

# THE TABLET: PALLIATIVE CARE PHARMACY TIPS



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Palliative Care  
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If you have a topic you  
would like the pharmacy  
team to answer, please  
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## TODAY'S TOPIC:

**Requested Topic: IV Acetaminophen for Acute Pain: How does it compare to other analgesics?**

### Background:

Acetaminophen (APAP) is one of the most used analgesics as it is cheap, available over the counter and in various formulations: oral, rectal, and intravenous (IV). Acetaminophen has been studied to have favorable efficacy and safety profiles and has a very low potential for severe drug interactions. Thus, it is widely used for pain management in patients with cancer, patients undergoing procedures, and patients in palliative care.

### Importance:

Pain management is an essential part of palliative care to achieve a better quality of life in patients with terminal illnesses. IV acetaminophen is widely used for pain control for various reasons due to its well-established safety and efficacy profiles. However, it is unclear whether IV acetaminophen offers advantages over oral acetaminophen or other analgesics in managing acute pain.

### The Literature:

#### **Question #1: Does IV acetaminophen perform better than PO acetaminophen in the setting of acute pain?**

[Can J Hosp Pharm. 2015 May-Jun;68\(3\):238-47.](#)

##### **Intravenous versus Oral Acetaminophen for Pain: Systematic Review of Current Evidence to Support Clinical Decision-Making.**

- > No strong evidence suggesting superiority of IV APAP administration over oral routes
- > Pettersson et al. (2005): significantly lower use of rescue opioids postoperatively in the IV group ( $17.4 \pm 7.9$  mg vs.  $22.1 \pm 8.6$  mg;  $p < 0.05$ ) than with the oral APAP

[J Arthroplasty. 2017 Apr;32\(4\):1125-1127.](#)

##### **Randomized Prospective Trial Comparing the Use of Intravenous versus Oral Acetaminophen in Total Joint Arthroplasty**

- > **Methods:** prospective, randomized trial
  - Patients undergoing hip and knee arthroplasty randomized to receive either intravenous or oral acetaminophen
- > **Results:** n = 120 patients (63 receiving IV and 57 receiving PO)
  - 24-hour average VAS scores in IV group were 3.00 and 3.40 in PO group ( $p = 0.06$ )
  - Only the first interval VAS scores (0-4 hour post-operatively) were significantly different and favored the IV group ( $p = 0.03$ )
  - 24-hour average hydromorphone equivalents given were not different between groups (3.71 vs 3.48) at 24 hours ( $p = 0.76$ )

[Br J Anaesth. 2005 May;94\(5\):642-8.](#)

##### **Onset of acetaminophen analgesia: comparison of oral and intravenous routes after third molar surgery**

- > **Methods:** double blind, randomized
  - Patients aged 18–50 years post third molar removal were given APAP as either 2-min IV bolus injection, 15-min IV infusion, oral or placebo
- > **Results:** n = 175 patients (50 in each active treatment group and 25 in placebo group)
  - IV APAP has shorter onset (3 min for bolus administration, 5 min for 15-min infusion) than oral APAP (11 min)
  - Active treatments (all acetaminophen) significantly better for pain relief, pain intensity, duration of analgesia than placebo
  - Adverse events occurred more frequent after IV APAP, especially pain at the injection site (52-90%)

#### **Question #2: Are there any other comparison studies of IV acetaminophen and other analgesics?**

[Ann Emerg Med. 2022 Nov;80\(5\):432-439.](#)

##### **A randomized study of intravenous hydromorphone versus intravenous acetaminophen for older adult patients with acute severe pain.**

- > **Methods:** double blind, parallel group, randomized trial
  - Patients aged 65 years or more with acute pain in the EDs were given either 1000mg IV acetaminophen or 0.5mg IV hydromorphone
- > **Outcomes:**
  - Primary outcome: improvement in a 0 to 10 pain scale from baseline to 60 minutes later
  - Secondary outcomes: need for additional analgesic medication and adverse events
- > **Results:** n = 162 patients
  - Primary outcome:
    - Minimum clinically important difference: 1.3
    - Baseline median pain score: 10
    - By 60 minutes: difference was not clinically significant
      - APAP improved by 3.6 (+/- 2.9)
      - Hydromorphone improved by 4.6 (+/- 3.3)
  - Secondary outcomes: need for additional analgesic and adverse events
    - Additional analgesic needed in
      - 37 APAP patients
      - 31 hydromorphone patients
    - Adverse events (dizziness, drowsiness, headache, nausea)
      - 6 APAP patients
      - 10 hydromorphone patients

**CLINICAL PEARL: IV acetaminophen does not seem to be superior to PO acetaminophen or other analgesics (ie. opioids)**



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[Br J Aneasth. 2006 Jun;96\(6\):790-5.](#)

**Effects of intraoperative i.v. acetaminophen vs i.m. meperidine on post-tonsillectomy pain in children**

- > **Methods:** double blind, randomized study
  - Patients aged 3-16 year were given either IV APAP or IM meperidine
- > **Results:** n = 80 patients (40 patients in each group)
  - IV APAP provided adequate analgesia, less sedation and earlier readiness for recovery room discharge than IM meperidine
    - Shorter median (IQR) time to readiness for PACU discharge in APAP group than meperidine group [15 (0–20) min vs. 25 (15–30) min]
    - Ramsay sedation scores were 3 (SEM 0.2) and 4 (SEM 0.3) for the acetaminophen and meperidine groups

[Arch Pediatr Adolesc Med. 2004 Jun;158\(6\):521-6.](#)

**Efficacy and Safety of Acetaminophen vs Ibuprofen for Treating Children's Pain or Fever**

- > Meta-analysis of 17 blinded, randomized controlled trials with children (<18 years) receiving either acetaminophen or ibuprofen to treat fever or moderate to severe pain
- > Similar efficacy and safety in relieving moderate to severe pain between ibuprofen (4-10 mg/kg) and APAP (7-15 mg/kg)
  - Point-estimate of the weighted mean was 1.14 (95% confidence interval [CI], 0.82-1.58) after 2 hours, and 1.11 (95% CI, 0.89-1.38) after 4 hours, slightly favoring ibuprofen
  - 95% CIs include values favoring APAP

**Bottom Line:**

- IV acetaminophen has not been well-studied in the palliative care population, it is unclear if these studies are totally generalizable to our population
- IV acetaminophen provides faster onset of analgesia than PO formulation with questionable clinical significance (3-5 mins versus 11 mins) although degree of analgesia did not seem to differ between IV and PO formulations
- IV acetaminophen comes with possibility of injection site reactions, need for IV access, and can contribute to fluid volume especially in end-of-life setting
- Recent RCT in ED showed no significant difference in pain reduction between one time dose of IV acetaminophen and IV hydromorphone (10mg OME)

	<b>IV Acetaminophen versus PO Acetaminophen</b>	<b>IV Acetaminophen versus other analgesics</b>
<b>Safety</b>	IV: more administration site reactions	Opioids: more sedation
<b>Tolerability</b>	IV: nausea, dizziness, malaise PO: well-tolerated	Opioids: more dizziness, drowsiness, headache, nausea
<b>Efficacy</b>	IV: 3-5 min for analgesia onset PO: 11 min for analgesia onset Similar degree of analgesia	No clinically significant difference in pain scores after 1 time doses
<b>Price</b>	IV: \$0.09-0.45 PO: \$0.05	Oral acetaminophen remains the cheapest
<b>Simplicity</b>	IV requires IV-line access	All available in IV and PO formulations Hydromorphone available as PCA Meperidine given more frequently (Q3-4H)