

Evaluation of an Intravenous Acetaminophen Protocol in the Emergency Department

Received 11/22/2023
Review began 12/19/2023
Review ended 01/09/2024
Published 01/25/2024

© Copyright 2024

Deutsch et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Aaron B. Deutsch¹, John D. DelBianco², Patrick Fagan¹, Kimberly Sharpe³, Jason Laskosky³, Laura Koons³, Gillian A. Beauchamp², Kenneth D. Katz²

1. Department of Emergency and Hospital Medicine, Lehigh Valley Health Network/University of South Florida (USF) Morsani College of Medicine, Allentown, USA 2. Department of Emergency and Hospital Medicine, Division of Medical Toxicology, Lehigh Valley Health Network/University of South Florida (USF) Morsani College of Medicine, Allentown, USA 3. Department of Pharmacy, Lehigh Valley Health Network/University of South Florida (USF) Morsani College of Medicine, Allentown, USA

Corresponding author: Gillian A. Beauchamp, gillian.beauchamp@lvhn.org

Abstract

Background: Acute pain is a leading reason for Emergency Department (ED) evaluation, accounting for nearly half of all ED visits. Therefore, providing effective non-opioid analgesics in the ED is critical. Oral acetaminophen (APAP) is commonly administered in the ED but is limited to patients tolerating oral intake. Intravenous (IV) APAP provides significant pain reduction parenterally. The purpose of this quality assessment project was to evaluate the frequency of opioid use in patients receiving IV APAP, the safety of IV APAP, and compliance with an ED IV APAP protocol.

Methods: This study included all patients who received IV APAP in the ED of a tertiary care, level I trauma center, during a three-month period. The protocol required ED patients to be NPO (nil per os), 18 years or older, and administered with a single 1000 mg dose. The adverse reactions within 24 hours post-IV APAP, ED length of stay (LOS), and opioid administration within four hours post-IV APAP were assessed.

Results: Ninety-four patients received IV APAP. All patients received a 1000 mg dose. One patient received more than one dose, but this patient had a 22-hour ED LOS. Two patients received oral medications within one hour of IV APAP (one received an antacid, and the other received carbamazepine and lamotrigine). An opioid was administered to 22 of the 94 (23.4%) patients during the four-hour protocol period. There were no reports of adverse reactions.

Conclusions: The results show excellent compliance with the protocol. IV APAP was safe and well-tolerated. Notably, most patients did not receive an opioid within four hours of IV APAP. IV APAP can be safely and effectively utilized as an analgesic and lessen ED opioid use.

Categories: Emergency Medicine, Pain Management

Keywords: patient safety, opioid epidemic, parenteral analgesia, emergency department analgesia, intravenous acetaminophen

Introduction

Acute pain is a leading cause of presentation to the Emergency Department (ED) [1]. In 2020, there were approximately 151 million ED visits, with one study showing that about 42% of ED visits are related to pain [1,2]. Patient co-morbidities may limit pain-management options, requiring consideration of alternative modalities. For example, nonsteroidal anti-inflammatory medications (NSAIDs) are contraindicated in patients with acute or chronic kidney disease [3]. Other factors, such as pregnancy and the ability to tolerate oral medications, can further limit the pharmacological options to treat pain [4,5].

Acetaminophen is a common analgesic used in the ED. Intravenous acetaminophen (IV APAP) provides a significant reduction in both pain intensity and time to meaningful pain improvement [6]. Published data generally have not proven IV APAP superior to oral APAP, although IV APAP remains an option when other routes of administration are not viable [7,8]. A randomized, placebo-controlled trial by Bektas et al. found similar efficacy between IV APAP and IV morphine for treating renal colic [9]. These findings suggest that IV APAP may be beneficial for treating pain in the ED and could serve as an alternative to IV opioids for parenteral analgesia when NSAIDs are contraindications.

Both patients and clinicians may have concerns about opioid use, given there were over 80,000 opioid-associated deaths in the United States in 2021, according to the National Center for Health Statistics (NCHS) [10]. The rising incidence of opioid use disorder and overdose deaths involving opioids has been with both illicit and prescribed opioids, with patients being almost twice as likely to use opioids in the future after an initial opioid prescription [11]. Therefore, non-opioid treatment for pain is an important consideration. Alternatives to opioids, such as IV APAP, may be utilized to decrease the frequency and number of opioids

How to cite this article

Deutsch A B, DelBianco J D, Fagan P, et al. (January 25, 2024) Evaluation of an Intravenous Acetaminophen Protocol in the Emergency Department. Cureus 16(1): e52934. DOI 10.7759/cureus.52934

required in the ED.

This study describes a hospital-implemented protocol for the use of IV APAP in the ED. The percentage of patients receiving opioids in addition to IV APAP, adverse events related to IV APAP, and ED provider compliance with the protocol were evaluated.

This article was previously presented in part as an abstract at the Pennsylvania College of Emergency Physicians Scientific Assembly in Pocono Manor, Pennsylvania, United States, on May 5, 2023.

Materials And Methods

Study design

This study included all patients who received IV APAP during a three-month period in the ED of Lehigh Valley Health Network, Allentown, Pennsylvania, United States, a tertiary care, level I trauma center. The protocol required patients to be NPO (nil per os), 18 years or older, and administered a single 1000 mg IV dose. This quality assessment project was designated as nonhuman subjects research by the Institutional Review Board. This study was approved by the Lehigh Valley Health Network Institutional Review Board (approval number: STUDY000001169).

Data collection

The adverse reactions within 24 hours post-IV APAP, ED length of stay (LOS), oral medication administration within one hour post-IV APAP, and opioid administration within four hours post-IV APAP were tracked. Cases were retrieved from the electronic medical record via standard pharmacy processes based on orders for IV APAP. Cases of IV APAP administration were documented per standard hospital pharmacy protocol, de-identified, and stored in a password-protected spreadsheet on a secure drive within a secure server.

Results

Ninety-four patients received IV APAP as first-line treatment for acute pain. All patients received a 1000 mg dose. Protocol adherence was observed in 91 of the 94 (96.8%) cases, with the remaining three cases involving protocol violations (Table 1). An opioid was administered to 22 of the 94 (23.4%) patients during the four-hour protocol period. There were no reports of adverse reactions, side effects, or incorrect dosing administrations.

Cases Violating Protocol	Nature of Violation
Patient A	Received two doses of IV APAP (had 22-hour ED LOS)
Patient B	Received oral medication (aluminum-magnesium hydroxide with simethicone) within one hour of IV APAP
Patient C	Received oral medication (carbamazepine and lamotrigine) within one hour of IV APAP

TABLE 1: Protocol violations

IV APAP: Intravenous acetaminophen; ED: Emergency department; LOS: Length of stay

Discussion

This study demonstrates that ED clinicians complied with the IV APAP protocol as the first-line therapy for acute pain. There were no reports of adverse reactions. Notably, only 23.4% of the patients received an opioid within four hours of IV APAP. In comparison, according to data from the NCHS, an opioid was given or prescribed for 30.9% of pain-related ED visits nationally [12]. It may represent an opioid-sparing effect with the use of IV APAP, which is consistent with studies that have evaluated the efficacy of IV APAP in the postoperative setting [13,14]. However, IV APAP may not completely supplant opioid use as other studies find that IV APAP alone is less effective than opioids and does not augment the analgesic effects of opioids [15,16].

Nevertheless, decreasing opioid use is an important goal for both patient safety and economic reasons. Opioids are associated with substantial adverse effects, including constipation, nausea, vomiting, and potentially fatal respiratory depression [17]. Opioid overdose deaths may involve both illicit substances and prescribed medications; one study demonstrated that 36% of patients with opioid use disorder had at least one opioid prescription within the past year [18]. Additionally, studies show that patients are almost twice as likely to use opioids in the future after receiving an initial prescription [11]. IV APAP, in contrast, has largely minor adverse effects [13]. Although there were no reports of adverse reactions in this study, IV APAP has

been associated with hypotension in severely ill patients [19]. IV APAP dosing errors, some resulting in hepatic injury, have occurred. These errors are more common in the pediatric population because of the calculations required with weight-based dosing. Experts recommend approaching IV APAP overdose in the same manner as an oral APAP overdose, administering N-acetylcysteine when treatment is indicated, according to the Rumack-Matthew nomogram [20,21].

Opioid use also takes an economic toll. It has been estimated that the cost to society of harmful prescription opioids is over \$8.6 billion [22]. Moreover, postoperative opioid prescriptions are associated with higher costs [23]. Some institutions have implemented cost-saving initiatives to reduce IV APAP use in the inpatient setting; however, compared to opioid monotherapy, IV APAP reduces hospital costs without any significant difference in pharmaceutical costs [24,25]. IV APAP was associated with fewer side effects and adverse drug events for patients, which may further reduce healthcare costs [14,26].

Emergency medicine clinicians treat a diverse patient population with complex medical histories and comorbidities, which may limit pharmaceutical options for pain relief. For example, clinicians often avoid NSAIDs for patients with kidney disease, coronary artery disease, history of gastrointestinal hemorrhage, or those currently taking anticoagulant medications [27]. Pregnancy is another condition commonly encountered in the ED that requires careful consideration regarding analgesics. The American College of Obstetricians and Gynecologists (ACOG) has identified APAP as one of the safe pain relievers for pregnant individuals [28]. Nausea and vomiting are common symptoms in pregnancy. The utility of IV APAP in individuals who cannot tolerate oral intake, particularly in pregnancy, seems beneficial [4,29].

Limitations of this study include that it was retrospective and conducted at one hospital system, limiting the generalizability of the results. Additionally, this study excluded those under the age of 18.

Conclusions

This study demonstrates the successful implementation of an IV APAP protocol in the ED. Nearly all cases maintained protocol compliance. IV APAP was found to be safe, with no adverse effects reported. In addition, most patients receiving IV APAP did not also receive opioids.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Acquisition, analysis, or interpretation of data: Gillian A. Beauchamp, Aaron B. Deutsch, Jason Laskosky, Laura Koons, Kimberly Sharpe, Patrick Fagan

Drafting of the manuscript: Gillian A. Beauchamp, Aaron B. Deutsch, John D. DelBianco, Kenneth D. Katz, Patrick Fagan

Critical review of the manuscript for important intellectual content: Gillian A. Beauchamp, Aaron B. Deutsch, John D. DelBianco, Jason Laskosky, Kenneth D. Katz, Laura Koons, Kimberly Sharpe

Concept and design: John D. DelBianco, Kenneth D. Katz

Supervision: Kenneth D. Katz

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Lehigh Valley Health Network Institutional Review Board issued approval STUDY000001169. The Institutional Review Board determined that, as submitted, the project referenced above does not meet the regulatory requirements for human subject research as defined by 45 CFR 26.102(d). **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

Acknowledgements

Authors would like to thank Katelyn McLain and Stephanie Shara for editing and formatting assistance.

References

- Pletcher MJ, Kertesz SG, Kohn MA, Gonzales R: Trends in opioid prescribing by race/ethnicity for patients seeking care in US emergency departments. *JAMA*. 2008, 299:70-8. [10.1001/jama.2007.64](https://doi.org/10.1001/jama.2007.64)
- Cairns C, Ashman JJ, King JM: Emergency department visit rates by selected characteristics: United States, 2020. *NCHS Data Brief*. 2022, 452:1-8. [10.15620/cdc:121837](https://doi.org/10.15620/cdc:121837)
- Lucas GN, Leitão AC, Alencar RL, Xavier RM, Daher EF, Silva Junior GB: Pathophysiological aspects of nephropathy caused by non-steroidal anti-inflammatory drugs. *J Bras Nefrol*. 2019, 41:124-30. [10.1590/2175-8239-JBN-2018-0107](https://doi.org/10.1590/2175-8239-JBN-2018-0107)
- Black E, Khor KE, Kennedy D, Chutatape A, Sharma S, Vancaillie T, Demirkol A: Medication use and pain management in pregnancy: a critical review. *Pain Pract*. 2019, 19:875-99. [10.1111/papr.12814](https://doi.org/10.1111/papr.12814)
- Lee NM, Saha S: Nausea and vomiting of pregnancy. *Gastroenterol Clin North Am*. 2011, 40:309-34, vii. [10.1016/j.gtc.2011.03.009](https://doi.org/10.1016/j.gtc.2011.03.009)
- Wininger SJ, Miller H, Minkowitz HS, Royal MA, Ang RY, Breitmeyer JB, Singla NK: A randomized, double-blind, placebo-controlled, multicenter, repeat-dose study of two intravenous acetaminophen dosing regimens for the treatment of pain after abdominal laparoscopic surgery. *Clin Ther*. 2010, 32:2348-69. [10.1016/j.clinthera.2010.12.011](https://doi.org/10.1016/j.clinthera.2010.12.011)
- Hickman SR, Mathieson KM, Bradford LM, Garman CD, Gregg RW, Lukens DW: Randomized trial of oral versus intravenous acetaminophen for postoperative pain control. *Am J Health Syst Pharm*. 2018, 75:367-75. [10.2146/ajhp170064](https://doi.org/10.2146/ajhp170064)
- Furyk J, Levas D, Close B, et al.: Intravenous versus oral paracetamol for acute pain in adults in the emergency department setting: a prospective, double-blind, double-dummy, randomised controlled trial. *Emerg Med J*. 2018, 35:179-84. [10.1136/emered-2017-206787](https://doi.org/10.1136/emered-2017-206787)
- Bektas F, Eken C, Karadeniz O, Goksu E, Cubuk M, Cete Y: Intravenous paracetamol or morphine for the treatment of renal colic: a randomized, placebo-controlled trial. *Ann Emerg Med*. 2009, 54:568-74. [10.1016/j.annemergmed.2009.06.501](https://doi.org/10.1016/j.annemergmed.2009.06.501)
- Spencer MR, Miniño AM, Warner M: Drug overdose deaths in the United States, 2001-2021. *NCHS Data Brief*. 2022, 457:1-8. [10.15620/cdc:122556](https://doi.org/10.15620/cdc:122556)
- Hoppe JA, Kim H, Heard K: Association of emergency department opioid initiation with recurrent opioid use. *Ann Emerg Med*. 2015, 65:493-499.e4. [10.1016/j.annemergmed.2014.11.015](https://doi.org/10.1016/j.annemergmed.2014.11.015)
- Schappert, SM, Santo L: QuickStats: percentage of emergency department visits for pain at which opioids were given or prescribed, by geographic region of the hospital-United States, 2005-2017. *MMWR Morb Mortal Wkly Rep*. 2020, 69:53. [10.15585/mmwr.mm6902a6](https://doi.org/10.15585/mmwr.mm6902a6)
- Sinatra RS, Jahr JS, Reynolds LW, Viscusi ER, Groudine SB, Payen-Champenois C: Efficacy and safety of single and repeated administration of 1 gram intravenous acetaminophen injection (paracetamol) for pain management after major orthopedic surgery. *Anesthesiology*. 2005, 102:822-31. [10.1097/0000542-200504000-00019](https://doi.org/10.1097/0000542-200504000-00019)
- Aryaie AH, Lalezari S, Sergent WK, Puckett Y, Juergens C, Ratermann C, Ogg C: Decreased opioid consumption and enhance recovery with the addition of IV acetaminophen in colorectal patients: a prospective, multi-institutional, randomized, double-blinded, placebo-controlled study (DOCIVA study). *Surg Endosc*. 2018, 32:3432-8. [10.1007/s00464-018-6062-y](https://doi.org/10.1007/s00464-018-6062-y)
- Pouraghaei M, Imamverdizadeh P, Moharramazadeh P, Vahdati SS: Effect of intravenous acetaminophen on pain and peritoneal irritation signs in patients with acute surgical abdomen in the emergency department. *ABC Med*. 2019, 7:12-15. [10.7575/aiac.abcm.v.7n.1p.12](https://doi.org/10.7575/aiac.abcm.v.7n.1p.12)
- Bijur PE, Friedman BW, White D, et al.: Randomized clinical trial of intravenous (IV) acetaminophen as an adjunct to IV hydromorphone for acute severe pain in emergency department patients. *Acad Emerg Med*. 2020, 27:717-24. [10.1111/acem.13947](https://doi.org/10.1111/acem.13947)
- Berde C, Nurko S: Opioid side effects--mechanism-based therapy. *N Engl J Med*. 2008, 358:2400-2. [10.1056/NEJMe0801783](https://doi.org/10.1056/NEJMe0801783)
- Hawk K, D'Onofrio G, Fiellin DA, et al.: Past-year prescription drug monitoring program opioid prescriptions and self-reported opioid use in an emergency department population with opioid use disorder. *Acad Emerg Med*. 2018, 25:508-16. [10.1111/acem.13352](https://doi.org/10.1111/acem.13352)
- Maxwell EN, Johnson B, Cammilleri J, Ferreira JA: Intravenous acetaminophen-induced hypotension: a review of the current literature. *Ann Pharmacother*. 2019, 53:1035-41. [10.1177/1060028019849716](https://doi.org/10.1177/1060028019849716)
- Dart RC, Rumack BH: Intravenous acetaminophen in the United States: iatrogenic dosing errors. *Pediatrics*. 2012, 129:349-55. [10.1542/peds.2011-2345](https://doi.org/10.1542/peds.2011-2345)
- Beringer RM, Thompson JP, Parry S, Stoddart PA: Intravenous paracetamol overdose: two case reports and a change to national treatment guidelines. *Arch Dis Child*. 2011, 96:307-8. [10.1136/adc.2010.192005](https://doi.org/10.1136/adc.2010.192005)
- Birnbaum HG, White AG, Reynolds JL, et al.: Estimated costs of prescription opioid analgesic abuse in the United States in 2001: a societal perspective. *Clin J Pain*. 2006, 22:667-76. [10.1097/01.ajp.0000210915.80417.cf](https://doi.org/10.1097/01.ajp.0000210915.80417.cf)
- Brummett CM, England C, Evans-Shields J, et al.: Health care burden associated with outpatient opioid use following inpatient or outpatient surgery. *J Manag Care Spec Pharm*. 2019, 25:973-83. [10.18553/jmcp.2019.19055](https://doi.org/10.18553/jmcp.2019.19055)
- Howell KA, Ruggles CA, Thompson M, Metzger KZ, Christopher JA, Bigham MT: Using quality improvement to reduce IV acetaminophen use in a PICU. *Pediatr Crit Care Med*. 2020, 21:550-6. [10.1097/PCC.0000000000002301](https://doi.org/10.1097/PCC.0000000000002301)
- Maiese BA, Pham AT, Shah MV, Eaddy MT, Lunacsek OE, Wan GJ: Hospitalization costs for patients undergoing orthopedic surgery treated with intravenous acetaminophen (IV-APAP) plus other IV analgesics or IV opioid monotherapy for postoperative pain. *Adv Ther*. 2017, 34:421-35. [10.1007/s12325-016-0449-8](https://doi.org/10.1007/s12325-016-0449-8)
- Sin B, Wai M, Tatunchak T, Motov SM: The use of intravenous acetaminophen for acute pain in the emergency department. *Acad Emerg Med*. 2016, 23:543-53. [10.1111/acem.12921](https://doi.org/10.1111/acem.12921)
- Risser A, Donovan D, Heintzman J, Page T: NSAID prescribing precautions. *Am Fam Physician*. 2009, 80:1371-1378.

28. ACOG Response to Consensus Statement on Paracetamol Use During Pregnancy . (2021). Accessed: December 15, 2023: <https://www.acog.org/news/news-articles/2021/09/response-to-consensus-statement-on-paracetamol-use-during-pregnancy>.
29. Festin M: Nausea and vomiting in early pregnancy . *BMJ Clin Evid.* 2014, 2014:1405.