

CADTH Reference List

Post-Discharge Outcomes Following Intravenous Acetaminophen Treatment in Acute Care Settings

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Key Message

- Seven randomized controlled trials and 3 non-randomized studies were identified regarding the clinical effectiveness of intravenous acetaminophen used in acute care settings for adult patients with any acute pain condition.

Research Question

What is the clinical effectiveness of intravenous acetaminophen used in acute care settings for adult patients with any acute pain condition?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE and Embase via OVID, the Cochrane Database of Systematic Reviews, the international HTA database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were intravenous acetaminophen and acute care settings. No filters were applied to limit the retrieval by study type. Comments, newspaper articles, editorials, conference abstracts, and letters were excluded. Where possible, retrieval was limited to the human population. The search was also limited to English-language documents published between January 1, 2016 and April 16, 2021. Internet links were provided, where available.

Selection Criteria and Summary Methods

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. The Overall Summary of Findings was based on information available in the abstracts of selected publications.

Results

Seven randomized controlled trials¹⁻⁷ and 3 non-randomized studies⁸⁻¹⁰ were identified regarding the clinical effectiveness of intravenous acetaminophen used in acute care settings for adult patients with any acute pain condition. No health technology assessments or systematic reviews were identified.

Additional references of potential interest that did not meet the inclusion criteria are provided in Appendix 1.

Table 1: Selection Criteria

Criteria	Description
Population	Adult patients with any acute pain condition (surgical and non-surgical) in acute care settings (e.g., emergency department, intensive care unit, inpatient cancer unit, surgical unit)
Intervention	Acetaminophen alone given intravenously or in combination with other pain medications given by any route of administration (e.g., oral, rectal, transdermal)
Comparator	<ul style="list-style-type: none"> • Nonsteroidal anti-inflammatory drugs alone or in combination with other pain medications given by any route • Opioids alone or in combination with other pain medications given by any route • Acetaminophen alone given by any route other than intravenously or in combination with other pain medications given by any route • Placebo alone (e.g., intravenous saline) or in combination with other pain medications given by any route
Outcomes	Post-discharge clinical effectiveness outcomes (e.g., pain score, change in opioid use/abuse, overdose and overdose-related harms, other adverse events, re-hospitalization)
Study designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies

Overall Summary of Findings

One randomized controlled trial (RCT)¹ and 2 non-randomized studies^{8,9} IV acetaminophen to oral acetaminophen. In the RCT,¹ no difference was found between groups on opioid use, while both non-randomized studies^{8,9} reported that IV acetaminophen was associated with lower 30-day readmission rates. Two RCTs^{2,3} and 1 non-randomized study¹⁰ compared IV acetaminophen to alternative pain medications. One RCT² reported the IV acetaminophen group did not differ from patients who received other pain medications on chronic pain over a 2-month follow-up period; the non-randomized study¹⁰ reported that patients who received IV acetaminophen tended to use fewer opioids after discharge compared to the control group. One RCT³ reported no adverse events occurred in any group during the 2-week follow-up period. Four RCTs⁴⁻⁷ compared IV acetaminophen to placebo. Two RCTs^{5,7} reported improved outcomes in the IV acetaminophen group, with fewer emergency department visits 30 days post-operatively,⁵ lower persistent incisional pain scores at 3 months, significantly better DN4 questionnaire scores, and mental health-related quality of life,⁷ although no difference was found for physical health-related quality of life.⁷ The remaining 2 RCTs^{4,6} reported no statistically significant differences between groups on self-reported pain, nausea, and post-operative oral opiates taken after discharge,⁴ or incisional pain 30 and 90 days after surgery.⁶ A detailed summary of the identified studies can be found in Table 2.

Table 2: Summary of Included Studies

First author, year	Study characteristics and population	Intervention and comparator(s) of interest	Relevant outcome(s)	Authors' conclusions
Randomized controlled trials				
Patel et al. (2020) ¹	Study design: RCT Population: Patients undergoing any laparoscopic unilateral hernia repair surgery in the ambulatory setting N = 100	Intervention: IV acetaminophen (1,000 mg) Comparator(s): Oral acetaminophen (975 mg)	Home opioid MME	No statistically significant difference was found on home opioid MME use
Kamel et al. (2018) ²	Study design: RCT Population: Cardiac surgery patients N = 90	Intervention: IV acetaminophen and ketorolac Comparator(s): 0.125% bupivacaine and 5% magnesium sulphate; or 0.125% bupivacaine, only	Chronic post-sternotomy pain over 2 months	Incidence of chronic pain did not differ between groups, but it was more pronounced in the IV acetaminophen and ketorolac group
Pathan et al. (2016) ³	Study design: RCT Population: Patients presenting to the emergency department with renal colic N = 1,645	Intervention: IV acetaminophen (1g/100 mL) Comparator(s): Intramuscular diclofenac (75 mg/3 mL) or IV morphine (0.1 mg/kg)	Additional adverse events during a 2-week follow-up period	No additional adverse events were noted in any group
Rindos et al. (2019) ⁴	Study design: RCT Population: Laparoscopic hysterectomy patients N = 183	Intervention: IV acetaminophen (1,000 mg) Comparator(s): Placebo	Post-operative oral opiates taken after discharge	No significant differences were found between groups
Koyuncu et al. (2018) ⁵	Study design: RCT Population: Abdominal hysterectomy patients N = 140	Intervention: IV acetaminophen Comparator(s): Saline placebo	At 3 months after surgery: persistent incisional pain scores, DN4 questionnaire score, mental health- and physical health-related quality of life (SF-12)	Acetaminophen group had lower persistent incisional pain scores, and better DN4 scores and mental health-related quality of life but not physical health-related quality of life
Turan et al. (2017) ⁶	Study design: RCT Population: Patients undergoing cardiac surgery via median sternotomy N = NR	Intervention: IV acetaminophen (4 doses of 1 g) Comparator(s): IV placebo (4 doses of 1 g)	Self-reported incisional pain severity 30 and 90 days after surgery	Acetaminophen had no effect on 30- and 90-day incisional pain; both groups reported low pain severity, neuropathic pain, and interference at both time points

First author, year	Study characteristics and population	Intervention and comparator(s) of interest	Relevant outcome(s)	Authors' conclusions
El Chaar et al. (2016) ⁷	Study design: RCT Population: Bariatric surgery patients N = 100	Intervention: IV acetaminophen + IV narcotics Comparator(s): IV placebo	Presentation to the emergency department in the first 30 days post-operatively	Using IV acetaminophen reduced ED visits in the first 30 days post-operatively
Non-randomized studies				
Mont et al. (2019) ⁸	Study design: Cohort study Population: Patients undergoing total knee arthroplasty N = 190,691	Intervention: IV acetaminophen Comparator(s): Oral acetaminophen	30-day readmission rates	Patients who received IV acetaminophen had lower readmission rates than those who received oral acetaminophen
Hansen et al. (2017) ⁹	Study design: Retrospective cohort study Population: Spine surgery patients N = 112,586	Intervention: IV acetaminophen Comparator(s): Oral acetaminophen	30-day readmission	Patients who received IV acetaminophen had lower readmission rates than those who received oral acetaminophen
Blok et al. (2021) ¹⁰	Study design: Prospective cohort study Population: Patients presenting to the emergency department with painful conditions N = 116	Intervention: IV acetaminophen + opioids Comparator(s): Opioids only	Opioid consumption in MEUs during 24 hours after discharge	Patients who received additional IV acetaminophen trended toward reduced opioid requirement 24 hours after discharge

ED =emergency department; MEU = morphine equivalent unit; MME = morphine milligram equivalents; RCT = randomized controlled trial; SF-12 = 12-Item Short Form Health Survey.

References

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

No literature identified.

Randomized Controlled Trials

Comparator – Oral Acetaminophen

1. Patel A, Pai BHP, Diskina D, Reardon B, Lai YH. Comparison of clinical outcomes of acetaminophen IV vs PO in the peri-operative setting for laparoscopic inguinal hernia repair surgeries: a triple-blinded, randomized controlled trial. *J Clin Anesth.* 2020;61:109628. [PubMed](#)

Comparator – Alternative Pain Medication

2. Kamel EZ, Abd-Elshafy SK, Sayed JA, Mostafa MM, Seddik MI. Pain alleviation in patients undergoing cardiac surgery; presternal local anesthetic and magnesium infiltration versus conventional intravenous analgesia: a randomized double-blind study. *Korean J Pain.* 2018;31(2):93-101. [PubMed](#)
3. Pathan SA, Mitra B, Straney LD, et al. Delivering safe and effective analgesia for management of renal colic in the emergency department: a double-blind, multigroup, randomised controlled trial. *Lancet.* 2016;387(10032):1999-2007. [PubMed](#)

Comparator – Placebo

4. Rindos NB, Mansuria SM, Ecker AM, Stuparich MA, King CR. Intravenous acetaminophen vs saline in perioperative analgesia with laparoscopic hysterectomy. *Am J Obstet Gynecol.* 2019;220(4):373.e371-373.e378. [PubMed](#)
5. Koyuncu O, Hakimoglu S, Ugur M, et al. Acetaminophen reduces acute and persistent incisional pain after hysterectomy. *Ann Ital Chir.* 2018;7:15. [PubMed](#)
6. Turan A, Karimi N, Zimmerman NM, Mick SL, Sessler DI, Mamoun N. Intravenous acetaminophen does not decrease persistent surgical pain after cardiac surgery. *J Cardiothorac Vasc Anesth.* 2017;31(6):2058-2064. [PubMed](#)
7. El Chaar M, Stoltzfus J, Claros L, Wasyluk T. IV Acetaminophen results in lower hospital costs and emergency room visits following bariatric surgery: a double-blind, prospective, randomized trial in a single accredited bariatric center. *J Gastrointest Surg.* 2016;20(4):715-724. [PubMed](#)

Non-Randomized Studies

Comparator – Oral Acetaminophen

8. Mont MA, Lovelace B, Pham AT, et al. intravenous acetaminophen may be associated with reduced odds of 30-day readmission after total knee arthroplasty. *J Knee Surgery.* 2019;32(5):414-420. [PubMed](#)
9. Hansen RN, Pham AT, Boing EA, Lovelace B, Wan GJ, Miller TE. Comparative analysis of length of stay, hospitalization costs, opioid use, and discharge status among spine surgery patients with postoperative pain management including intravenous versus oral acetaminophen. *Curr Med Res Opin.* 2017;33(5):943-948. [PubMed](#)

Comparator – Alternative Pain Medication

10. Blok Z, Ridderikhof ML, Goddijn H, Berendsen M, Hollmann MW. Intravenous acetaminophen does not have an opioid sparing effect in emergency department patients with painful conditions. *Am J Emerg Med.* 2021;39:1-5. [PubMed](#)

Appendix 1: References of Potential Interest

Systematic Reviews and Meta-analyses

Alternative Population – Patients With Fever

11. Lewis SR, Baker PE, Andrews PJ, et al. Interventions to reduce body temperature to 35 0C to 37 0C in adults and children with traumatic brain injury. *Cochrane Database Syst Rev.* 2020;10:CD006811. [PubMed](#)

Randomized Controlled Trials

Alternative Population – Pediatric Patients

12. Dhebaria T, Sivitz A, Tejani C. Does intravenous acetaminophen reduce opioid requirement in pediatric emergency department patients with acute sickle cell crises? *Acad Emerg Med.* 2020;06:06. [PubMed](#)
13. Juujarvi S, Kallankari H, Patsi P, et al. Follow-up study of the early, randomised paracetamol trial to preterm infants, found no adverse reactions at the two-years corrected age. *Acta Paediatr.* 2019;108(3):452-458. [PubMed](#)

Unclear Comparator

14. Reagan KML, O'Sullivan DM, Gannon R, Steinberg AC. Decreasing postoperative narcotics in reconstructive pelvic surgery: a randomized controlled trial. *Am J Obstet Gynecol.* 2017;217(3):325.e321-325.e310. [PubMed](#)

Unclear Outcome

15. Truelove EC, Urrechaga E, Fernandez C, Fowler JR. Prospective, double-blind evaluation of perioperative intravenous acetaminophen and ketorolac for postoperative pain and opioid consumption after endoscopic carpal tunnel release. *Hand (NY).* 2020:1558944720906501. [PubMed](#)
16. Wang VC, Preston MA, Kibel AS, et al. A prospective, randomized, double-blind, placebo-controlled trial to evaluate intravenous acetaminophen versus placebo in patients undergoing robotic-assisted laparoscopic prostatectomy. *J Pain Palliat Care Pharmacother.* 2018;32(2-3):82-89. [PubMed](#)

Non-Randomized Studies

Alternative Population – Pediatric Patients

17. Gornitzky AL, Flynn JM, Muhly WT, Sankar WN. A rapid recovery pathway for adolescent idiopathic scoliosis that improves pain control and reduces time to inpatient recovery after posterior spinal fusion. *Spine Deform.* 2016;4(4):288-295. [PubMed](#)

Unclear or No Comparator

18. Vuong B, Dusendang JR, Chang SB, et al. Outpatient mastectomy: factors influencing patient selection and predictors of return to care. *J Am Coll Surg.* 2021;232(1):35-44. [PubMed](#)
19. Connolly KP, Kleinman RS, Stevenson KL, Neuman MD, Mehta SN. Delirium reduced with intravenous acetaminophen in geriatric hip fracture patients. *J Am Acad Orthop Surg.* 2020;28(8):325-331. [PubMed](#)
20. Mattern HP, Reichert JC, McConnell KJ. The effect of intravenous acetaminophen on patient outcomes within a large integrated delivery network. *Pharmacotherapy.* 2020;40(4):301-307. [PubMed](#)
21. Vu V, Baker WL, Tencza EM, Rochon C, Sheiner PA, Martin ST. Intravenous acetaminophen for postoperative pain management in patients undergoing living laparoscopic living-donor nephrectomy. *Ann Pharmacother.* 2017;51(1):21-26. [PubMed](#)

Unclear Outcomes

22. Kawakami J, Abe T, Higaki E, et al. Scheduled intravenous acetaminophen versus nonsteroidal anti-inflammatory drugs (NSAIDs) for better short-term outcomes after esophagectomy for esophageal cancer. *Surg Today.* 2020;50(10):1168-1175. [PubMed](#)
23. Wesmiller SW, Bender CM, Conley YP, et al. A prospective study of nausea and vomiting after breast cancer surgery. *J Perianesth Nurs.* 2017;32(3):169-176. [PubMed](#)