

Pain Management in Racing Greyhounds

Pain

Pain is a syndrome consisting of multiple organ system responses, and if left untreated will contribute to patient morbidity and mortality. Greyhounds incur a wide variety of injuries during races, ranging from minor lacerations to catastrophic long bone and joint fractures.

Severe soft tissue injuries and traumatic fractures cause moderate to severe pain requiring rapid, potent analgesia. The drug and dose for initial management are determined by the severity and instability of the injury and any concurrent haemodynamic instability or organ dysfunction.

On Track Veterinarians (OTVs) are faced with the task of providing, rapid, effective and safe analgesia to dogs which are hypertensive or hypotensive, tachycardic, possibly dehydrated and distressed by injury.

OTVs are also frequently required to undertake procedures on injured greyhounds (for example, bandaging or suturing) requiring a combination of sedation and analgesia to perform competently and humanely.

Management protocols will vary with the severity of the injury but will generally involve:

- combining opioids with sedatives
- combining opioids with NSAID's
- combining opioids with alpha2agonists
- NSAID's only

Remember: Injury and associated anxiety and fear induce a "stress response" which is counterproductive or even deleterious, and prolongs recovery.

PAIN = STRESS = POOR AND PROLONGED RECOVERY

Opioids - overview

Opioids are primarily used to provide profound analgesia and a degree of sedation in animals with pre existing pain and can reduce the anxiety and fear that contribute to pain and suffering (by blocking noxious stimuli).

Opioids are also frequently used as part of safe and effective sedation protocols (neuroleptanalgesia).

Opioids can act at mu (u) receptor sites and kappa (k) receptor sites located throughout the central and peripheral nervous system. Drugs can be

- pure agonists (inducing a maximal response once bound to the receptor)
- partial agonists (inducing a submaximal response once bound to the receptor)
- antagonists (inducing no response once bound to the receptor)

Opioids with a high affinity for the receptor (eg buprenorphine) have a relatively long duration of action which is unrelated to the plasma half life.

mu agonists	kappa agonists	Partial mu agonist	mu antagonists
Morphine	Butorphanol	Buprenorphine	Butorphanol
Methadone			Naloxone
Fentanyl			
Pethidine			

The desirable effects of opioids are ANALGESIA and SEDATION

The potential undesirable side effects are CNS excitation, bradycardia, hypotension, respiratory depression, vomiting/nausea and gastrointestinal stasis.

ANALGESIA is most predictably produced at mu receptor sites with mu receptor selective agonists being the most effective analgesics. SEDATION can be considered a side effect when using opioids primarily as analgesics. The most effective SEDATIVES are reported to be BUTORPHANOL and MORPHINE .

CNS excitation can be an uncommon undesirable side effect, but despite this potential, use of mu agonists in animals that are in pain will result in calming of the animal.

Opioids – commonly used

Morphine

- mu selective agonist
- excellent analgesic and effective sedative
- duration of action 4-6 hours
- dose rate 0.2-1.0mg/kg I/M, S/C, or SLOW I/V
- will not generally induce vomiting in animals already in pain (compared to use as a premedicant)
- may cause excitement in greyhounds?
- **GOOD ANALGESIA, GOOD SEDATION-THE GOLD STANDARD OPIOID ANALGESIC FOR SEVERE PAIN IN DOGS**

Methadone

- mu selective agonist
- equipotent to morphine but less effective sedative
- combined with acepromazine, diazepam or midazolam, it provides effective sedation.
- dose rate 0.1-0.5mg/kg I/M or S/C, can be given I/V for more rapid onset of action
- duration of action 4-6 hours
- **GOOD ANALGESIA, MODERATE SEDATION**

Pethidine

- selective mu agonist
- does not cause bradycardia
- half as potent as morphine
- rapid onset of action
- short duration of action (30-60 minutes). The need for frequent dosing makes it a poor choice for ongoing pain management
- useful as a premedicant
- dose rate 3-5mg/kg I/M only.
- **MILD ANALGESIA, MILD SEDATION**

Fentanyl

- potent mu agonist
- rapid onset of action (2-5 minutes)
- short duration of action (5-20 minutes) dose rate 0.005-0.02mg/kg I/M , S/C or I/V
- can be used as transdermal patches but take approximately 18-24 hours to achieve optimum plasma concentration. Effective for 72 hours.
- GOOD ANALGESIA, MODERATE SEDATION

Buprenorphine

- mu selective partial agonist
- slow onset of action (30-60 minutes for peak effect regardless of route of administration).
- S/C injection does not result in fast enough uptake so must be given I/M or I/V
- moderate duration of action (4-8 hours)
- dose rate 0.01-0.03mg/kg I/M or I/V
- binds very strongly and dissociates from receptor sites slowly making reversal or concurrent use of other opioids difficult.
- MODERATE ANALGESIA, MODERATE SEDATION

Butorphanol

- kappa selective agonist and mu selective weak antagonist (can be used to partially reverse the respiratory depressant effects of pure mu agonists (morphine, methadone)
- effective sedative
- rapid onset of action
- duration of action 1-2 hours
- dose rate 0.2-0.4mg/kg I/M, I/V or S/C
- poor analgesic for somatic pain, traumatic injuries
- MILD ANALGESIA, MODERATE SEDATION

Tramadol

Tramadol is a synthetic opioid agonist which is an analogue of codeine. It is not a controlled substance. There is diversity among specialist surgeons as to its effectiveness with a “ best of the rest” opinion prevailing. Its effects are attributed to both the direct opioid effect (mu receptors only) and the inhibition of re-uptake of serotonin and noradrenaline. Its analgesic

potency is one-fifth to one-tenth that of morphine. Hepatic metabolism of tramadol produces o-desmethyl tramadol which possesses 200-300 times the affinity for mu receptors than tramadol itself and this metabolite is largely responsible for the analgesia attributed to tramadol. There is a rapid and effective production of this first metabolite following intravenous injection. Equipotent doses of tramadol (2mg/kg I/V) and morphine (0.2mg/kg I/V) resulted in similar post operative pain scores in dogs undergoing ovariohysterectomy, while anecdotal evidence suggests similar analgesia can be obtained with equipotent doses of tramadol and morphine for mild to moderate pain.

Tramadol is available for injection as a 50mg/ml solution and can be given I/V, I/M or S/C. It is also available in capsules, slow release tablets and liquid. Used I/V or I/M it may be a useful pain relieving medication for those On Track Veterinarians reluctant to carry controlled substances on racetracks, however it is not suitable for management of fractures or severe injury. It is extremely safe and can be combined with benzodiazepines, acepromazine and medetomidine for sedation.

The severity of the injury will determine the choice of opioid and sedative to be used.

Mild pain (lacerations)	Moderate to severe pain (fractures, severe soft tissue injury)
Butorphanol	Morphine
Buprenorphine	Methadone
Pethidine	Fentanyl
Tramadol	

Alpha-2 agonists

Alpha 2 agonist drugs such as xylazine, medetomidine and the newer dexmedetomidine are reliable and predictable sedative agents. They are often combined with opioids to enhance their sedative effects. They are powerful analgesics as well. The analgesic effect of alpha 2 agonists is believed to be mediated by similar pathways to opioids, inhibiting the passage of painful stimuli through the central nervous system.

The major disadvantage associated with using alpha 2 agonists for analgesia is their potent cardiovascular side effects. Recommended sedative doses result in a hypotensive, vasoconstricted and bradycardic patient often with an arrhythmia. Most specialist anesthetists discourage the use of xylazine in dogs, citing incidents of sudden death up to 24 hours after use.

Microdoses of medetomidine (1-5ug/kg equating to 0.03-0.15ml for a 30kg dog) given I/V or I/M will give mild sedation but will provide short term analgesia. These micro doses may reduce the cardiovascular effects allowing use in a wider range of patients. If difficulties arise the drug can be quickly reversed using Atipamerzole

Dexmedetomidine is the new generation alpha 2 agonist . Literature suggests it has fewer cardiovascular effects but comparable sedative and analgesic properties given at half the dose for medetomidine.

Use of medetomidine should be restricted to young healthy, normotensive, normovolemic dogs if used at all. Xylazine is not an appropriate choice of medication for dogs.

Sedatives

Sedatives will potentiate the analgesia produced by analgesic drugs but on their own they have NO analgesic properties.

Diazepam and Midazolam

Benzodiazepines are the safest supplements to opiate sedation. I/M absorption of midazolam (Hypnovel) is better than that of diazepam and is preferred for the I/M route. Either is suitable for I/V administration.

- dose rate 0.2-0.3mg/kg I/V (preferred), I/M
- duration of action 2-5 hours.

Acepromazine

Acepromazine can be combined with morphine and methadone for severe pain and with butorphanol for milder pain to provide additional sedation.

- dose rate 0.01-0.05mg/kg I/V, 0.02-0.1mg/kg I/M,S/C
- duration of action 4-6 hours.

Sedative/opioid combinations and dose rates

Medication Combinations	Dose rate (mg/kg)	Route of administration	Comments
Acepromazine + Methadone	0.01 – 0.03 0.1-0.3mg/kg	IV, IM, SC IV, IM, SC	OR morphine
Diazepam + Methadone	0.2 0.3	IV IM, IV	OR midazolam OR morphine
Acepromazine + Butorphanol	0.02 0.2	IV, IM, SC IV, IM, SC	Slow onset IM or SC (20-30 minutes)
Diazepam + Fentanyl	0.1 – 0.2 0.01	IV IV	OR midazolam Rapid onset/short duration of action
Medetomidine + Butorphanol	0.005- 0.01 0.1	IV, IM IV, IM	Rapid onset of action resulting in recumbency for 1 hour
Diazepam + Tramadol	0.2 1 -2	IV IV, IM	OR Midazolam OR Acepromazine 0.03mg/kg

Non steroidal anti-inflammatories (nsaids)

- NSAIDS are generally less analgesic than opioids (except perhaps pethidine)
- provide analgesia without sedation
- effective for inflammatory pain (musculoskeletal or wound pain) not visceral pain
- delayed onset of action (2-4 hours) make them unsuitable for pain management in the acutely traumatised patient
- **POTENTIALLY NEPHROTOXIC IN DEHYDRATED, HYPOVOLEMIC AND HYPOTENSIVE PATIENTS**
- potential to cause gastric ulceration.

Administration of NSAID's should be carefully approached and monitored in patients with possible dehydration. The maintenance of blood supply to the kidneys is mediated by prostaglandin E2, which may be inhibited by the use NSAID's

NSAID's are most useful

- in the treatment of mild pain
- combined with opioid analgesia in moderate to severe injuries
- as continuing analgesia after discontinuation of opioids.
- in patients with no potential for concurrent haemodynamic instability (for example in dehydration or blood loss)

Conclusion

The best welfare outcome for injured Greyhounds will be achieved by prompt administration of analgesic medications which will prevent or limit pain as much as possible and avoid long term side-effects.