WHAT’S COMING DOWN THE PIPELINE?
NEWER AND FUTURE ANESTHETIC AND ANALGESIC DRUGS FOR THE SMALL ANIMAL PRACTITIONER.

ANESTHESIA AND ANALGESIA

- Looking for the next “great” tool in the box
- New drugs and new uses for old drugs
- Improve patient care and maximize outcomes

WHAT IS OLD IS NEW...

- Methadone
- Fentanyl (topical)
- Buprenorphine (transmucosal)
- Etomidate
- Meloxicam (transmucosal spray)
- Robenaxicib
WHAT IS NEW IS NEW...

- Propoflo 28® (propofol with an increased shelf life)
- Remifentanil
- Alenza
- Simbadol™ - Long acting buprenorphine
- Alfaxan®- CD (alfaxalone)

METHADONE

- Pure μ agonist opioid (synthetic)
- NMDA antagonist
  - May be best opioid for chronic pain
  - Better analgesic than buprenorphine for 8 hours post operatively
  - Less vomiting and panting than hydromorphone and morphine in dogs
  - Does not seem to elicit aggressive behavior in cats
  - Can be expensive, cannot be administered orally (unlike in humans)
- Dosages
  - Dogs 0.25 to 0.5 mg/kg, IM or IV
  - Cats 0.1 mg/kg, IM or IV

FENTANYL (TOPICAL)

- Recuvyra™
- Transdermal solution
  - Topical application in dogs only
  - 50 mg/ml fentanyl (Class II controlled substance)
- Risk Minimization Action Plan (RiskMAP)
  - Educational materials to veterinarian, staff and owners
Fentanyl (Topical)

RiskMAP
- Owner must read and sign client information sheet before application
- Only available through a restricted distribution program
  - Certified distributors
  - Veterinarian must take online training prior to being able to purchase
- High potential for human abuse and safety risks

Use
- Administered by two trained veterinarians or staff
  - Protective clothing – gloves, lab coats, and glasses or face shield
- Applied directly to the skin in the dorsal scapular area.

Dries in 5 minutes after application
- Application notice card placed on cage
- Provides up to three days of analgesia
- Applied 2 hours preoperatively
- Risk of contact for 72 hours
  - Can not be given to animals released to homes with children
  - Owners must make sure other animals don’t lick and wash hands after contact

Provides up to three days of analgesia
- Applied 2 hours preoperatively
- Risk of contact for 72 hours
  - Can not be given to animals released to homes with children
  - Owners must make sure other animals don’t lick and wash hands after contact
**Fentanyl (Topical)**
- Applied 2 to 4 hours prior to surgery
- Analgesia lasts 72 to 96 hours
- Effective for:
  - Cruciate ligament repair, ovariohysterectomy, lateral ear resection, laparotomy, liver biopsy, kidney removal, tumor removal
- Adverse reaction:
  - Tachypnea, Bradypnea, Hypertension, Hypotension, Tachycardia
  - Hypothermia, Bradycardia, Pyrexia cardiac arrhythmia, Reduced SPO2

**Buprenorphine (Transmucosal)**

**Cats**
- 0.02 mg/kg
  - Deposited in cheek
- Bioavailability is nearly 100%
- pH of feline oral cavity is between 8 and 9
- Can be combined with dexmedetomidine for transmucosal delivery and achieve good sedation
  - Dexmedetomidine 0.04 mg/kg

**Dogs**
- Bioavailability is 38±12%
- Dose for dogs to achieve analgesic effect is 0.12 mg/kg
ETOMIDATE

- Imidazole GABA agonist
- Rapidly acting induction agent
  - Used similar to propofol
  - Hypnosis lasts 8 to 20 minutes
- Produces no change in heart rate, blood pressure, or myocardial performance
- Decreases CMRO₂ (brain protective)

ETOMIDATE

- May be the agent of choice for trauma patients, cardiac disease, intracranial disease or Cesarean sections
- Side effects
  - Respiratory depression (rate and dose dependent)
  - Myoclonus
    - Administer after benzodiazepine or opioid
  - Single dose suppresses steroidal genesis for up to 3 hours
    - Do not use repeated dosing or CRI

MELOXICAM (TRANSMUCOSAL)

- OroCAM™
  - Meloxicam transmucosal oral delivery spray
  - Indicated for the control of pain and inflammation associated with osteoarthritis in dogs
    - DO NOT USE IN CATS!!!
  - Spray pump delivers uniform spray pattern and consistent droplet size for oral mucosal contact
  - Highly vascular oral mucosa allows for rapid absorption into systemic circulation
**MELOXICAM (TRANSMUCOSAL)**

- Mucosal uptake
  - Bypasses digestive tract and first pass metabolism
  - Spray is applied to cheek space
  - Well tolerated and may improve client compliance

**MELOXICAM (TRANSMUCOSAL)**

- Dosage based on weight
  - Three bottle sizes with different concentrations
    - Blue bottle – 0.25 mg/spray
    - Orange bottle – 0.50 mg/spray
    - Green bottle – 1.075 mg/spray

**MELOXICAM (TRANSMUCOSAL)**

- Side effects
  - Similar to other NSAIDs
  - Vomiting
  - Increased liver enzymes
  - Diarrhea
  - Lethargy
  - Inappetance
  - Hematuria
  - Polydipsia
  - Dehydration
ROBENACOXIB

- COX-2 preferential NSAID
- Labeled for 3 consecutive day use in cats
  - Oral administration once daily
  - Only oral NSAID approved for use in cats in USA
- $IC_{50}$ COX-1/$IC_{50}$ COX-2 ratios is 66.9:1
  - 1:107 for ketoprofen.
- Carboxylic acid nature of drug contributes to prolonged COX-2 inhibition in exudate, despite short half-lives in blood

Use

- Dosage 1 to 2.4 mg/kg PO q24h
- More effective than meloxicam or ketoprofen for inflammatory pain

Safety

- High safety index compared to other NSAIDs in cats
- Short residence time in the central compartment

Reported Side effects

- Inappetence, weight loss, incision site bleeding, incision site infection, decreased activity, lethargy, cystitis, hematuria, hair loss, excoriation, bruising, vomiting, hematochezia, diarrhea, respiratory, cardiac arrest, incoordination, weakness

Avoid in cats with:

- Renal, hepatic, gastrointestinal, bleeding disorders
**PROPOFLO 28**
- Propofol with 28 day shelf life after opening
  - 20 and 50 ml multidose vials
  - Bacterial growth inhibited by benzyl alcohol (20 mg/ml)
  - Licensed only for dogs
  - Benzyl alcohol may be toxic to cats
    - Anecdotal reports of use as induction agent in cats with no effects
  - Avoid repeated dosing or CRI

**REMIFENTANIL**
- Pure μ opioid
  - Ultrashort acting synthetic
  - Similar potency to fentanyl
- Available in 1, 2, and 5 mg vials
  - Dilute to 20 µg/ml (1 mg in 50 ml saline)

**REMIFENTANIL**
- Metabolized in the blood stream
  - Completely independent of liver or kidney disease
  - Cardio-protective effects in dogs with ventricular arrhythmias
  - Half-life of 3 to 5 minutes
REMIFENTANIL

- Administered at a CRI
  - 2 to 10 µg/kg/hr
- May be opioid of choice for:
  - Renal disease
  - Hepatic disease
  - Neurosurgery
    - Combined with propofol CRI
    - Results in rapid recovery for neuro-assessment

ALENZA

- "Multi-system support for whole body comfort in aging and active dogs"
- Chewable tablet
  - Vexadol™
    - Naturally occurring bioflavonoids
    - Baicalin from Scutellaria baikalensis
    - Catechin from Acacia catechu
  - Boswellia serrata
  - Antioxidants (Vit C, selenium, Vit E)

ALENZA

- Baicalin and Catechin
  - Naturally found in Blue Skull Cap, Koala Nut, Cocoa
  - Act as dual inhibition of COX and LOX
- Other effects
  - Neuroprotection
  - MAO inhibitor
  - Reduces muscle fatigue
**ALENZA**

- Not a pharmaceutical
- May be more effective than other chondroprotective medications
- Available in tablet formulations based on dogs size

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boswellia serrata</td>
<td>150 mg</td>
</tr>
<tr>
<td>Proprietary blend of Boswellia serrata, Alpha Lipic Acid and Copper Proteinate</td>
<td>148 mg</td>
</tr>
<tr>
<td>Ascorbic Acid (Vitamin C)</td>
<td>125 mg</td>
</tr>
<tr>
<td>Zinc (as Zinc Proteinate)</td>
<td>1.8 mg</td>
</tr>
<tr>
<td>Selenium (as Sodium Selenite)</td>
<td>24 mcg</td>
</tr>
<tr>
<td>d-Alpha Tocopheryl Acetate (Vitamin E)</td>
<td>100 IU</td>
</tr>
</tbody>
</table>

**SIMBADOL™**

*Introducing the first and only FDA-Approved buprenorphine for surgical pain control in cats*

**Product Details**

- Controlled Substance: Schedule II
- See human safety warnings, including complete boxed warning. SIMBADOL™ (buprenorphine) is potentially similar to other Schedule II opioids.
- Concentration = 1.6 mg/mL, buprenorphine
- 50 vials (1 mL per vial) in each case
- 21 month expiration date
- 28 day shelf life after first puncture
- Approximately 15 doses per vial
ALFAXALONE

- Injectable neurosteroid that has anesthetic properties
  - Similar in structure to progesterone
  - Well developed metabolic pathways exist in mammals
    - Results in rapid clearance from circulation and short duration of effect

ALFAXALONE

- History
  - Saffan was available in the 1970’s and 1980’s
  - Combination of alfaxalone and alphadalone
    - Solubilised in Cremophor EL
      - Causes massive histamine release
      - Vasodilation
      - Hypotension
      - Swollen paws in cats
    - Althesin – similar product for humans
  - Removed from the market in the late 1980’s

2-HPβCD

- In Alfaxan, the alfaxalone molecule is solubilised in cyclodextrin
  - Cyclodextrins are round complex sugars derived from starch
  - Lipophilic (fat soluble) drugs like alfaxalone can be hidden inside to allow the complex to be dissolved in water

- 2-HPβCD is
  - Inert
  - Does not cause histamine release
  - Is eliminated unchanged via the kidneys

2-hydroxypropyl β-cyclodextrin (2-HPβCD)
ALFAXALONE

- Alfaxalone 10 mg/ml
  - In 2000, Jurox formulated a solution using beta-cyclodextrin
  - No histamine release
  - Mechanism of action is through GABA-A activation and enhancement
    - Similar to other induction agents
      - Barbiturates
      - Propofol
      - Etomidate

http://www.youtube.com/watch?feature=player_embedded&v=dOf4hXZMx

ALFAXALONE

- Induction agent for dogs and cats
  - Clear, colorless solution in multi-dose vial
  - Can be administered IV or IM (no tissue irritation)
    - IV for dogs (volume to large for IM use)
      - 2 mg/kg
    - IV or IM for cats
      - 5 mg/kg IV
      - 10 mg/kg (approx 1 ml) into quadriceps muscles (high blood flow)
        - Deep sedation/light anesthesia
        - Aggressive cats
        - Abscess or wound repair
**Induction Dose Rates**

**Alfaxan Induction dose guidelines: CATS**

<table>
<thead>
<tr>
<th>Preanesthetic</th>
<th>Average Alfaxan® Induction dose (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pre-anesthetic</td>
<td>4.0 ± 2.9 mg/kg</td>
</tr>
<tr>
<td>Opioid + premedications</td>
<td>2.2 ± 1.8 mg/kg</td>
</tr>
<tr>
<td>NMDA antagonist + premedications</td>
<td>3.6 ± 3.7 mg/kg</td>
</tr>
<tr>
<td>Propofol + opioid premedication</td>
<td>3.0 ± 2.2 mg/kg</td>
</tr>
<tr>
<td>Thiopental + opioid premedication</td>
<td>3.4 ± 1.5 mg/kg</td>
</tr>
<tr>
<td>Thiopental + amnestic + premedication</td>
<td>2.1 ± 0.8 mg/kg</td>
</tr>
</tbody>
</table>

Administer slowly over 60 seconds.

**Maintenance Dose Rates**

**Alfaxan Maintenance dose guidelines: CATS**

<table>
<thead>
<tr>
<th>Dose and Duration</th>
<th>Pre-anesthetized cats</th>
<th>Un-pre-anesthetized cats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintenance anesthesia doses</td>
<td>1.5-2.5 mg/kg</td>
<td>1.5-3.5 mg/kg</td>
</tr>
<tr>
<td>Mean duration of anesthesia</td>
<td>7-8 minutes</td>
<td>3-5 minutes</td>
</tr>
</tbody>
</table>

**Alfaxan Maintenance dose guidelines: DSB**

<table>
<thead>
<tr>
<th>Dose and Duration</th>
<th>Pre-anesthetized cats</th>
<th>Un-pre-anesthetized cats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintenance anesthesia doses</td>
<td>12.6 ± 1.7 mg/kg</td>
<td>13.3 ± 2 mg/kg</td>
</tr>
<tr>
<td>Mean duration of anesthesia</td>
<td>3-5 minutes</td>
<td>3-6 minutes</td>
</tr>
</tbody>
</table>

**ALFAXALONE**

- Respiratory depression similar to propofol
- Recommend oxygen support
- Intubation for deep, surgical anesthesia
- Good cardiovascular stability
- Maintenance of cardiac index
- Packaged in 10 ml single use vials
- No preservative
- Store at room temperature
Caveats for use

1. Better administered slowly over 60 seconds
   • Decreases the risk of apnoea and allows the patient to choose the dose required for induction

2. Not analgesic
   • Ensure to address pain

3. Rapidly cleared
   • Can result in very rapid and uncontrolled recoveries if not well premedicated

4. Minimise stimulation in the recovery period
   • Keep the recovery area quiet

QUESTIONS?