Multimodal Analgesic Options to Minimize Post-Cesarean Pain

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Patient Preferences for Anesthesia Outcomes Associated with Cesarean Delivery

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Rank</th>
<th>Relative Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain During Cesarean</td>
<td>8.4 ± 2.2</td>
<td>27 ± 18</td>
</tr>
<tr>
<td>Pain After Cesarean</td>
<td>8.3 ± 1.8</td>
<td>18 ± 10</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7.8 ± 1.5</td>
<td>12 ± 7</td>
</tr>
<tr>
<td>Nausea</td>
<td>5.8 ± 1.7</td>
<td>11 ± 7</td>
</tr>
<tr>
<td>Cramping</td>
<td>6.0 ± 1.9</td>
<td>10 ± 8</td>
</tr>
<tr>
<td>Itching</td>
<td>5.6 ± 2.1</td>
<td>9 ± 8</td>
</tr>
<tr>
<td>Shivering</td>
<td>4.6 ± 1.7</td>
<td>6 ± 6</td>
</tr>
<tr>
<td>Anxiety</td>
<td>4.1 ± 1.9</td>
<td>5 ± 4</td>
</tr>
<tr>
<td>Somnolence</td>
<td>2.9 ± 1.4</td>
<td>3 ± 3</td>
</tr>
</tbody>
</table>

Benefits of Postoperative Analgesia

- Improves functional recovery and sleep
- Less DVT and shorter hospital stay
- Breastfeeding success
- Maternal interaction with newborn
- ↓ Chronic persistent post-cesarean pain

Incidence: ± 10%


Opioids Post-Cesarean

Panch-Ma et al. Anesthesiology 1994
Harrison. Anesthesiology 1988; 68: 454-7

Intrathecal Opioids Post-Cesarean


Dose of Neuraxial Morphine


- Analgesic ceiling, dose-related side effects
  - Intrathecal: 50-200 mcg
  - Epidural: 2-4 mg

- Pain Intensity (1 - 4)
- Pain After Cesarean
- Vomiting
- Nausea
- Cramping
- Itching
- Shivering
- Anxiety
- Somnolence

PCA use

Dose of Neuraxial Morphine

- Epidural
- Intrathecal
- Spinal Morphine
ELEM (DepoDur®) Post-Cesarean

Total Narcotic Medication Usage
0 - 48 h (IV MS equivalents in mg)

*p<0.05

ELEM 10 mg vs. Epidural Morphine 4 mg
Single-dose, post-delivery
Carvalho, Anesth Analg 2007; 105: 176-83

ELEM (DepoDur®) Post-Cesarean
Limited Use

• Epidural or CSE only
• Side-effects
• Respiratory depression
• Cost
• Familiarity
• Marketing
• Potential local anesthetic interaction

Carvalho et al. Anesth Analg 2005; 100: 1150-8

Opioid Side-Effects
IT Morphine for Cesarean Delivery

• Pruritus: Incidence 40-90%, dose-dependent
• Nausea and Vomiting: 20-30%
• Respiratory Depression:
  Very low incidence 1: ± 3-500 (mild) → 1: ± 2-5000
  Neuraxial opioids benefits far outweigh risks
  Risk not increased compared to IV opioids

Carvalho B. Anesth Analg. 2008; 107: 956-61

Oral Opioids vs. Intravenous PCA
Post-Cesarean

• Oxycodone-acetaminophen (5/325 mg) 1 to 2 tablets vs.
• Morphine PCA 1 mg, 6 min lock-out, 1 mg/h background

• Less pain at 6 and 24 h
• Less nausea and drowsiness at 6 h


NSAIDs Post-Cesarean

• Numerous post-CS studies show analgesic and opioid-sparing advantage
• Naproxen, indomethacin, diclofenac, ketorolac, tenoxicam, ketoprofen (NNT 1.8-2.7)
• Opioid sparing: 30 - 50%
• ↓ Opioid-related SEs (vomit, sedation ↓ 30%)
• Low breast milk transfer: RID = 0.2-0.6

2. http://www.jr2.ox.ac.uk/bandolier/

Carvalho et al. Anesth Analg 2005; 100: 1150
Carvalho B. Anesth Analg. 2008; 107: 956-61

Oral
IV

*p = 0.04

n=36/gr
**Cox-2 Inhibitors: Celecoxib**

- Cox-2 analgesic efficacy similar to non-selective NSAIDs
- Celecoxib pain relief NNT: 4.2 (200 mg) and 2.5 (400 mg)
- No difference in pruritus and analgesia (secondary endpoint)
- Breast Milk Transfer: RID = 0.3%


**Acetaminophen**

- 10 - 20% opioid-sparing effect
- COX-3 activity
- Synergistic with oral opioids
- Additive effect than NSAIDs alone
- IV preparation
- Good side-effect profile

1. Remy. BJA 2005;94(4):505-513

**Local Anesthetic Wound Infiltration**

- Varying analgesic success reported
- Wound and peritoneal spraying
- Some benefits after cesarean under general anesthesia
- Minimal benefit post-cesarean under spinal anesthesia

Bamigboye AA, Hoffmyr GJ. Cochrane Database Syst Rev. 2009

**Long-Acting Local Anesthetics**

- Microspheres
- Uni and/or multi-layered Liposomes
- Multi-chambered Liposomes

Bamigboye AA, Hoffmyr GJ. Cochrane Database Syst Rev. 2009

**Continuous Local Anesthetic Wound Instillation**

- Disposable pumps
- ↓ Opioid use and rescue analgesia
- Reduced pain scores on activity
- Rate 2-5 ml/h

Bamigboye AA, Hoffmyr GJ. Cochrane Database Syst Rev. 2009

**Wound Instillation of Local Anesthetics**

- Multiorifice catheter
- Inserted by surgeon
- Ropivacaine 5 ml/h for 48 h
- Between unclosed parietal peritoneum and transversalis fascia

Intraperitoneal lidocaine reduces cesarean pain
Multimodal Wound Infiltration

Incisional Wound Nociceptive and Inflammatory Biochemical Mediator Release Following Cesarean Delivery

Transversus Abdominis Plane Block

Blind Technique

TAP Block: Ultrasound-Guided

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No Intrathecal Morphine

• Spinal anesthetic (bupivacaine + fentanyl)
• Diclofenac and acetaminophen

Blind Technique

Ultrasound-Guided

• 24 hours post-CS:
  • ↓ Morphine use (18 vs. 32 mg)
  • ↑ Satisfaction (96 vs. 77 mm)
  • ↓ Antiemetics


Costello et al. RAPM 2009;34(6)

TAB Block Post-Cesarean

With IT morphine

- 50 patients per group for 48 h
- 20 ml ropivacaine 0.375% (per side) vs. saline control
- Morphine for breakthrough pain

Kanazi et al. Anesth Analg 2010

TAP Block Vs. IT Morphine

- TAP (bupivacaine 0.375%) vs. IT morphine 200 mcg
- Multimodal analgesic (NSAIDs, acetaminophen)

Intrathecal morphine

- Superior post-cesarean analgesia at cost of increased opioid-related side effects
- Visceral (cramping) and somatic (wound) pain

TAP Block: Indications

Routine Use vs. Selected Patients
(e.g. GA, midline incision, opioid-dependent, no NSAIDs / opioid)
vs. Breakthrough Pain

- Limited duration unless catheter-based
- Reduces incisinal not deep visceral pain

Gabapentin / Pregabalin

The Good

- Gabapentin: Analgesic and opioid-sparing acute postoperative period
- Pregabalin: Dose-related reduction in postoperative opioid

Cesarean Delivery:
- Single-dose, 600 mg
- Chronic pain similar

Gabapentin

The Bad

- Pre-delivery: Mean (SD) umbilical vein to maternal vein ratio: 0.86 (0.12)
- Breastfeeding: Relative infant dose: 2.34%
- Maternal side-effects: Sedation

Ketamine

- Subanesthetic doses of ketamine reduce opioid use for 24 h after surgery
- Effective: 0.15 mg/kg IV during general or spinal anesthesia for cesarean
- Not effective: 10 mg IV after cesarean with spinal and multimodal analgesia

2. Zhang et al. BJA 2011; 106: 454-62
4. Bauch et al. IJOA 2011; 20: 3-9
Ketamine Effect on Postoperative Pain
Preoperative Temporal Summation

Lavand’homme. ASA and SOAP Best Paper 2009
Evaluates CNS sensitization and nociceptive hyperexcitability

Neuraxial Adjuvants

• Clonidine, Neostigmine, Etc.
• Modest analgesic prolongation
• Side-effects and toxicity limit routine use
• Fetal concerns
• ? Decrease pain sensitization and “wind-up” → persistent post-operative pain


Targeted or Individualized Treatment Plans

• Stratify patients
• Dosage adjustments or tailor treatment around patient’s needs
• Pain modifying agents (e.g. gabapentin, ketamine, clonidine)
• Early intervention
• Resource allocation

Predicting Post-Cesarean Pain and Analgesic Use
Current Knowledge

• Demographic, psychological and surgical factors: Younger, anxious, depressed, neurotic, preoperative pain, poor fetal outcome
• Experimental pain tests are promising
• Genetics of postoperative pain disappointing
• No prediction test or model has been developed for routine clinical use
• Severe acute postoperative pain is associated with chronic pain

Post-Cesarean Analgesia
Summary

• No “wonder drug” → Multi-modal approach
• Standard Management:
  IT or EPI Morphine
  NSAIDS + Acetaminophen
  Oral opioids for breakthrough pain
• Additional Medication:
  TAP blocks and LA instillation
  EREM and adjuvants (Gabapentin)
• Individualized Treatment Plans

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