




Pain Management for Pregnant & Nursing Cats & Dogs



Analgesia and Anesthesia for the **Ill** or **Injured** **Dog and Cat**

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Evidence Based Veterinary Studies



- ★ **None on acute, sub-acute to chronic** use of analgesics in pregnant and lactating dogs and cats



- ★ Many peri-caesarian section analgesic/anesthetic regimens have been recommended and used with no apparent ill effects





PREGNANT AND NURSING CATS & DOGS

★ May

- Sustain injuries
- Require a surgical procedure
- Acquire a painful illness

★ All require analgesic management





Factors that may alter drug absorption during pregnancy



- ★ Decreased gastrointestinal motility → ↓
- ★ Esophageal reflux and vomiting → ↓
- ★ ↑ cutaneous blood flow may enhance absorption of transdermally administered drugs BUT
 - ↑ total body water → ↑ volume distribution
 - ↑ total body fat → ↑ volume distribution
- ★ Reduced serum albumin – due to dilution
- ★ Altered hepatic enzymatic activity – drug dependent
- ★ Increased renal function – drug dependent
 - Wunsch MJ Clin J Pain 2003;19(3):148–55.



Placental Transfer of Medications



★ ↑ or ↓ placental blood flow influences transfer of medications



★ Water soluble, protein-bound, polar or ionized ↓ transfer across the placenta

★ Placental thickness ↓ as placenta ages
→ ↑ diffusion



★ Fetal acidosis ↑ fetal opioid concentration
★ the placenta



Placental Transfer of Opioids



- ★ Highly lipophilic drugs have more rapid placental transfer
 - Transfer of meperidine>sufentanil>butorphanol, buprenorphine,nalbuphine>fentanyl>methadone > hydromorphone>oxymorphone>morphine
 - Fetal-to-maternal transfer is also rapid
- ★ Short term administration not a problem



What Dose of Analgesic For Pregnant Animals?



★ During pregnancy progesterone levels
↑ with some analgesic effect



★ A standard dose of analgesic – opioid
– may be too high for the same level
of pain in non-pregnant animals



★ How good are we at assessing pain?
– Not 100% accurate
– Not 100% of the time



Opioid Administration



- ★ All ill or injured patients should have IV access
 - Facilitate administration of medication
 - Always titrate an opioid slowly to effect to
 - avoid nausea, vomiting, dysphoria, panting
 - avoid morphine in cats due to slow action
 - Where pain still exists, add another class of analgesic



Post-op Laparotomy





*Titrate To Effect******





Opioid Selection

★ Methadone safe

- **Dogs** IV & IM routes only
- **Cats** IV, IM & oral transmucosal route

★ Fentanyl

- Transfer → fetal brain
 - Fentanyl patch in 2 human patients minimal fetal effect

★ Sufentanil > transfer than fentanyl

- ↑ reuptake back into the maternal circulation



Opioid Selection

★ Hydromorphone

- May → fetal tachycardia → caesarian

★ Morphine

- Fetal withdrawal syndrome, respiratory depression
- avoid IV in cats

★ Butorphanol

- Rapidly crosses placenta → neonatal concentration $\uparrow 0.4-1.4X$ maternal plasma





Opioid Selection

★ Buprenorphine

– Concentrates within placenta

- transplacental transfer to fetus very low
- effect on fetus dependent on serum levels
- Mild to non-existent withdrawal symptoms in newborn of mothers treated for several weeks during pregnancy

Nanovskaya T J Pharmacology & Expt Therap
2002;300:26-33

★ Tramadol → ↑ fetus

– Very poor analgesic



Opioid Reversal

Naloxone does not alter transfer or clearance of morphine across placenta

– Retention of naloxone by placenta

- Prolonging fetal exposure of opioid

– Antagonism likely by direct actions on fetal mu receptors

- Kopecky E Life Sciences 1999;65;2359-2371





NSAIDs



- ★ High fetal serum levels
- ★ Pulmonary hypertension
- ★ ? Cardiac, orofacial defects in babies
- ★ Prolonged gestation
- ★ Very little known about current NSAIDs in cats and dogs
- ★ Bottom line – do not administer



Ketamine

- ★ Rapidly crosses to the fetus in animals
 - no fetal defects observed in rats, mice, rabbits & dogs
- ★ No reports in the veterinary or human literature examining the effects on the mother or fetus at doses used for analgesia (0.2-1.0mg/kg/h)
 - 2mg/kg administered to human mothers prior to delivery → profound respiratory depression and ↑ muscle tone of the infant at birth
- ★ Increases uterine contractions
 - Oats JN et al Br J Anaesth 1979;51:11636





Miscellaneous – not recommended



★ Acupuncture

- ★ Can induce labour
 - Not recommended during pregnancy



★ Alpha-2s

- xylazine, medetomidine, dexmedetomidine
 - Not recommended



★ Thiobarbiturates - Not recommended

★ Amantadine – Not recommended



Miscellaneous

★ Gabapentin

- Did not → ↑ adverse effects in a human study
- Short term use appears safe
 - Case study pregnant mare 2.5mg/kg for 6 days due to neuropathic pain
 - Normal foal

★ Pregabalin not recommended due to adverse fetal effects



Caesarean - opioids



★ Epidural administration of fentanyl or sufentanil did not alter vigour of babies

★ Combined with bupivacaine

• Loftus JR Anesthesiology 1995;83():300-308



★ Engorged epidural blood vessels → ↓ epidural space by 30-50% → ↓ volume of drug admin





Caesarean - opioids



- ★ Epidural morphine reduces post-op analgesic requirements in humans
- ★ Avoid buprenorphine beyond immediate post-op → ↓ milk production



Caesarean - Opioids

★ Retention of morphine by placenta ~ 60 mins after administration ceases

- Prolonging fetal exposure

- Kopecky E Life Sciences 1999;65;2359-2371

★ Should lack of vigor or respiratory depression occur in puppies or kittens due to opioid administration

- one-drop of naloxone (0.4 mg/ml) under the tongue with further titration to effect will reverse adverse effects



Caesarean



★ Local anesthetics

- No effect on neonate
- Recommended



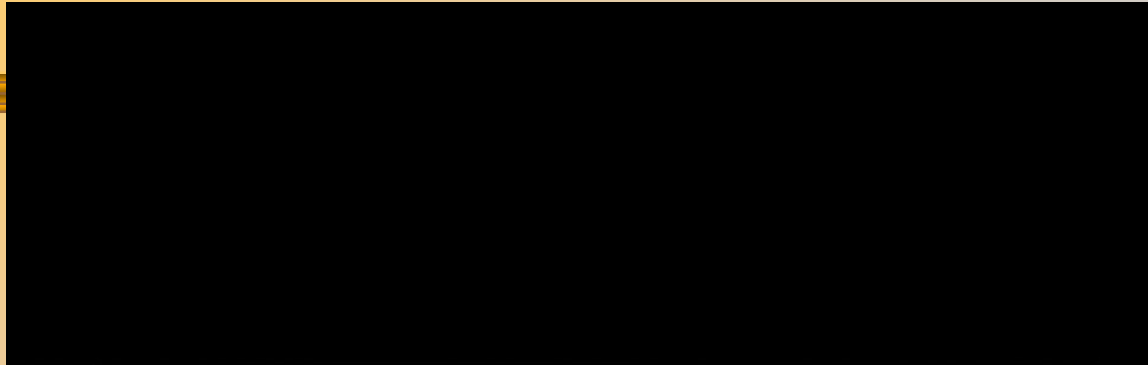
★ Post-C-Section

- NSAIA: DOGS carprofen 2mg/kg
 - Less concern for hemorrhage
 - Undetectable levels in milk





Nursing Patients





Nursing Patients



- ★ Characteristics of a drug which facilitate secretion into milk, similar to placenta and blood-brain barrier
- ★ It is estimated that the neonate receives approximately 1% to 2% of the maternal dose of a drug

– Britt R. Am J Nurs 1999;99(9):20



Nursing Patients

- ★ Morphine & metabolite in colostrum low
- ★ Methadone, oxymorphone OK
- ★ Hydromorphone in breast milk less than 1/10 of a recommended dose for neonate
- ★ Acetaminophen (**not cats**) & methadone (**oral not absorbed in dogs**) levels do not justify interruption of nursing

- Baka N-E Anesth Analg 2002;94:184-187
- Edwards JE et al Pharmacotherapy 2003;23:153-158



*Oxymorphone safe for this
litter*





Avoid

★ Meperidine

- Highly lipophilic
- Single dose is of no risk, repeated dosing may be a problem

• Wittels B et al Anesthesiology 1990;73:864

★ Buprenorphine → ↓ milk production

– Lindemalm S J Hum Lact. 2009;25(2):199-205

★ Diazepam → neonatal sedation

★ Amantadine – not recommended





NSAIDs



★ COX-2 required for kidney development

★ Veterinary approved drug levels measured in cows' milk is an indication of drug presence in breast milk

– Carprofen **not detected** in cows' milk

– Meloxicam **high levels** in cows' milk





NSAIDs Carprofen

★ Post-caesarean

- 2mg/kg SC followed with
- 2mg/kg PO q12h for 6 days
- Milk assays performed daily ~ 4 hrs post-administration of carprofen
 - all levels below low-end limit of analyzer range

★ **Follow-up on puppies 5 -106 (41.9) months**

- Serum creatinine on all subjects within normal reference ranges

★ SR Escobar Proceedings for the Society for Theriogenology September 2016;8(3): 191



Tramadol

- ★ Short-term in humans has low potential for adverse effects in breastfed infants
 - Bloor M et al Int J Obstetric Anesthesia 2012;21:163–167
- ★ Anecdotal evidence in dogs
 - **RARE** potential efficacy
 - **MORE COMMONLY** extreme sedation and inability to care for the puppies





Amitriptyline



- ★ Less toxicity than imipramine
 - low concentrations in breast milk
 - ★ May be administered to manage pre-existing chronic or neuropathic pain
 - do not administer with tramadol
 - seizure may occur
-
- Newman K. American Journal of Psychiatry. 1980;137:855–856.
 - Misri A. International Journal of Psychiatry in Medicine, 1991;21:157–171



Local Anesthetics



- ★ At therapeutic doses the concentration of lidocaine & metabolites in breast milk are small & not a risk for the infant
- ★ No risks have been reported in veterinary patients following line block for C-section
- ★ Bupivacaine diffusion catheters in humans safe levels for infants
- ★ Protect catheter from puppies and kittens



Ketamine



- ★ No reports on measurements but expected to pass into breast milk
- ★ Post-C-section suckling in humans no reported adverse effects



Herbal Medications



★ Due to the multi-ingredients & lack of information on toxicity in infants



★ **Not to prescribe**



- Ostrea EM. *Pediatr Clin N Am* 51 (2004) 539– 579



Do Not Withhold Analgesics



★ **Opioids & others**

- ★ nurse at trough level, avoid nursing at peaks



★ **If analgesia is essential** with concerns for potential toxicity in the offspring

- ★ pump & discard milk for 12 hours before resuming suckling
- ★ puppies and kittens should be bottle fed





Non-Pharmaceutical



★ Physio, comfort, hot or cold packs etc



★ Nursing releases **oxytocin** which **MAY** be a slight **adjunct analgesic**



