CADTH Evidence Driven.

Codeine for Acute Pain: A Synopsis of the Evidence

Acute pain is pain that lasts for minutes to weeks. There are many interventions available for the management of acute pain. Opioids are one of the potential treatment options and there are many opioids available. Opioid prescribing practices have come under scrutiny in recent years as Canada battles with an opioid epidemic. Overprescribing of opioids and the diversion of non-consumed supplies has created a need to optimize opioid prescribing. Specifically, the evidence surrounding codeine for acute pain is being reviewed here. Codeine is a weak opioid that is metabolized by the liver to become various metabolites, including morphine. The conversion to morphine accounts for some of codeine's painrelieving effects. How fast the liver metabolizes codeine varies in the general population, which is why some patients experience good pain relief with codeine and others do not. Codeine may also be combined with acetaminophen for an additive analgesic effect.

CADTH has reviewed the evidence regarding the clinical effectiveness for codeine, with or without acetaminophen, versus various comparators, for the management of acute pain in various patient populations.

In this report, you will find a summary of the evidence for:

- · Codeine for acute pain for urological or general surgery patients
- · Codeine for pediatric patients with acute pain
- · Codeine for acute pain in patients undergoing orthopedic surgery



Codeine for Acute Pain for Urological or General Surgery Patients: A Review of Clinical Effectiveness (2019)

cadth.ca/codeine-acute-pain-urological-or-general-surgery-patients-review-clinical-effectiveness-0

Issue: Surgical procedures can cause inflammation, tissue injury, or nerve injury that result in pain. The therapeutic options for post-operative pain are multimodal and tailored to the patient's characteristics, needs, and the level of pain associated with the surgery. Opioids, including codeine, are the most widely used treatment for post-operative pain management. Patients can experience varying pain-relieving effects with codeine because there is variability in how quickly an individual's liver will metabolize the drug. A review of the clinical effectiveness of codeine, with or without acetaminophen, versus various comparators, may help inform decisions on the use of codeine-containing products for acute pain after urological, or general surgeries.

CADTH Assessed Relevant Evidence Found In: zero publications

Key Messages:

- No relevant literature was identified regarding the use of codeine, with or without acetaminophen, versus relevant comparators, for patients with acute pain due to urological or general surgery.
- More research is needed to examine the comparative clinical effectiveness of codeine, with or without acetaminophen, for patients with acute pain after urological or general surgery.

Codeine for Pediatric Patients with Acute Pain: A Review of Clinical Effectiveness (2019)

cadth.ca/codeine-pediatric-patients-acute-pain-review-clinical-effectiveness-0

Issue: Various organizations around the world have issued warnings regarding the use of codeine for pain in pediatric patients. In 2013, Health Canada recommended against the use of codeine in children younger than 12 after reviewing the safety of prescription pain and cough medications containing codeine. A review of the clinical effectiveness of codeine, with or without acetaminophen, may help inform decisions on the use of codeine-containing products for pediatric patients with acute pain.

CADTH Assessed Relevant Evidence Found In: one systematic review, three randomized controlled trials, and one non-randomized study

Key Messages:

- Adverse events for codeine for acute pain in pediatric patients did not differ significantly from ibuprofen or hydrocodone based on the findings from one systematic review and one non-randomized study.
- There were mixed results across outcome measures (adverse events, pain, treatment failure, and functional outcomes) for codeine with acetaminophen compared to ibuprofen or acetaminophen monotherapies for acute pediatric pain.
 - Compared to ibuprofen, codeine with acetaminophen had similar results in pediatric pain severity and treatment failure (statistical significance was not tested for this outcome) and had significantly more adverse events. Codeine with acetaminophen was significantly less effective compared with ibuprofen for some functional outcomes (playing and eating); however, between-group differences for other functional outcomes (i.e., school and sleep) were unclear (i.e., no data or statistical comparisons reported).



- Compared with acetaminophen, pediatric patients who received codeine with acetaminophen had lower pain and distress.
- High-quality studies on the clinical effectiveness of codeine compared with nonsteroidal antiinflammatory medications are needed.
- Additional high-quality studies may further aid in making definitive conclusions about the role of codeine with acetaminophen for the management of acute pain in pediatric patients.

Codeine for Acute Pain in Patients Undergoing Orthopedic Surgery: A Review of Clinical Effectiveness (2019)

cadth.ca/codeine-acute-pain-patients-undergoing-orthopedic-surgery-review-clinical-effectiveness

Issue: Surgical procedures can cause inflammation, tissue injury, or nerve injury that result in pain. The therapeutic options for post-operative pain are multimodal and tailored to the patient's characteristics, needs, and the level of pain associated with the surgery. Opioids, including codeine, are the most widely used treatment for post-operative pain management. Patients can experience varying pain-relieving effects with codeine because there is variability in how quickly an individual's liver will metabolize the drug. A review of the clinical effectiveness of codeine, with or without acetaminophen, versus various comparators, may help inform decisions on the use of codeine-containing products for acute pain after orthopedic surgeries.

CADTH Assessed Relevant Evidence Found In: two systematic reviews

Key Messages:

- Two systematic reviews for the management of pain after orthopedic surgery were identified. These reviews did not contain any relevant literature regarding the clinical effectiveness of codeine, with or without acetaminophen, versus relevant comparators, for pain management in patients who have undergone orthopedic surgery.
- More research is needed to examine the comparative clinical effectiveness of codeine, with or without acetaminophen, for patients with acute pain after orthopedic surgery.



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