Intraoperative Interventions to Reduce Postoperative Pain

Matthias Behrends, MD
Associate Professor
Department of Anesthesia & Perioperative Care
University of California San Francisco

Disclosures
I have nothing to disclose

The Question
Can the anesthesia provider achieve improved and prolonged postoperative analgesia with anesthetic interventions?

Revisited: Preemptive Analgesia
J Katz: Anesthesia & Analgesia. 2011
The End of Preemptive Analgesia

The review revealed a lack of evidence for preemptive treatment with NSAIDs, intravenous opioids, intravenous ketamine, peripheral local anesthetics, and caudal analgesia to be of any benefit with respect to postoperative pain relief. ... overall interpretation of all continuous epidural regimens did not support the hypothesis that preemptive analgesia is of greater benefit than analgesia administered after the onset of the surgical procedure.

Causes of Postoperative Pain

<table>
<thead>
<tr>
<th>preoperative</th>
<th>intraoperative</th>
<th>postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>genetic predisposition</td>
<td>intraoperative nociceptive afferents carrying injury discharges such as cutting skin, fascia and muscle, tendons, nerves, viscera, and bone</td>
<td>postoperative afferent inputs from regenerating wounded tissues</td>
</tr>
<tr>
<td>psychological vulnerability</td>
<td>wound retraction</td>
<td>inflammatory response</td>
</tr>
<tr>
<td>non-genetic environmental variables</td>
<td>manipulation of organs</td>
<td>neuropathic ectopic neural activity from regenerating afferent nerves</td>
</tr>
<tr>
<td>- expectations</td>
<td>chemical irritation</td>
<td>- pain</td>
</tr>
<tr>
<td>- cultural, - dietary</td>
<td>inflamed tissues</td>
<td>- preoperative noxious inputs</td>
</tr>
<tr>
<td>- preoperative noxious inputs</td>
<td>- in inflamed tissues</td>
<td>- postoperative noxious inputs</td>
</tr>
<tr>
<td>- pain</td>
<td>- in inflamed tissues</td>
<td>- postoperative noxious inputs</td>
</tr>
</tbody>
</table>

Preventive Analgesia

How can an anesthetic intervention result in prolonged analgesia?

By preventing sensitization.
**Nociceptive Transmission**

- Nociceptor Central Terminal
- Kainate
- AMPA
- Brain
- Pain
- Inhibitory Interneuron

**Central Sensitization – Acute Phase**

- Pain
- Hypersensitivity

**Disinhibition**

- Reduced Inhibitory Transmitter
- Loss of Inhibitory Interneuron
- Altered Descending Modulation from Brain

**Perioperative Interventions**

- Regional Anesthesia
  - Peripheral Nerve Blocks
  - Neuraxial Blocks
- Pharmacological Analgesic Interventions/ Anesthetic Adjuvants
  - Intravenous Local Anesthetics
  - Ketamine
  - Magnesium
  - Dexamethasone
  - COX-2 Inhibitors
  - TIVA
Regional Anesthesia

Review of 89 studies investigating the effects of peripheral nerve blocks on postoperative pain.

Peripheral nerve blocks decreases pain for the expected duration of the regional anesthetic and beyond:
Most of the cited studies examined pain scores and/or opioid consumption for 24 to 48 hours after surgery and local anesthetic administration.

Anesthesia & Analgesia, 2013, 116: 1141-1161
Regional Anesthesia and Chronic Postoperative Pain

23 RCTs studying regional for the prevention of chronic pain after surgery.

The data was considered too sparse for evidence synthesis for limb amputation, laparotomy, C-section, hernia repair, bone graft harvesting, and vasectomy.

Intravenous Local Anesthetics

16 randomized, double-blind, placebo controlled studies were identified that examined the IV use of lidocaine and its effect on postoperative pain.

A total of 678 patients were enrolled.

13 of 16 trials reported a preventive analgesic effect of intravenous lidocaine.
Ketamine

Mechanism of Action

- Non-competitive antagonist on the N-methyl-d-aspartate (NMDA) receptor
- Affects opioid receptors and monoaminergic receptors at higher doses
- Systemically administered ketamine has local anesthetic action
- Spinal effects have been documented
- Anti-inflammatory effects: shown to inhibit TNF and IL-6 gene expressions LPS-activated macrophages

Preventive analgesia by intraoperative ketamine was demonstrated in multiple studies

Magnesium

Mechanism: NMDA antagonist

Magnesium has been used for many years in an attempt to minimize postoperative pain. In 1963, Anstett reported on the effect of magnesium chelates on painful postoperative pulmonary scars.

<table>
<thead>
<tr>
<th>Meta-analysis evaluating the effect of systemic magnesium on late pain scores (24 h) at rest compared with control.</th>
</tr>
</thead>
</table>

**Steroids:**

Dexamethasone
COX inhibitors

- Acetaminphen
- NSAIDs (Ketorolac)
- COX-2 Inhibitors/ Coxibs

Thirty-six studies involving 3896 patients were included. 37% of patients receiving propacetamol or i.v. paracetamol experienced at least 50% pain relief over 4 h compared with 16% receiving placebo. The number of patients in propacetamol or i.v. paracetamol groups experiencing at least 50% pain relief diminished over 6 h. Patients receiving propacetamol or paracetamol required 30% less opioid over 4 h and 16% less opioid over 6 h than those receiving placebo. The reduction in opioid consumption did not translate to a reduction in opioid-induced adverse events (AEs).

Thirteen randomized clinical trials with 782 subjects were included. Ketorolac when compared to Placebo reduced early pain at rest by -0.64 (-1.11 to -0.18) but not late pain at rest --0.29 (-0.88 to 0.29).

Opioid consumption was decreased by the 60-mg dose, with a mean (95% CI) IV morphine equivalent consumption of -1.64 mg (-2.90 to -0.37 mg). Postoperative nausea and vomiting were reduced by the 60-mg dose, with an odds ratio (95% CI) of 0.49 (0.29–0.81).
Total Intravenous Anesthesia (TIVA)

Summary

Interventions that provide analgesia for 24 hours

- Intraoperative Lidocaine Infusions
- Intraoperative Magnesium Infusions
- Single Dose Systemic Dexamethasone
Summary

Interventions that reduce the risk for chronic postsurgical pain

- Regional Anesthesia
- Intraoperative Ketamine Infusion
- TIVA