Advances in Acute Pain Management

Lee Wilson
Consultant Pharmacist
Bassetlaw Hospital
What’s Coming Up?

- ‘Advances’ in Acute Pain Management
  - Novel ways of administering old medicines
  - Some new therapies and evidence
- What do we already know about acute pain management?
  - Multimodal analgesia
- Brief overview of PONV prophylaxis
Why Manage Acute Pain?

- To prevent negative psychological and physiological consequences
  - Pain and suffering (incl. persistent pain)
  - Pneumonia
  - Impaired GI motility
  - Impaired wound healing
  - Tachycardia/Hypertension
  - Prevent ongoing pain
## Incidence of Persistent Pain following Surgical Procedures

<table>
<thead>
<tr>
<th>Type of Operation</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amputation</td>
<td>30 to 85</td>
</tr>
<tr>
<td>Thoracotomy</td>
<td>5 to 67</td>
</tr>
<tr>
<td>Mastectomy</td>
<td>11 to 57</td>
</tr>
<tr>
<td>Cholecystectomy</td>
<td>3 to 56</td>
</tr>
<tr>
<td>Inguinal Hernia</td>
<td>0 to 63</td>
</tr>
<tr>
<td>Vasectomy</td>
<td>0 to 37</td>
</tr>
<tr>
<td>Dental Surgery</td>
<td>5 to 13</td>
</tr>
</tbody>
</table>
Advances in Acute Pain Management

- Slow progress despite considerable Pharma investment
  - Potential they may withdraw completely?
- Most new analgesic therapies look to reduce the adverse effects of current therapies\(^1\)
Recent Analgesic Developments

- Paracetamol IV
  - (Propacetamol)
  - Perfalgan
- Diclofenac IV (Dyloject)*
- COXIBs
  - Celecoxib
  - Etoricoxib
  - Lumaricoxib
  - Parecoxib (IV)
  - Rofecoxib
  - Valdecoxib
- Targinact
  - Oxycodone plus Naloxone MR
- Tapentadol
  - New opioid analgesic
  ?effect on NeuP
- Ionsys
  - Fentanyl iontophoretic transdermal system
- Depodur
  - Epidural MR morphine
Paracetamol IV

- Reduce dose in low weight patients
- Manufacturers state: <50kg, use 15mg/kg²
- Analgesia not now thought to be blocked by ondansetron³

We use doses based on weight ranges:

<table>
<thead>
<tr>
<th>Wt (kg)</th>
<th>&lt;30</th>
<th>30-44</th>
<th>45-50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose (mg)</td>
<td>500 tds</td>
<td>500 qds</td>
<td>1000 tds</td>
</tr>
</tbody>
</table>
Dyloject (Diclofenac IV⁴)

- **Advantages**
  - Voltarol requires dilution and buffering before IV admin.
  - Onset of action better than with Voltarol (bolus vs 30 min inf.)
  - Non-inferiority demonstrated

- **Disadvantages**
  - More expensive than Voltarol*
  - Confusion if multiple diclofenac preps kept
  - Withdrawn in May 2010 following the presence of white particulate matter⁴ᵃ
Coxibs

- Initially, widely adopted nationally
- Withdrawal of rofecoxib and valdecoxib signalled massive U-turn
- Along with risks, benefits not as pronounced as hoped
- Etoricoxib and lumaricoxib rarely prescribed
- Note, Pfizer’s patent expires in Nov 2014
Updates to the Evidence Base

- Regular Opioids in Post-Operative Pain
  - Evidence base poor but audit data may support use

- Spinal Opioids

- Ketamine
- Clonidine
- Dexamethasone\(^4\)
- Adjuvants for NeuP
  - Gabapentinoids
Dexamethasone

- Widely prescribed for PONV
- Recent meta-analysis:\(^4\):
  - Examined high (\(=>0.21\text{mg/kg}\)), medium (0.11 to 0.2\text{mg/kg}) or low (\(<=0.1\text{mg/kg}\)) doses
  - Reduced post-operative pain in the treatment groups
    - Low dose failed to achieve a statistically significant effect on pain at early (0-4h) pain at rest \((-0.33 [-0.70 \text{ to } 0.04])\)
  - High and medium doses reduced opioid consumption
  - Pre-operative administration appears to produce a more consistent analgesic effect
Epidural Analgesia (incl. PCEA)
Bandolier League Table of Analgesics

Notes:
- In single doses, codeine is not an effective analgesic
- Tramadol 50mg less effective (NNT=8.3)
- NSAIDs all have similar efficacy (use the safest!)
- Don’t use IM morphine*
Other Potential Options and Future Therapies

- Ketamine (in sub-anaesthetic doses)
- Acupuncture
- Local anaesthetic infusion devices
  - e.g. ON-Q soaker
- Capsaicin
  - Injectable preparation being trialled in post-operative pain
- Patient-controlled regional anaesthesia
So Where Does This Leave Us?
Multimodal Analgesia$^{5,6}$

Morphine

Reduced doses of each analgesic
Improved effectiveness due to synergistic/additive effects
May reduce severity of side effects of each drug

NSAIDs$^7$, Paracetamol$^7$
Nerve Blocks
Enhanced Recovery

FULFILLING THE POTENTIAL
A BETTER JOURNEY FOR PATIENTS AND A BETTER DEAL FOR THE NHS

Published on behalf of the Enhanced Recovery Partnership by NHS Improvement
Enhanced Recovery: Anaesthetic Protocol

- Standardised protocol
- Spinal block
  - Epidural/Spinal
- Rationale
  - Blocks autonomic afferent pathways
  - Pain control
  - Reduce dose of inhalational/IV anaesthetics
Enhanced Recovery: Post-Operative Analgesia

- Keep opioids to a minimum
- Avoid PCA
- Epidural < 48 hours
- IV paracetamol/oral NSAIDs
  - NSAIDs - with or after food?
Tried and Tested Therapies

- **Prescribe Regularly:**
  - Paracetamol
  - NSAIDs (ibuprofen or naproxen - where not contraindicated) in short courses eg. 3/7

- **With Strong Opioid prescribed PRN:**
  - eg. oral/sc morphine*

- **Place for Other Modalities:**
  - Nerve Blocks and Epidurals (& PCEA)
  - PCA or Regular Strong Opioids*

*Aim to limit dose esp. in ERAS; Opioid dose may need reducing in elderly, frail and renal pts & increasing for those on regular strong opioids (including IVDUs)
Resources

- Acute Pain Management: Scientific Evidence
- Clinical Pharmacy and Therapeutics
  - Chapter on Pain by R. Knaggs and G. Hobbs
  - Edited by R. Walker and C. Edwards
Family mis-Fortunes

We asked 100 patients what their main concern about post-operative recovery was.

Our survey said....

1.
2.
3.
4.
5.
What do patient’s want?
Concerns during post-op recovery

<table>
<thead>
<tr>
<th>Importance of factor</th>
<th>Principal factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emesis</td>
<td>40%</td>
</tr>
<tr>
<td>Pain/aches</td>
<td>29%</td>
</tr>
<tr>
<td>Dysphoria</td>
<td>16%</td>
</tr>
<tr>
<td>Extra cost</td>
<td>10%</td>
</tr>
<tr>
<td>Mental acuity</td>
<td>5%</td>
</tr>
</tbody>
</table>
Apfel Risk Scoring System

- Patient Scores One Point for Each Risk Factor
  - Female Gender
  - Non-Smoking Status
  - Post-Operative Opioid Use
  - Previous History of PONV or Motion Sickness

- Good Correlation between Incidence of PONV and Number of Risk Factors
Correlation between risk factors and PONV

Apfel suggested that any patient scoring 2 or more should receive prophylaxis
Consensus Guidelines (Gan *et al*, 2003<sup>12</sup>)

<table>
<thead>
<tr>
<th>Risk Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>PONV Risk</td>
<td>10%</td>
<td>20%</td>
<td>40%</td>
<td>60%</td>
<td>80%</td>
</tr>
<tr>
<td>Antiemetics</td>
<td>0</td>
<td>0</td>
<td>1/2/3</td>
<td>2/3</td>
<td>2/3</td>
</tr>
</tbody>
</table>
Evidence Base – Impact\textsuperscript{13}

- Large Patient Numbers (n=5199)
- All High Risk Patients
  - risk score=2 or more
- Most (n=4123) were randomised to received combination of 6 prophylactic interventions
  - 64 different treatment combinations (2\textsuperscript{6})
  - Remainder received comb.’s of first 4 interventions
Evidence Base – Impact^{13}

- Ondansetron 4mg
- Dexamethasone 4mg
- Droperidol 1.25mg
- Propofol
- Nitrogen
- Remifentanyl

- No Ondansetron
- No Dexamethasone
- No Droperidol
- Inhaled Anaesthetic
- Nitrous Oxide
- Fentanyl
# Evidence Base – Impact

<table>
<thead>
<tr>
<th>Antiemetics (number)</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of PONV</td>
<td>52</td>
<td>37</td>
<td>28</td>
<td>22</td>
</tr>
</tbody>
</table>
Evidence Base – Impact Trial\textsuperscript{13}

- Each agent reduced incidence of PONV by around a quarter (26%)
- No agent was found to be more effective than any other
- Combination of avoiding nitrous oxide and propofol use (TIVA) reduced risk by 26%
- No advantage with remifentanil
PONV: Summary

- Prophylaxis indicated for high risk patients using a combination of anti-emetics
  - I would suggest all should receive one agent
- There is little to choose between antiemetics used*
- Anti-emetics used for treatment should target a different site of action to those used for prophylaxis
- Sufficient evidence is now available to guide management of PONV
- Prophylaxis is key - Treatment is often difficult: use policies
Take Home Messages

- Multimodal analgesia is still important
- Opioids widely used but low opioid techniques may reduce adverse effects and length of stay
- Modified-release opioids may have a place
- Ketamine may be a useful adjunct in resistant pain cases
Take Home Messages
(for discussion)

- Developments in acute pain management are few and far between in recent years
- Acute pain management is often less complex than it is time-consuming*
- Good quality pain assessment is key
  - Along with pain scoring and action when scores are high
Take Home Messages (for discussion)

- Chronic pain patients continue to present some of the biggest challenges
- This includes opioid users
  - If on regular opioids, may need increased PRN doses
  - Recreational users often most difficult to manage
    - Continue regular opioid (nb. Subutex)
    - Baseline analgesia (adding tramadol may help)
References

4a. See http://www.dyloject.co.uk
References


6. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. BJA 78: 606-17 (via http://bja.oxfordjournals.org/content/78/5/606.full.pdf)


References

11. Apfel CC et al. A simplified risk score for the prediction of postoperative nausea and vomiting. Anesthesiology, 91(3): 693-700 (via http://www.ponv.org)