ADVERSITY

That which Does Not Kill Me Postpones the Inevitable.

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Topics:

• Post-operative analgaesia techniques
• Analgaesic and adjunctive agents
• Persistent post-operative pain
Post-operative analgesia techniques
Post-operative analgesia techniques

• Interventional regional anaesthesia
• Systemic pharmacological therapies
• Non-pharmacological strategies
  – Catastrophisation increases post-operative pain scores¹
  – Pre-operative provision of appropriate information
  – Pre and post operative cognitive therapies
  – Relaxation
  – Attentional techniques
  – Hypnosis (mainly studied in acute procedural pain)
  – TENS / acupuncture / various ‘physical therapies’

¹Sullivan et al, 2001, Theoretical perspective on the relation between catastrophising and pain

Clinical Journal of Pain 17:52-64
Interventional regional anaesthesia

- Central neuraxial:
  - Spinal
  - Epidural
- Plexus block (Cervical, paravertebral, brachial, lumbar):
  - Catheter
  - Single shot
- Peripheral nerve block
  - Catheter
  - Single shot
- Topical / wound / surgical site
  - Infiltration
  - Infusion

Largely covered in this morning’s presentation – Hope you were paying attention
Systemic Pharmacological Therapies
Systemic Pharmacological Therapies

• Opioids
  – Specific agents, Specific considerations
  – Routes of administration

• Non-opioid analgaesics and adjuvant agents
Opioids:

Specific agents, Specific considerations

• Morphine
• Fentanyl
• Oxycodone
• Hydromorphone
• Methadone
• Codiene
• Buprenorphine
• Tramadol
• ?Tapentadol (Phase III clinical trials)
Opioid Choice Considerations

• Availability / cost / preparations
• Opioid receptor effect
  – Agonist / partial agonist
  – Which receptors?
• Other receptor effects and drug interactions
• Metabolite activity
• Bioavailability (enteral administration)
• Mode(s) of elimination and effect offset
Opioids: Routes of Administration

- Oral – Often preferable, but ‘Dumping effect’
- Intravenous – Rapid titration, short duration
- Intramuscular and subcutaneous – Impaired absorption in shock and hypothermia
- Rectal – Variable absorption and 1st pass metabolism, cultural resistance
- Transdermal – Fentanyl: Time to peak levels 17 to 48 hours, Terminal half-life 13 to 25 hours, Transdermal fentanyl not suitable in acute pain setting
- Transmucosal – Intranasal, sublingual, buccal, pulmonary
  - Generally lipid soluble opioids (note – nebulised morphine)
  - Patient-controlled devices
- Central neuraxial
Other Analgesics and Adjunctive Agents

A Segway

- Paracetamol
- NSAIDS
- COX-2 inhibitors
- NMDA antagonists
- Antidepressants
- Anticonvulsants
- Membrane stabilisers
- Alpha-2 agonists
- Calcitonin
- Cannabinoids
- Complementary / alternative medicines

A Segue
Non-Opioid Analgesics

• Paracetamol:
  – A para-aminophenol
  – Mechanism of action poorly understood, Probably central cyclooxygenase inhibition (COX-3)\(^1\)
  – Parenteral formulations, similar efficacy to NSAIDS in dental surgery
  – Good efficacy evidence in multiple studies with opioid combination therapy

Non-Opioid Analgesics

• NSAIDS:
  – Non-selective reversible COX inhibitors
  – COX role in:
    • Gastric mucosal protection
    • Renal tubular function
    • Intrarenal vasodilation
    • Endothelial prostacyclin (COX-2) and platelet thromboxane (COX-1) production
    • Bronchodilation
  – Efficacy in renal colic, back pain, minor surgery pain
  – Opioid sparing effect in severe post-operative pain
  – Lack of evidence for interference with bone healing
  – Caution in presence of hypotension, hypovolaemia, renal impairment, diabetes
Non-Opioid Analgesics

• COX-2 Inhibitors:
  – Selective inhibition of inducible cyclooxygenase
  – Similar efficacy to NSAIDS
  – Similar effects to NSAIDS on renal function
  – Do not impair platelet function
  – Gastric ulcer rate similar to placebo
  – Lack of evidence for interference with bone healing
  – Use associated with adverse cardiovascular events¹

¹Graham D (Editorial) JAMA. 2006;296
Non-Opioid Analgesics

• N-methyl-D-aspartate antagonists:
  – Spinal NMDA receptors play role in allodynia and hyperalgesia
  – NMDA receptor activation by glutamate augments propagation of nociceptive impulses
  – Ketamine, dextromethorphan, methadone are NMDA antagonists
  – Preventative analgesic effects
  – Ketamine:
    • Opioid-sparing in post-operative pain (But no reduction in SFX)
    • Improved analgesia in opioid-resistant pain and opioid-tolerant patients
Non-Opioid Analgesics

• Anticonvulsants and tricyclic antidepressants (TCA’s):
  – No data for use in acute neuropathic pain
  – Both groups show efficacy in chronic neuropathic pain (NNT 2.5-3)¹
  – Gabapentin effective in treatment of post-amputation pain²

Non-Opioid Analgesics

• Membrane Stabilisers:
  – Lignocaine may exert some preventive effect on post-operative pain
  – Lignocaine shown to reduce pain and allodynia in chronic neuropathic pain and after nerve trauma

• Alpha 2 agonists:
  – Systemic use reduces opioid requirements in post-operative pain and ICU sedation
  – Significant hypotension and sedation
  – No analgesic efficacy when used as systemic monotherapy in chronic pain¹

• Calcitonin:
  – Bone pain - Pain reduction in vertebral fractures (‘nuff said)

Non-Opioid Analgaesics

- Cannabinoids:
  - No benefit with 5mg oral THC in post-operative pain¹
  - Wide range of SFX:
    - Mood elevation, appetite stimulation, antiemetic
    - Dysphoria, sedation, impaired psychomotor performance


Pain 106:169-72
More Segue:

Novel Agent, Novel Administration
The Perplexing Problem of Persistent Postoperative Pain: Algaesia, Allodynia or Alliteration?
Persistent Postoperative Pain: Day Surgery

• Incidence severe pain 5.3% in first 24 hours¹

• Predictors:
  – High BMI
  – Increased duration of anaesthesia
  – Poor initial pain control
  – Type of surgery: Orthopaedic, open inguinal hernia, laparoscopy, plastic

¹Beauregard et al, 1998, Severity and impact of pain after day-surgery.

*Canadian Journal of Anesthesia* 45:304-11
Chronic Pain / Persistent Pain:

A pain by any other name would smell the same

- Refers to pain persisting beyond 3 months or beyond period of nociceptive stimulus
- Many persistent / chronic pain patients relate an acute onset
- Acute pain events often associated with progression to persistent pain:
  - Surgery / trauma
  - Acute back pain
  - Acute zoster
## Incidence of Chronic Pain After Surgery

<table>
<thead>
<tr>
<th>Operation</th>
<th>Incidence of Chronic Pain (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amputation</td>
<td>30-85</td>
</tr>
<tr>
<td>Thoracotomy</td>
<td>5-67</td>
</tr>
<tr>
<td>Mastectomy</td>
<td>11-57</td>
</tr>
<tr>
<td>Cholecystectomy</td>
<td>3-56</td>
</tr>
<tr>
<td>Inguinal hernia</td>
<td>0-63</td>
</tr>
<tr>
<td>Vasectomy</td>
<td>0-37</td>
</tr>
<tr>
<td>Dental surgery</td>
<td>5-13</td>
</tr>
</tbody>
</table>

¹Adapted from *Acute Pain Management: Scientific Evidence* 2nd Ed 2005
# Predictors of Chronic Post-Surgical Pain¹

<table>
<thead>
<tr>
<th>Preoperative Factors</th>
<th>Moderate to severe pain &gt; one month</th>
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<tbody>
<tr>
<td></td>
<td>Repeat surgery</td>
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<td></td>
<td>Psychologic vulnerability</td>
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<td></td>
<td>Worker’s compensation</td>
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<tr>
<td>Intraoperative Factors</td>
<td>Surgical approach / Risk of nerve damage</td>
</tr>
<tr>
<td>Postoperative Factors</td>
<td>Moderate to severe acute pain</td>
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<tr>
<td></td>
<td>Radiation therapy to surgical site</td>
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<td>Neurotoxic chemotherapy</td>
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<td>Depression</td>
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<td>Psychologic vulnerability</td>
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<td></td>
<td>Neuroticism</td>
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<tr>
<td></td>
<td>Anxiety</td>
</tr>
</tbody>
</table>

¹Perkins and Kehlet, 2000, Chronic pain as an outcome of surgery – A review of predictive factors. *Anesthesiology* 93:1123-33
Mechanisms of Progression to Persistent Pain

- Peripheral inflammatory response
- Amplification of afferent nociceptor response (‘Central sensitisation’)
- Sympathetic nervous system response
- Loss of descending pathway inhibition
- It’s complicated and has a lot to do with neuroplasticity
Strategies to Limit Progression to Persistent Pain

- ‘Pre-emptive’ analgesia:
  - Effective in some laboratory models
  - No benefit in clinical studies
- ‘Preventative’ analgesia:
  - Earlier interventions more effective
- NMDA antagonists show preventative benefit in number of studies (particularly ketamine)
- Psychological / cognitive therapies in acute pain patients probably merit much more attention:
  - Anxiety, sleep deprivation, loss of autonomy all contribute to persistent pain
  - Animal modeling suggests 30% of population have genetic susceptibility to persistent pain induced behavioral disturbance¹

¹Monassi, C, Bandler, R, Keay, K. A subpopulation of rats show social and sleep-waking changes typical of chronic neuropathic pain following peripheral nerve injury. *The European Journal of Neuroscience*. 2003; 17:1907-20
The Known and the Unknown

• “There are known knowns. These are things we know that we know. There are known unknowns. That is to say, there are things that we know we don't know. But there are also unknown unknowns. There are things we don't know we don't know.”
  -Donald Rumsfeld

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Hunter Integrated Pain Service (HIPS):
A Final Thought:

THOUGHT FOR THE DAY
Never hold your farts in.
They travel up your spine, into your brain,
and that is where shitty ideas come from!!!!