time. Setting the timer reminds everyone it is time to re-assess the patient, and to administer more drugs if needed. Verbalizing the analgesia plan to the team helps to ensure the re-assessment and re-dosing occurs.

DRUGS AND ADMINISTRATION

Opioids have traditionally been the cornerstone of pain management in severely injured and critically ill animals, and remain the primary class of drugs used in these patients. They can be dosed intermittently or as a CRI, and should be used as part of a multi-modal approach rather than as sole agents. The pure mu-agonists are preferred over the partial mu-agonists and the agonist-antagonist agents in critically ill patients as the pure mu-agonists are more easily reversed using naloxone and provide stronger analgesia that either the partial or agonist-antagonist agents. Additionally, if a patient is tolerating the pure-mu-agonist poorly, the effects can be reversed (fully or partially) by administration of either buprenorphine or butorphanol, while keeping a lesser-degree of analgesia compared to reversal with naloxone which removes the analgesic properties as well.

Constant rate infusions (CRI) of pain relievers, usually an opioid with or without adjunct drugs, are very useful in the most critically ill patients. By using a CRI the dose can be titrated quickly and easily based on the patient's needs at any given time giving more minute-to-minute control of pain relief and sedation than administration of intermittent dose pain relievers. The rate can be increased during painful procedures or when the patient's level of awareness of an injury increases (for example after a walk outside), and decreased when resting quietly and comfortably in the cage. Drugs delivered as a CRI need to be administered as a loading dose immediately followed by start of the CRI. A general rule of thumb for loading doses is calculate the volume of the CRI solution to be given over 1 hour and give that IV over 2-5 minutes as the loading dose, then start the CRI at the desired rate.

Non-steroidal anti-inflammatory drugs are excellent pain relievers. Studies in humans have shown them to be superior to morphine for single bone fractures (not major poly-trauma) and renal colic. NSAIDs can be safely used in severely injured animals however they generally should not be initiated until the patient's blood pressure is stable off of vasopressors. Acetaminophen is a controversial medication. Pharmacokinetic studies suggest dogs may not convert enough of the parent drug into active metabolite to achieve therapeutic drug concentrations. Other studies have shown benefit for dogs with mild to moderate pain. The author feels it is worth considering in dogs (*never* cats) who cannot take a classic NSAID.

Local blocks and regional anesthesia are an often underutilized but powerful tool that can be used very safely in unstable animals. Landmark-guided or ultrasound-guided nerve blocks provide regional anesthesia for fractures, wounds, etc. Ultrasound-guided techniques are accessible to individuals with basic ultrasound skills. Use of the ultrasound to perform a nerve block, or to inject a fracture or deep wound site allows precision-delivery of the local anesthetic. Transverse abdominis plane (TAP) block provides analgesia to the ventral abdominal wall and is effective for surgical incisions and other body wall trauma. It can be a useful adjunct in patients with severe peritonitis. Dental blocks can be utilized for animals with severe oral and facial trauma. Lidocaine can be injected into a fracture site prior to fracture reduction or splint placement. Liposomal bupivicaine, which may provide analgesia for up to 3 days, can be injected at surgical sites, around rib fractures or for intercostal blocks, around

thoracostomy tube insertion sites, and around soft tissue wounds. Wound soaker catheters can be placed into wound beds early in the course of critical care to provide topical analgesia.

Epidural analgesia and anesthesia is also extremely useful in critically ill patients. An epidural may be used for patients with most painful abdominal conditions - surgical procedures, pancreatitis, major abdominal trauma, etc. Sacrococcygeal epidurals can be used to pass urinary catheters and perform otherwise painful procedures on the perineum with only mild sedation. For patients expected to have a painful condition for several days epidural catheters can be placed for repeated administration of epidural medications.

NON-PHARMACOLOGIC INTERVENTIONS AND OTHER CONSIDERATIONS

There are many non-pharmacologic interventions that are readily available and quite effective. Areas of inflammation may be amenable to application of cold packs (first 24 hours following injury), warm compressing, and focal hydrotherapy. Stabilization of fractures, sprains, and unstable joints can reduce noxious stimulation and pain in the acute setting and are encouraged. Long-term immobilization can lead to muscle wasting and contracture – once the acute injury is resolved exercise should begin to return normal range of motion to the affected region. Non-ambulatory patients should have assisted range of motion exercises as part of their routine nursing care to reduce joint stiffness and discomfort.

Relieving anxiety, preventing anticipation of a painful event, and providing drugs that will cause the patient to have amnesia regarding a painful event or procedure are an integral part of the patient's pain control package. Severely traumatized patients needing wound assessment or major movement may benefit from trazodone, low-dose ketamine and/or midazolam (in addition to pain relievers) immediately prior to wound assessment and cleaning. Dosed properly the patient will still be awake and in control of the airway but should be quite cooperative (particularly if also has received good analgesia) and will hopefully not remember the procedure occurred once the drugs wear off. There is huge benefit to the patient and the medical team from this - patients who do not remember the painful procedure occurring will not experience anticipatory pain when caretakers approach to change the bandages again, and patients who are not expecting their caretakers to do painful things to them are much more cooperative patients. It is considered a standard of care to administer major burns patients (both human and veterinary) amnesia-inducing drugs prior to every bandage change to reduce anticipatory pain and wind-up pain. It seems reasonable for this to become the standard of care for all painful wound care, or other painful procedures.

KEY THERAPEUTIC DRUGS

Pure mu-agonist opioids

Drug (duration)	Route	Dose for dog	Dose for cat	Notes
Fentanyl	IV CRI	2-5mcg/kg/h	2-5mcg/kg/h	Dose titrated to desired effect
Fentanyl (15-20 min)	IV	2-5mcg/kg	2-5mcg/kg	
Hydromorphone	IV CRI	0.015-0.05mg/kg/h	0.015-0.05mg/kg/h	

Hydromorphone (2-6h)	IV, IM, SC	0.05-0.2mg/kg	0.05-0.1mg/kg	
Methadone (2-6h)	IV, IM, SC	0.2-0.5mg/kg	0.2-0.5mg/kg	Also NMDA receptor antagonist
Morphine	IV CRI	0.1-0.3mg/kg/h	0.1-0.2mg/kg/h	
Morphine (2-4h)	IV (slowly), IM, SC	0.5-1mg/kg	0.2-0.5mg/kg	Give slowly IV
Oxymorphone (2-4h)	IV, IM, SC	0.05-0.4mg/kg	0.02-0.1mg/kg	
Common side effects include panting, nausea, sedation, mydriasis, hypothermia, hyperexcitability, bradycardia, respiratory depression. Urine retention has been reported with fentanyl. IV – intravenous; IM - intramuscular; SC - subcutaneous				

Partial mu-agonist opioids

Drug (duration)	Route	Dose for dog	Dose for cat	Notes
Buprenorphine (6-12h)	IV, IM, SC	5-20mcg/kg	5-20mcg/kg	Sedation apparent in 15 minutes but requires 30-45min for analgesia to occur
Buprenorphine [Simbadol] (24h)	SC	NA	0.24mg/kg	Note mg, not mcg
Buprenorphine	OTM	NA	10-20mcg/kg	OTM bioavailability in dogs is ~5% and not recommended
The partial mu-agonists antagonize the pure mu-agonists OTM – oral transmucosal				

Agonist-antagonist opioids

Drug (duration)	Route	Dose for dog	Dose for cat	Notes
Butorphanol (1-4h)	IV, IM, SC	0.1-0.4mg/kg	0.1-0.4mg/kg	
Butorphanol	IV CRI	0.03-0.4mg/kg/h	0.03-0.4mg/kg/h	0.1-0.4mg/kg IV
Moderate to strong sedative depending on dose, generally weak analgesic. Will antagonize pure-mu agonists.				

Local Anesthetic Drugs

Drug (duration)	Route	Dose for dog	Dose for cat	Notes
Bupivicaine	Local infiltration, Nerve blocks, IA	Up to 2mg/kg	Up to 1mg/kg	Can dilute 1:1 with saline

Lidocaine	Local infiltration, Nerve blocks, IA	Up to 12mg/kg Total dose	Up to 6mg/kg Total dose	
Lidocaine	IV CRI	30-80mcg/kg/min (1.8-5mg/kg/h)	Not recommended	1-2mg/kg IV loading dose
Cats are more sensitive to the cardiac depression and CNS effects of local anesthetics compared to dogs. Use with caution IV in cats. Do NOT use preparations with epinephrine IV.				

NSAIDS

Drug (duration)	Route	Dose for dog	Dose for cat	Notes
Acetaminophen	PO	10-15mg/kg q8-12h	Do NOT use in cats	
Carprofen	SC, PO	2-4.4mg/kg/d	Off label in USA	
Deracoxib	PO	1-2mg/kg q24h		
Etodolac	SC, PO	5-15mg/kg q24h		
Meloxicam	IV, SC, PO	0.1-0.2mg/kg q24h	0.1-0.2mg/kg ONCE	
Robenacoxib	SC, PO	1-2mg/kg q24h	1-2.4mg/kg q24h	
Critically ill or injured patients: should have normal blood pressure and kidney function for 12-24h, off vasopressors, prior to starting NSAIDs.				

Other Analgesic Drugs

Drug (duration)	Route	Dose for dog	Dose for cat	Notes
Amantadine	PO	2-5mg/kg q24h	2-5mg/kg q24h	
Dexmedetomidine	IV, IM	125-250mcg/m^2	150-300mcg/m^2	
Dexmedetomidine	IV CRI	0.5-2mcg/kg/h	1-2mcg/kg/h	
Gabapentin	PO	3-10mg/kg q8-24h	2-5mg/kg q8-12h	
Ketamine	Intermittent IV	0.5mg/kg	0.5mg/kg	
Ketamine	IV CRI	0.3-1.2mg/kg/h	0.3-1.2mg/kg/h	
Trazodone	PO		25-50mg total dose per cat	Anxiolytic, not analgesic