The WHY and HOW of Acute Pain Control

Principles of Pain Management
- Pain control is good medicine
- Pre-emptive, intraoperative & postoperative, chronic analgesia
- Multimodal approach

Newer Terminology
- Adaptive pain: Biological purpose
  - Typically short term
  - Long term would be unusual
- Maladaptive pain
  - The body gone wrong
  - Short or long term

What is Adaptive Pain?
- Biological purpose
- Mild - moderate - severe
- Up to a month
- Related to a traumatic incident, surgery, medical problem
- Resolves as condition resolves

Newer Terminology
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**Adaptive Pain**

- Innocuous stimuli → Spinal cord → Brain
- Noxious stimuli → Spinal cord

**Wind Up**

- Innocuous stimuli → Spinal cord → Brain
- NMDA receptor-mediated

**Maladaptive Pain**

- Noxious stimuli → Spinal cord → Brain

**Pain & The Stress Response**

- Relatively Healthy Patients
- Sick Patients
  - Critically Ill Patients
- DEAD Patients

**The Stress Response is Detrimental**

**Pain Control is Good Medicine**

**Pain & The Stress Response**

- Increased ACTH & Cortisol
- Increased Renin
  - Aldosterone
  - Angiotensin II
- Decreased Catecholamines
- Decreased GI motility
- Retention of sodium, water
- Decreased oxygenation, ventilation
- General Catabolism, Lipolysis

**COMPLICATIONS**

<table>
<thead>
<tr>
<th>Finding</th>
<th>Intermittent Opioid</th>
<th>Continuous Opioid</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>11 (73%)</td>
<td>13 (43%)</td>
<td>0.055</td>
</tr>
<tr>
<td>Dysrhythmias</td>
<td>7 (47%)</td>
<td>6 (20%)</td>
<td>0.154</td>
</tr>
<tr>
<td>Sepsis</td>
<td>3 (20%)</td>
<td>0</td>
<td>0.032</td>
</tr>
<tr>
<td>DIC</td>
<td>3 (20%)</td>
<td>0</td>
<td>0.032</td>
</tr>
<tr>
<td>Death</td>
<td>4 (27%)</td>
<td>0</td>
<td>0.032</td>
</tr>
</tbody>
</table>

From Anand, KJS et al. NEJM 326:1-9, 1992
**Pre-emptive Analgesia**
• Preventative pain control
• Providing pain control prior to inflicting a noxious stimulus
• Always possible with elective procedures
• Not possible with injuries or trauma
• Easier to provide pain control later
• Prevent wind-up

**Multi-Modal Approach**
• Multiple drugs
• Different mechanisms
• Overall better analgesia

**Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)**

**Perioperative NSAIDs**

**Preop vs Postop Considerations**
• IV fluids
• Blood pressure measurement
• Duration of procedure
• Actual blood pressure
• Likelihood for bleeding
Preop NSAID Options

NSAIDs
- Aspirin
- Piroxicam
- Phenylbutazone
- Flunixin
- Ketoprofen

Opioids
- Morphine
- Hydromorphone / oxymorphone
- Fentanyl
- Remifentanil
- Buprenorphine
- Butorphanol
- Nalbuphine

Opioids
- Morphine is prototype
- Mu agonist
- Best analgesia
- Potency = 1

Mu Opioid Potency
- Morphine: 1
- Hydromorphone: 5
- Fentanyl: 100
- Remifentanil: 50

Potency refers only to relative dose to get equivalent effect
Opioids
• Analgesia and sedation
  • Dysphoria may require
    – Tranquilizer
    – Sedative
    – Partial reversal

Opioids- Benefits Plus....
• Minimal cardiovascular effects – allows less gas anesthesia!
• Bradycardia: Anticholinergics
• No respiratory depression unless combined with an inhalant....

Morphine
• Very inexpensive
• Premed 0.2-1.0 mg/kg SQ, IM
• Post-op 0.1-0.2 mg/kg/hr
• Relatively long lasting
• IV-> Histamine release in dogs
• Most likely to cause vomiting as premed

Morphine and Cats
• Morphine – 6 – glucuronide (M6G) necessary for analgesia
• Cats produce very little even when given IV
• Sedation and dysphoria but analgesia?

Methadone
• Similar potency as morphine
• Similar dose as morphine
• Virtually ZERO vomiting
• NMDA antagonist
• Feline EUPHORIA

Hydromorphone / Oxymorphone
• 5-10x more potent than morphine
• Less vomiting
• No histamine release concerns
• 0.1-0.2 mg/kg SQ, IM
• 0.05-0.1 mg/kg IV

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Fentanyl
• 100x more potent than morphine
• Short duration
  – 20 min IV
  – 40 min SQ
• Unlikely to induce vomiting
• Infusions
  – 2 ug/kg IV
  – 5-20 ug/kg/hr

Butorphanol
• Kappa agonist - mu antagonist
• Mild to moderate analgesia: NEVER the same as mu agonist
• 45 minute duration in dogs
• 4 hr duration in cats

Buprenorphine
• Partial mu agonist - antagonist
• Mild - moderate analgesia
• NOT good for severe pain
• Long duration 6-12 hrs
• Feline differences - better analgesia?

Long Term Approaches Challenges:
Efficacy
Duration
Client compliance

Tramadol
• Opioid like
• mu agonist effects
• Likely not very efficacious – DATA!
• Best with an NSAID – of course!
• 6-10 mg/kg PO QID (vs what we do)

Tramadol Data
• The Effect Of Oral Tramadol On Ground Reaction Forces In Dogs With Experimentally Induced Osteoarthritis. Westling M1; Millis DL1; Carr JG1; Westling W2
• Metabolism of the analgesic drug, tramadol hydrochloride, in rat and dog. Wu WN, McKown LA, Gauthier AD, Jones WJ, Raffa RB.
• Pharmacokinetics of tramadol and the metabolite O-desmethyltramadol in dogs. Kukanich B, Papich MG
• Pharmacokinetics and antinociceptive effects of oral tramadol hydrochloride administration in Greyhounds. Kukanich B, Papich MG
• Comparison of the analgesic efficacy of perioperative firocoxib and tramadol administration in dogs undergoing tibial plateau leveling osteotomy. Davila D, Kawanishi TP, Etoke R, Conzemius MG.
• Characterization of tramadol, morphine and tapentadol in an acute pain model in Beagle dogs. Kilgore B, Tardieu R, Schneider J.
• Cardiorespiratory, sedative and antinociceptive effects of desmethyltramadol alone or in combination with methadone, morphine or tramadol in dogs. Cardoso CG, Marques DR, da Silva TH, de Mattos-Juaima E.
**Codeine**
- 1-2 mg / kg PO BID – QID
- Analgesia may be better than tramadol but **CEILING effect**
- More likely to induce sedation / dysphoria

**Fentanyl Patches**
- Theoretical efficacy
- Good data in multiple species
- Must maintain good patch adherence
- Clinical effectiveness?

84% of clinical dogs have sub-therapeutic plasma levels
IOW: 16% efficacy

**Transdermal Fentanyl Solution**
- 96 hr duration
- Postoperative pain in dogs
- Apply 2-4 hrs prior to sx

**INDICATION:**
RECUVRA is indicated for the control of postoperative pain associated with surgical procedures in dogs.

**WARNING:**
Abuse Potential: RECUVRA contains fentanyl, a high concentration µ-opioid receptor agonist (50 mg/mL) and is a Class II controlled substance with high potential for abuse.

Risk Minimization and Action Plan: This product is distributed under a Risk Minimization Action Plan (RiskMAP) and its use is limited to certified veterinarians.

Human Safety:
SECONDARY EXPOSURE TO FENTANYL IN CHILDREN AND ADULTS: Strict adherence to the requirements of the RiskMAP and the INSTRUCTIONS FOR USE provided in this product insert is imperative in order to reduce the potential of secondary exposure to fentanyl from RECUVRA treated skin.

Animal Safety:
Individual dogs may be especially sensitive to the effects of fentanyl.


Before using this product, it is important to read the entire product insert. The following is an excerpt from the Boxed Warning which highlights important safety information.

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Penetration enhancer and active fentanyl become supersaturated.

Once in the skin, a slow rate of active ingredient is delivered into the bloodstream.

Recuvyra® (Transdermal fentanyl solution) Issues

- Dysphoria
  – Reversible with naloxone, nalbuphine, butorphanol, buprenorphine
  – Acepromazine
  – Trazadone!
- Manage Adverse Effects
  – Avoid Reversal
  – Maintain pain control

Recuvyra® Uses – Dogs

- OHE
- Dentistry
- Abd sx
- Stable trauma patients
- Routine orthopedics
- ASA I, II, ± III

Challenges solved: compliance + effectiveness + duration

Recuvyra® Uses – Cats

- Do NOT use in cats
- Different absorption
- Huge doses
- Dysphoria
- Mania
- Remember MORPHINE MANIA?

Recuvyra® Uses

- OHE
- Dentistry
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For Consultation

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