UPDATE ON POST-OP PAIN MANAGEMENT

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Case #1 - Trauma
• 29 male MBA ->
  – # L) wrist
  – # ribs 7-9 L) + minimal pneumothorax
  – # tibial plateau L)

• Smoker, occasional cannabis
• No other hx

• In pain on the ward, while waiting for surgery. Written up for “Morphine 2.5-10mg SCI/IV/IM” by Emergency dept staff.
• **Points for discussion:**
  
  1. Assessment of the patient in acute pain.
  2. Appropriateness of current regime for this patient.
  3. What are the alternatives.
  4. Role of co-analgesia.
  5. Role of patient controlled analgesia.
• Paracetamol
  • Mechanism of action unclear - ?central COX2 inhibition, ??modulation of descending serotoninergic pathways
  • Significant opioid sparing effects (dose requirement reduced by 20-32%) whether given orally or IV
  • Associated improvement in analgesia but no reduction in frequency of opioid SE
• NSAIDs
  – Significant morphine sparing effects (30-55%) with associated improvements in analgesia and reduction in opioid SE
  – Increased frequency of severe bleeding events with non selective agents
• You elect to commence patient controlled analgesia.

• **Points for discussion:**
  – Selection of drug, dose and settings
  – Initiation of therapy – loading dose
Bolus Dose:

- “Optimal” dose that provides consistent, satisfactory analgesia without producing excessive or dangerous side effects
- Optimal doses may be 1 mg for morphine or 30mcg for fentanyl over 5 minutes
- Dose will need titration depending on subsequent reports of pain or onset of SE
• Lockout Interval:
  – No difference in analgesia was shown with lockout intervals (for IV PCA) of 7 to 11 minutes for morphine and 5 to 8 minutes for fentanyl

• Loading Dose:
  – Enormous interpatient differences in loading dose requirements mean that individual titration of the loading dose is usually required prior to starting PCA
• Bg Infusions:
  – Do not improve analgesia or sleep
  – Increase the risk of respiratory depression

• Dose Limits:
  – No good evidence shows benefit (or otherwise) from the use of a dose limit
  – For PCA to be used effectively in all patients, a wide range of opioid doses may be required.
• You see the patient post-op the next day. His pain relief is borderline (having consumed 80mg of morphine in 16 hours), but he is nauseous, has vomited 3 times, and feels itchy. He is reluctant to use the PCA. The nursing staff have administered Metoclopramide but it hasn’t helped.
• Points for discussion:
  – complications of IV opiates administered via PCA
  – management of nausea and vomiting
  – management of itchiness (?rotation to another opiate)
  – variability of opioid response in patients
• SE of PCA Opiates:
  – Nausea 25%
  – Vomiting 20%
  – Excessive Sedation 3%
  – Pruritus 15%
  – Urinary Retention 23%
  – Resp Depression 0.3%
• Determinants of Opioid Response: Age
  — 2-4x decrease in opioid requirement with increasing age shown experimentally and in clinical setting
  — Predominantly due to pharmacodynamic factors

— Useful rule of thumb:
  • Expected daily Morphine Requirement (mg) 
    ~ 100 - AGE
Determinants of Opioid Response: Gender

- Poorly understood at present
- Women report consistently higher post-op pain scores, but impact on PCA consumption variable
- Women are more sensitive to opioids with Kappa activity
• Determinants of Opioid Response: Psychological Factors

– Pre-op Depression
– Pre-op Anxiety
– Pre-op Neuroticism
• Determinants of Opioid Response:
  Gen
• Determinants of Opioid Response: Genetics

<table>
<thead>
<tr>
<th>Polymorphism</th>
<th>Affected codon</th>
<th>Wild-type</th>
<th>Heterozygous</th>
<th>Variant</th>
<th>Frequency of occurrence* (variant)</th>
</tr>
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<tbody>
<tr>
<td>−172 G &gt; T</td>
<td></td>
<td>185</td>
<td>20</td>
<td>1</td>
<td>5.3%</td>
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<tr>
<td>118 A &gt; G</td>
<td>(N40D)</td>
<td>167</td>
<td>35</td>
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<tr>
<td>IVS2+31 G &gt; A</td>
<td></td>
<td>166</td>
<td>40</td>
<td>76</td>
<td>9.7%</td>
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<tr>
<td>IVS2+691 G &gt; C</td>
<td></td>
<td>30</td>
<td>100</td>
<td></td>
<td>61%</td>
</tr>
</tbody>
</table>

Pharmacological observations for 118 A > G genotype groups:

<table>
<thead>
<tr>
<th></th>
<th>Wild-type (AA)</th>
<th>Heterozygous (AG)</th>
<th>Variant (GG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine dose (mg 24 h⁻¹)</td>
<td>97 ± 89 (n = 78)</td>
<td>56 ± 50 (n = 17)</td>
<td>225 ± 143* (n = 4)</td>
</tr>
<tr>
<td>Morphine serum conc. (nmol L⁻¹)</td>
<td>71 ± 67</td>
<td>52 ± 46</td>
<td>117 ± 92</td>
</tr>
<tr>
<td>M6G serum conc. (nmol L⁻¹)</td>
<td>404 ± 449</td>
<td>267 ± 237</td>
<td>711 ± 517</td>
</tr>
<tr>
<td>M3G serum conc. (nmol L⁻¹)</td>
<td>2300 ± 2166</td>
<td>1666 ± 1462</td>
<td>3815 ± 2729</td>
</tr>
</tbody>
</table>
• Determinants of Opioid Response: Genetics

• Polymorphisms currently under investigation:
  – UGT2B7 Gene controlling Morphine glucuronidation
  – MDR1 Gene controlling Multi Drug Resistance Transporters in CNS
  – COMT
On post-op day 4, the surgeon sees the patient and instructs that the IV cannula be removed and PCA ceased. The patient has consumed 35mg of morphine over last 24h.

Points for discussion:
– conversion of PCA to oral therapy
– analgesia weaning program
**PARENTERAL**

- Morphine 10mg
- Hydromorphone 2mg
- Fentanyl 150mcg

**ORAL**

- Morphine 30mg
- Hydromorphone 10mg
- Oxycodone 20mg
• 8 Panadeine Forte / day:

  • ~ 200mg Tramadol
  • ~ 40mg Morphine
  • ~ 30mg Oxycodone
  • ~ 15mg Methadone
  • ~ 12mcg/h Fentanyl Patch
  • ~ 20mcg/h Buprenorphine Patch
Case #2 – Abdominal Hysterectomy
• 46 yo female presents for abdominal hysterectomy for fibroids and menorrhagia

• Bg:
  – Obese 92 kg
  – Depression – on Fluvoxamine
  – Chronic Mechanical Lumbar Pain:
    • Extensive laminectomy 1998 followed by L2 – L5 fusion 2 years later
    • Ambulates in an electric wheelchair outside of home because of pain
    • Rx MS Contin 60mg bd, Panadeine Forte up to 6/day
• She is worried about being treated like a “drug addict” and not receiving adequate postop pain relief
• She asks whether she will develop persistent pain from the surgery
Points for discussion:

- Addiction vs Dependence vs Tolerance
- Anaesthetic technique
- Post-op analgesia

- Persistent Pain after surgery
Patients on transdermal or implantable pumps
- Continue patch or pump
- Additional short-acting analgesia for acute pain
- Avoid risk of any agonist-antagonist reaction

Patient on high dose opioids

Patients on methadone maintenance
- Continue prescribed methadone
- Poly-opioid therapy for acute burden

Preoperative administration of maintenance opioid

Multimodal analgesia with local anaesthesia infiltration, nerve blocks, paracetamol, NSAIDs and adjuvant drugs

Short acting opioid PCA – large bolus dose with shorter lock out interval
The Analgesic Efficacy of Transversus Abdominis Plane Block After Abdominal Surgery: A Prospective Randomized Controlled Trial

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Anne Heffernan, MB, FCARCSI†
Camillus Power, MD, FCARCSI†
John G. Laffey, MD, MA, FCARCSI††

BACKGROUND: The transversus abdominis plane (TAP) block is a novel approach for blocking the abdominal wall neural afferents via the bilateral lumbar triangles of Petit. We evaluated its analgesic efficacy in patients during the first 24 postoperative hours after abdominal surgery, in a randomized, controlled, double-blind clinical trial.

METHODS: Thirty-two adults undergoing large bowel resection via a midline abdominal incision were randomized to receive standard care, including patient-controlled morphine analgesia and regular nonsteroidal antiinflammatory drugs and acetaminophen (n = 16), or to undergo TAP block (n = 16) in addition to standard care (n = 16). After induction of anesthesia, 20 mL of 0.375% levobupivacaine was deposited into the transversus abdominis neuro-fascial plane via the bilateral lumbar triangles of Petit. Each patient was assessed by a blinded investigator in the postanesthesia care unit and at 2, 4, 6, and 24 h postoperatively.

RESULTS: The TAP block reduced visual analog scale pain scores (TAP versus control, mean ± SD) on emergence (1 ± 1.4 vs 6.6 ± 2.8, P < 0.05), and at all postoperative time points, including at 24 h (1.7 ± 1.7 vs 3.1 ± 1.5, P < 0.05). Morphine requirements in the first 24 postoperative hours were also reduced (21.9 ± 8.9 mg vs 80.4 ± 19.2 mg, P < 0.05). There were no complications attributable to the TAP block. All TAP patients reported high levels of satisfaction with their postoperative analgesic regimen.

CONCLUSIONS: The TAP block provided highly effective postoperative analgesia in the first 24 postoperative hours after major abdominal surgery.

(Anesth Analg 2007;104:193-7)
Time to first request for morphine (min) | Control (n = 16) | TAP block (n = 16)
--- | --- | ---
24.1 ± 6.9 | 157.2 ± 27.9†

Mean 24 h morphine requirement (mg) | Control (n = 16) | TAP block (n = 16)
--- | --- | ---
80.44 ± 4.8 | 21.94 ± 2.2‡

Categorical pain severity | Control (n = 16) | TAP block (n = 16)
--- | --- | ---
PACU | 2.5 (2, 3) | 0 (0, 1)‡
2 Hours | 2 (2, 2) | 0 (0, 1)‡
4 h | 2 (1.5, 2) | 0 (0, 1)‡
6 h | 2 (1, 2) | 1 (0, 1)‡
24 h | 1 (1, 2) | 1 (0, 1)‡

Ordinal data are presented as medians and interquartile ranges (given in parentheses), and continuous variables are presented as mean ± SEM.

TAP = transverse abdominis plane; PACU = postoperative anesthesia care unit.
†P ≤ 0.01; and ‡P ≤ 0.001 when compared with control.
Do Surgical Patients Benefit from Perioperative Gabapentin/Pregabalin? A Systematic Review of Efficacy and Safety

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BACKGROUND: Gabapentin and pregabalin have antiallodynic and antihyperalgesic properties useful for treating neuropathic pain. These properties may also be beneficial in acute postoperative pain. In this study we evaluated randomized, controlled trials examining the analgesic efficacy, adverse effects, and clinical value of gabapentinoids in postoperative pain.

METHODS: A systematic search of Medline, PubMed, and Cochrane Central Register of Controlled Trials (CENTRAL) databases yielded 22 randomized, controlled trials on perioperative administration of gabapentinoids for postoperative pain relief.

RESULTS: Pain relief was better in the gabapentin groups compared with the control groups. The opioid-sparing effect during the first 24 h after a single dose of gabapentin 300–1200 mg, administered 1–2 h preoperatively, ranged from 20% to 62%. The combined effect of a single dose of gabapentin was a reduction of opioid consumption equivalent to 30 ± 4 mg of morphine (mean ± 95% CI) during the first 24 h after surgery. Meta-regression analysis suggested that the gabapentin-induced reduction in the 24-h opioid consumption was not significantly dependent on the gabapentin dose. Gabapentin reduced opioid-related adverse effects, such as nausea, vomiting, and urinary retention (number-needed-to-treat 25, 6, and 7, respectively). The most common adverse effects of the gabapentinoids were sedation and dizziness (number-needed-to-harm 35 and 12, respectively).

CONCLUSIONS: Gabapentinoids effectively reduce postoperative pain, opioid consumption, and opioid-related adverse effects after surgery. Conclusions about the optimal dose and duration of the treatment cannot be made because of the heterogeneity of the trials. Studies are needed to determine the long-term benefits, if any, of perioperative gabapentinoids.

(Austral Anaerg 2007;104:1545-56)
• Summary of Findings:

- Net opioid sparing effect 20-62%
- Reduction in opioid SE – NNT 25 (nausea), 6 (vomiting), 7 (urinary retention)
- Effect independent of Gabapentin dose used
- SE minimal – NNH 35 (sedation), 12 (dizziness)
PROGRESSION TO CHRONIC PAIN
<table>
<thead>
<tr>
<th>Type of 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>
• Preexisting pain
  – Central nervous system hyperexcitability
  – Opioid tolerance
• Physical nerve injury
  – Location of surgical procedure (e.g., chest wall)
  – Surgical technique
• Postoperative pain severity
  – Inadequate analgesia techniques
  – Extent of tissue injury
  – Psychological factors (e.g., depression)
  – Gender
  – Genetics including pharmacogenetics
• Impaired nerve repair (or aggravated injury)
  – Radiotherapy
  – Chemotherapy
• Other factors
  – Genetic
  – Psychological