Benefits and Limitations of Local Anesthetics in Postoperative Pain

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Discussion Topics

- Managing Severe Pain and Inflammation in the First 72 Hours Postoperatively
- Local Anesthetics: Benefits and Limitations
- Opioids Are Not the Optimal Solution
- Are There Opportunities for Improvement?
Managing Pain and Inflammation in the First 72 Hours Postoperatively
The first 72 hours after surgery are the most painful

Uncontrolled postoperative pain impedes patient recovery

- Negative impact on physical activity, sleep, and cognitive function
- Less likely to ambulate
- Delayed discharge
- Decreased patient satisfaction

References:
Types of postoperative pain

- Nociceptive pain
- Inflammatory pain
- Neuropathic pain

Inflammatory pain: peripheral sensitization

Local tissue damage activates a variety of cells, which release inflammatory mediators\(^1,2\)

- Inflammation can also modify the activity of the central nervous system’s pain pathways\(^1\)

- Inflammation is known to result in hyperalgesia\(^2\)

Inflammation is most active during the first 72 hours postoperatively

Inflammation peaks around 24 hours postoperatively and remains relatively high through the first 72 hours—and it is a significant component of postoperative discomfort.\textsuperscript{1,2}

Adequate treatment of pain and inflammation during the first 72 hours following surgery is critical.
Local Anesthetics:
Benefits and Limitations
Local anesthetics can be a strong foundation and first line of defense

- By allowing patients to come out of surgery with less severe pain, local anesthetics can provide a strong foundation for postoperative pain management.¹
  - Generic local anesthetics are not designed to provide pain relief beyond 8 to 12 hours¹
  - Longer-acting local anesthetics exhibit limited and inconsistent efficacy beyond 24 hours in part because the inflammatory process inhibits their ability to penetrate the nerve cell membrane²⁻⁶

Inflammation can inhibit the efficacy of local anesthetics such as bupivacaine

• To stop pain signals, bupivacaine must penetrate the nerve cell membrane\textsuperscript{1}
• The inflammatory process floods the wound with acidic metabolites, lowering pH at the surgical site\textsuperscript{2,3}
• Bupivacaine becomes ionized\textsuperscript{2}
• Ionized bupivacaine cannot penetrate and therefore cannot block pain signals\textsuperscript{2}

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The failure of local anesthetics to consistently manage pain beyond 24 hours has contributed to the extensive use of opioids\textsuperscript{1-9}

Opioids Are Not the Optimal Solution
The efficacy gap in postoperative pain management

**Defined as pain of >5 on 1-10 scale.**

* ~50 of the top procedures requiring post-op pain management (selected for analysis based on real-world post-op pain management usage).

The efficacy gap in postoperative pain management

Average Duration of Severe Pain¹,*

Duration of Action by Local Anesthetic¹

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Opioids work in the central nervous system—not at the site of injury

- 90% of patients are treated with opioids after surgery\(^1\)
- Opioids block pain centrally (at the brain), but they do not block transmission of the pain signals at the source\(^2\)
- Opioids can exacerbate postoperative pain, resulting in opioid-induced hyperalgesia and allodynia\(^3\)

**References:**
Opioids can have unintended consequences

- Opioids can cause serious adverse events (AEs), including respiratory depression\(^1\)
- Opioid-related AEs may increase length of hospital stay\(^2,3\)
- Opioids mask pain but cannot prevent the transmission of pain signals from the site of injury\(^4\)

How postoperative pain may contribute to the opioid crisis

As many as 6.5% of patients who take opioids to manage pain after surgery may become persistent opioid users.\(^1\)

That equals about 2.6 MILLION PEOPLE.\(^1\)

Of these 2.6 million persistent opioid users, approximately 440,000 will become addicted to opioids.\(^1,3\)

In addition, opioid discharge prescriptions filled by recovering surgical patients result in more than 1 billion unused pills.\(^1,2\)

70% of prescription opioids go unused by the patient.\(^2\)

90% of these pills remain inside the home.\(^4\)

32% of all opioid addicts report first opioid exposure through leftover pills.\(^5\)

More than $13 billion of the annual healthcare costs associated with addiction can be attributed to postoperative pain management.\(^1,3,6\)

Are There Opportunities for Improvement?
A longer-acting local anesthetic could reduce the treatment gap

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** ~50 of the top procedures requiring post-op pain management (selected for analysis based on real-world post-op pain management usage).

A longer-acting local anesthetic could impact the way we treat pain

• **Many experts agree:**
  It’s time to update the current WHO analgesic ladder¹-³

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**STEP 1:**
Acetaminophen, NSAIDs or Coxib Selective Inhibitors, Gabapentinoids, and Local/Regional Anesthesia

**STEP 2:**
Step 1 and Low Doses of Opioids

**STEP 3:**
Step 1 + Step 2 and Higher Doses of Opioids

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**Mild Pain**

**Moderate Pain**

**Severe Pain**

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A longer-acting local anesthetic could impact the way we treat pain

- A new proposed algorithm addresses the need for acute pain relief to avoid adverse outcomes and lowers risks associated with opioids

In conclusion

- Surgery causes nociceptive, inflammatory, and neuropathic pain\(^1\)
- Postoperative pain and inflammation are most severe in the first 72 hours following surgery\(^2,3\)
- Improperly managed postoperative pain can lead to delayed recovery\(^4\)
- Local anesthetics stop pain signals at the source\(^5\)
- Many products exhibit limited and inconsistent efficacy beyond 12 to 24 hours\(^5\)
- The inflammatory process inhibits current local anesthetics\(^7\)
- Many local anesthetic options fail after 24 hours, contributing to the extensive use of opioids for postoperative pain management\(^8\)
- Opioids are associated with adverse events and addiction\(^8,9\)
- Opioids do not stop pain signals at the source\(^10\)

The ideal solution:
- Longer-acting local anesthetic
- Reduction in opioid exposure

Thank You