Original Article

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Intravenous Acetaminophen Versus Morphine for Acute Limb Trauma Pain: A Randomized Double-Blind Clinical Trial

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Abstract

Introduction: Acute limb trauma is a frequent emergency department presentation that necessitates effective analgesia. Although intravenous morphine is widely used for moderate-to-severe pain, its adverse effect profile raises concerns. Safer non-opioid alternatives, such as intravenous acetaminophen, require further evaluation. This study aimed to compare the analgesic efficacy and safety of intravenous acetaminophen versus intravenous morphine in patients presenting to the emergency department with acute limb trauma.

Methods: In this randomized, double-blind, controlled clinical trial, 50 patients with acute limb trauma at Imam Reza Hospital, Birjand, Iran, were randomly assigned to two groups (n = 25 per group) to receive either 1 g of intravenous acetaminophen or 0.1 mg/kg of intravenous morphine. Pain was assessed using the Visual Analog Scale (VAS) at baseline, 5, 15, and 30 minutes post-treatment. Data were analyzed using Fisher's exact test, independent t-tests, and repeated-measures analysis of variance to evaluate pain reduction and hemodynamic stability over time.

Results: Pain scores decreased significantly over time in both groups ($P < 0.001$). No statistically significant differences in pain intensity or hemodynamic parameters were observed between groups ($P > 0.05$). However, the incidence of adverse effects was significantly higher in the morphine group compared to the acetaminophen group (36% vs. 4%, $P = 0.011$), with nausea and vomiting being the most frequent complications in patients receiving morphine. The need for rescue analgesia did not differ significantly ($P = 0.778$).

Conclusion: Intravenous acetaminophen is as effective as intravenous morphine in reducing acute pain from limb trauma within the first 30 minutes of administration. Given its superior safety profile characterized by significantly fewer gastrointestinal side effects and its hemodynamic stability, intravenous acetaminophen serves as a viable and preferred non-opioid alternative for early pain management in the emergency department.

Key words: Acetaminophen, Emergencies, Morphine, Pain management

Introduction

Acute limb trauma is a leading cause of emergency department visits globally and presents a major clinical challenge in emergency medicine (1, 2). Acute limb trauma refers to recent traumatic injuries of the upper or lower extremities, including fractures, dislocations, severe contusions, and soft tissue injuries requiring emergency analgesic management without immediate surgical intervention (2-4). Early and effective pain management not only reduces patient suffering but also mitigates adverse physiological responses, such as hemodynamic stress, prolonged hospitalization, and reduced patient satisfaction (5). Opioid analgesics, particularly intravenous morphine, have long been the mainstay for moderate to severe traumatic pain due to their rapid onset and potency (6). However, their use is increasingly scrutinized because of well-documented adverse effects, including nausea, vomiting, respiratory depression, hypotension, sedation, and risk of dependency (7, 8). In addition, the global rise in opioid-related complications and concerns regarding opioid overuse have encouraged the development of opioid-sparing strategies in emergency pain management (9-11).

Non-opioid analgesics with favorable safety profiles, such as intravenous acetaminophen, have

emerged as potential alternatives. Previous studies have demonstrated the efficacy of intravenous acetaminophen in acute pain conditions, such as postoperative pain and renal colic (12, 13). Some randomized trials suggest analgesic outcomes comparable to morphine with fewer adverse effects (14, 15). Several randomized clinical trials have compared intravenous acetaminophen with opioids in conditions, such as postoperative pain, renal colic, and rib fractures (5, 16, 17). However, evidence specifically focused on acute limb trauma in emergency department populations remains limited and inconsistent. Acute limb trauma represents a distinct clinical setting because patients frequently require rapid analgesia while simultaneously being vulnerable to opioid-related adverse effects, including sedation, nausea, hypotension, and respiratory depression, which may interfere with clinical evaluation and early stabilization. Pain intensity, a subjective and multifactorial experience, is most reliably measured using validated self-report instruments, such as the Visual Analog Scale (VAS) (18). Beyond pain reduction, contemporary pain management emphasizes outcomes, including hemodynamic stability, adverse-effect incidence, and rescue-analgesia requirement (5). Prior studies indicate that although opioids provide rapid analgesia, they are often accompanied by higher rates of side effects that complicate clinical management (8).

Despite the growing literature on non-opioid analgesia, several important gaps remain. First, relatively few randomized controlled trials have specifically evaluated patients with acute limb trauma in emergency department settings. Second, previous studies have reported inconsistent findings regarding the magnitude and timing of pain reduction, particularly during the first 30 minutes following drug administration. Third, evidence from Middle Eastern and Iranian emergency care settings is limited, where patient characteristics, prescribing patterns, and resource availability may differ from those of Western populations. Furthermore, the comparative effect of intravenous acetaminophen and morphine on short-term VAS reduction and early adverse effects in acute limb trauma has not been adequately clarified. The present study aimed to address these gaps by comparing the efficacy and safety of intravenous acetaminophen versus morphine in emergency department patients with acute limb trauma, using a randomized, double-blind, controlled design.

Methods

Trial Design

This study was designed as a randomized, double-blind, controlled clinical trial conducted in the emergency department of Imam Reza Hospital, Birjand, Iran. The primary objective was to compare the analgesic efficacy and safety of intravenous acetaminophen versus intravenous morphine in patients presenting with acute limb trauma. This randomized clinical trial followed the CONSORT guidelines for reporting randomized controlled trials. The Institutional Ethics Committee approved the study (IR.BUMS.REC.1402.540), and the study was prospectively registered in the Iranian Registry of Clinical Trials (IRCT20190618043934N26).

Participants

We assessed 50 patients for eligibility, and all met the inclusion criteria. Following informed consent, participants were randomly assigned in a 1:1 ratio to receive either intravenous acetaminophen (n = 25) or intravenous morphine (n = 25). All randomized participants received the allocated intervention. No participants were lost to follow-up, discontinued the intervention, or were excluded from the final analysis. Therefore, data from all 50 randomized participants were included in the intention-to-treat analysis. Figure 1 shows the participant flow throughout the trial, in accordance with the CONSORT 2010 guidelines. The sample size was calculated based on a two-sided comparison of mean pain intensity (VAS) between two independent groups using the standard formula for comparing two means.

To minimize selection bias, all eligible patients presenting consecutively to the emergency department during the study period were screened after initial triage and clinical stabilization. Enrollment followed predefined inclusion and exclusion criteria, and we did not select patients based on triage level or prehospital management decisions. This approach was applied uniformly to both study groups to reduce selection bias.

Patients were excluded if they had hypersensitivity to acetaminophen or morphine, opioid addiction, pregnancy, altered consciousness, respiratory distress, hemodynamic instability, hepatic or renal dysfunction, or if they had received analgesics within six hours before presentation. Baseline demographics and clinical parameters were recorded. To minimize the confounding effect of injury severity, we only included patients with

isolated limb trauma who were hemodynamically stable and did not require immediate surgical intervention. This ensured a more homogeneous study population regarding the potential intensity of the traumatic stimulus.

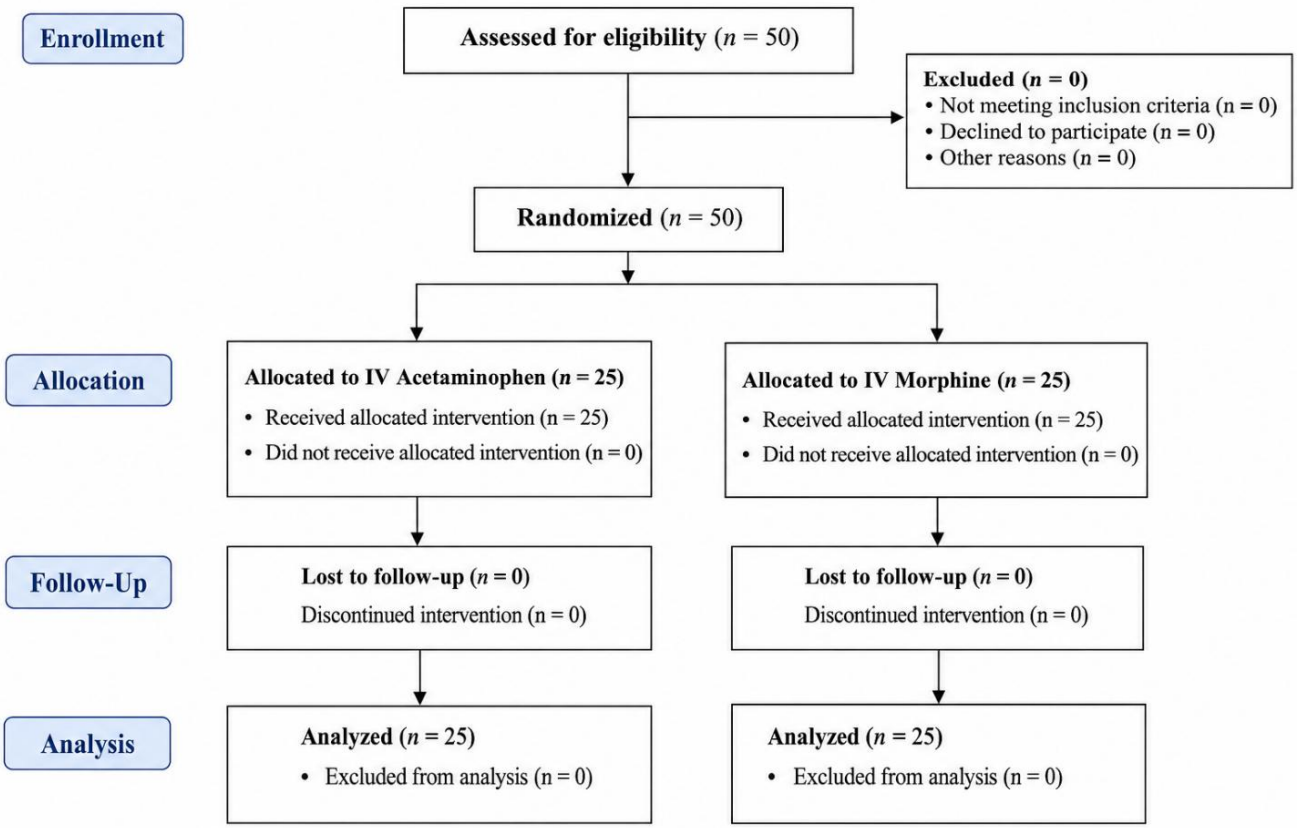

Figure 1. CONSORT Flow Diagram of Participants Through the Randomized Clinical Trial.

Data Collection Tools

Data were collected using a standardized case report form, which included patients' demographic characteristics, pain severity measured by the VAS at baseline, 5, 15, and 30 minutes post-administration, as well as hemodynamic parameters (systolic and diastolic blood pressure, heart rate, respiratory rate, and oxygen saturation) and adverse effects recorded at the same time points. The VAS is a validated and reliable instrument, as confirmed by extensive research conducted both nationally and internationally.

Interventions

Participants were randomly assigned to receive either:

Group 1 (Intervention group – intravenous acetaminophen)

Step 1: Baseline pain and vital signs were recorded.

Step 2: Patients received intravenous acetaminophen 1 g diluted in 100 mL normal saline.

Step 3: The drug was infused over 15 minutes via a peripheral intravenous line.

Step 4: No additional analgesic was administered during the 30-minute observation period unless rescue analgesia was required.

Step 5: Pain scores and hemodynamic parameters were assessed at 5, 15, and 30 minutes.

Group 2 (Control/comparator group – intravenous morphine)

Step 1: Baseline pain and vital signs were recorded.

Step 2: Patients received intravenous morphine sulfate 0.1 mg/kg diluted in 100 mL of normal saline.

Step 3: The drug was infused over 5 minutes via a peripheral intravenous line.

Step 4: No additional analgesic was administered during the 30-minute observation period unless rescue analgesia was required.

Step 5: Pain scores and hemodynamic parameters were assessed at 5, 15, and 30 minutes.

Outcome

The primary outcome was pain intensity, assessed using the VAS (0–10) at baseline (T0), 5 (T5), 15 (T15), and 30 (T30) minutes post-administration. The VAS is a validated and widely used instrument for assessing acute pain intensity in emergency department settings, with demonstrated reliability and sensitivity to change in previous trauma and emergency analgesia studies (18).

Secondary outcomes included:

Hemodynamic parameters: systolic and diastolic blood pressure, heart rate, respiratory rate, and oxygen saturation.

Adverse effects: nausea, vomiting, dizziness, hypotension, or respiratory depression.

Need for rescue analgesia is defined as the administration of additional opioid or non-opioid analgesics within 30 minutes after the initial dose (5, 16).

Trained research nurses performed all assessments using standardized protocols.

Sample Size

The calculation was informed by previous randomized clinical trials evaluating intravenous acetaminophen versus morphine in acute pain settings, including Craig et al.(5) and Serinken et al. (19), assuming a clinically meaningful difference in VAS score, standard deviation from prior literature, $\alpha = 0.05$, and study power of 80%.

Accordingly, the minimum required sample size was estimated to be 23 participants per group. To account for potential attrition, an additional 10% was considered, resulting in a final target sample size of 25 participants per group (total n = 50).

Randomization

The dosing regimens were selected based on previously published randomized controlled trials and clinical guidelines in emergency pain management, including studies by Sinatra et al.(20), Serinken et al.(19), and Lvovschi et al.(21), which support the use of 1 g intravenous acetaminophen and 0.1 mg/kg intravenous morphine as standard emergency analgesic doses.

The randomization sequence was generated using computerized block randomization. Block randomization with variable block sizes was used to ensure balanced group allocation throughout the study period. Allocation concealment was ensured via sealed opaque envelopes.

These envelopes were prepared by an independent researcher who was not involved in patient recruitment, intervention administration, or outcome assessment. Both patients and healthcare providers were blinded to group assignment.

In addition, a nurse not involved in data collection prepared study medications in identical syringes and infusion bags, and outcome assessors were blinded to treatment allocation to maintain full double-blind conditions.

Statistical Analysis

Data were analyzed using IBM SPSS (version 19.0). The normality of continuous variables was assessed using the Kolmogorov–Smirnov test and visual inspection of histograms. Descriptive statistics were reported as mean ± standard deviation for normally distributed data.

For between-group comparisons, the independent samples t-test was employed for normally distributed continuous data. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. To evaluate the changes in pain scores and hemodynamic parameters over time within and between groups, a repeated-measures analysis of variance (ANOVA) was performed. The assumption of sphericity was checked using Mauchly's test; if violated, Greenhouse-Geisser corrections were applied. Post-hoc analyses were conducted using the Bonferroni correction to adjust for multiple comparisons. A two-sided $P < 0.05$ was considered statistically significant.

Results

All 50 enrolled patients completed the study. Baseline demographic and clinical characteristics were comparable between groups ($P > 0.05$) (Table 1). The mean age was 34.8 ± 10.2 years in the acetaminophen group and 36.5 ± 9.8 years in the morphine group. Male patients constituted 56% and 60% of the acetaminophen and morphine groups, respectively.

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants.

Variable	Acetaminophen (n = 25)	Morphine (n = 25)	P value
Age (y)	34.8 ± 10.2	36.5 ± 9.8	0.567
Sex, No. (%)			0.742
Male	14 (56)	15 (60)	
Female	11 (44)	10 (40)	
BMI (kg/m²)	24.9 ± 3.1	25.3 ± 3.0	0.648
Baseline SBP (mmHg)	125.36 ± 4.78	124.60 ± 4.39	0.561
Baseline DBP (mmHg)	81.12 ± 5.54	79.80 ± 6.15	0.429
Baseline HR (bpm)	80.92 ± 5.36	79.04 ± 7.03	0.333
Baseline RR (breaths/min)	14.44 ± 0.82	17.12 ± 2.10	0.667

Abbreviations: BMI, body mass index.

Both groups experienced a significant reduction in pain intensity over time. The mean VAS scores decreased from 6.12 ± 0.88 to 2.76 ± 1.71 in the acetaminophen group and from 7.08 ± 1.03 to 2.52 ± 1.93 in the morphine group over the 30-minute follow-up period. Repeated-measures ANOVA demonstrated a significant time effect for pain reduction in both groups (P<0.001). However, no statistically significant overall difference was observed between the acetaminophen and morphine groups (group effect: P > 0.05), and the interaction between time and treatment group was not statistically significant (time × group interaction: P>0.05). In addition, no statistically significant between-group differences were observed at baseline, 5, 15, or 30 minutes after treatment (all P values>0.05) (Table 2).

Table 2. Changes in Pain Intensity Measured by Visual Analog Scale (VAS) Over Time.

Time (min)	Acetaminophen Mean ± SD	Morphine Mean ± SD	P value
Baseline	6.12 ± 0.88	7.08 ± 1.03	0.333
5	6.00 ± 0.95	5.72 ± 1.33	0.333
15	3.88 ± 1.12	3.84 ± 1.21	0.999
30	2.76 ± 1.71	2.52 ± 1.93	0.667
Repeated measure	P < 0.001	P < 0.001	

These findings indicate that no statistically significant difference in pain reduction was observed between intravenous acetaminophen and morphine during the first 30 minutes following acute limb trauma.

Systolic and diastolic blood pressure, heart rate, and respiratory rate remained stable in both groups throughout the study period (P > 0.05). No clinically significant deterioration was observed, indicating favorable hemodynamic safety profiles for both interventions (Table 3).

Adverse effects occurred in one patient (4%) in the acetaminophen group and nine patients (36%) in the morphine group, with nausea and vomiting being the most commonly reported events (P = 0.011; Fisher's exact test). The requirement for rescue analgesia did not differ significantly between groups (44% vs. 52%; P = 0.778; Fisher's exact test). However, given the relatively small sample size, these findings should be interpreted cautiously, particularly for secondary outcomes, such as adverse effects and rescue analgesia, because the study may have been underpowered to detect modest between-group differences.

Table 3. Adverse Effects and Requirement for Rescue Analgesia.

	Outcome	Acetaminophen (n = 25)	Morphine (n = 25)	P value
Any adverse effect, No. (%)	Nausea	0 (0)	5 (20)	0.011
	Vomiting	0 (0)	3 (12)	
	Dizziness	1 (4)	1 (4)	
	Hypotension	0 (0)	0 (0)	
	Total	1 (4)	9 (36)	
	Need for rescue analgesia	11 (44)	13 (52)	0.778

Discussion

The primary aim of this randomized double-blind clinical trial was to compare the analgesic efficacy and safety of intravenous acetaminophen versus intravenous morphine in patients presenting with acute limb trauma in the emergency department setting. The present study specifically addressed the limited and inconsistent evidence regarding analgesic management in patients with acute limb trauma presenting to the emergency department. While previous studies have evaluated intravenous acetaminophen in conditions, such as postoperative pain and renal colic, comparatively few investigations have focused specifically on acute limb trauma, despite its unique clinical challenges and the need for rapid, safe analgesia in emergency settings. In the current study, both intravenous acetaminophen and morphine produced rapid and significant pain reduction during the first 30 minutes after administration, with no statistically significant difference observed between groups. These findings contribute to filling an important clinical knowledge gap in emergency trauma pain management. Previous studies have reported mixed findings regarding the relative speed of onset and peak analgesic effects of acetaminophen versus opioids. Some trials suggest that opioids may provide slightly faster initial pain relief during the first few minutes after administration, whereas others have reported no clinically significant differences between the two agents during the first 30–60 minutes.

Pain intensity decreased significantly in both groups over the 30-minute observation period, with no statistically significant difference between acetaminophen and morphine at any measured time point. Previous randomized clinical trials have reported that intravenous acetaminophen may provide analgesic effects comparable to opioids in certain acute pain settings, particularly traumatic extremity injuries and selected emergency department populations. In addition, systematic and evidence-based reviews have suggested that intravenous acetaminophen can be considered a potential opioid-sparing strategy in acute pain management (14, 17, 22). The comparable efficacy observed in this study suggests that acetaminophen can be considered a first-line option for moderate acute pain in emergency departments, particularly when opioid use is contraindicated or poses additional risks.

The analgesic effects of intravenous acetaminophen are believed to involve central mechanisms, including modulation of central prostaglandin pathways and pain signaling processes (23). Unlike opioids, acetaminophen does not act on μ-opioid receptors, which explains its lack of respiratory depressant and sedative effects, making it particularly suitable for emergency care in patients with comorbidities or hemodynamic instability.

One of the most clinically significant findings of this study is the markedly lower incidence of adverse effects in the acetaminophen group compared to the morphine group (4% vs. 36%). Opioid-related adverse effects, including nausea, dizziness, sedation, hypotension, and respiratory depression, are well recognized in emergency pain management and may complicate patient stabilization and monitoring in acute trauma settings (24). Acetaminophen's reduced side-effect profile not only improves patient comfort and satisfaction but also reduces the need for additional interventions to manage complications, such as antiemetics or intravenous fluids.

Hemodynamic parameters remained stable in both groups throughout the study period, and no clinically significant deterioration was observed following administration of either intravenous acetaminophen or morphine. These findings suggest that both analgesic approaches were generally well tolerated from a hemodynamic perspective during early emergency management of acute limb trauma, although previous studies have reported that intravenous acetaminophen may occasionally be associated with transient hemodynamic changes,

particularly in critically ill patients (25). This finding is particularly important in acute trauma patients, especially those at risk of hypovolemia, occult bleeding, or hemodynamic compromise, in whom additional hypotension or respiratory depression associated with opioids may complicate early stabilization and clinical assessment in the emergency department.

The findings support the integration of opioid-sparing strategies in acute pain management protocols. By providing effective analgesia without opioid-related respiratory and sedative effects, intravenous acetaminophen may contribute to opioid-sparing approaches in emergency pain management and potentially reduce opioid exposure in selected patients (26).

Moreover, the comparable need for rescue analgesia between groups suggests that initial administration of acetaminophen does not compromise overall pain management. These findings suggest that intravenous acetaminophen may be used either as a standalone analgesic or as part of a multimodal pain management strategy aimed at optimizing analgesic efficacy while minimizing opioid-related adverse effects (27).

Previous studies comparing non-opioid and opioid analgesic strategies in acute pain settings have reported variable findings regarding the onset and magnitude of analgesic effects, with some studies demonstrating comparable short-term pain reduction between treatment approaches (28). In the present study, pain reduction in both groups was rapid and sustained, suggesting that acetaminophen is sufficient for early trauma pain control in most patients.

Additionally, prior research often focused on specific pain conditions, such as renal colic or postoperative pain, which may not accurately reflect pain mechanisms in limb trauma. The current study addresses this gap by providing evidence specifically for acute limb trauma, a common and distinct population in emergency medicine, thereby enhancing the clinical applicability of the findings.

Although intravenous acetaminophen demonstrated a favorable short-term safety profile in the present study, important safety considerations should be acknowledged. Acetaminophen dosing must remain within recommended therapeutic limits (generally not exceeding 4 g/day in adults), and caution is warranted in patients with hepatic dysfunction, chronic alcohol use, malnutrition, low body weight, or other conditions associated with increased susceptibility to hepatotoxicity. In addition, the short observation period of the present emergency department study was not designed to evaluate delayed hepatic adverse effects, which may not become clinically apparent during early follow-up.

Despite the strengths of a randomized, double-blind design, several limitations warrant consideration. A key limitation is the short follow-up period (30 minutes), which was designed to assess early analgesic response in the emergency department setting. While this timeframe is appropriate for evaluating rapid-onset analgesia and immediate adverse effects, it does not fully capture the longer duration of action of morphine compared with intravenous acetaminophen. Therefore, the findings primarily reflect short-term analgesic efficacy rather than sustained pain control. Additionally, pain assessment relied on self-reported VAS scores, which, although validated, remain inherently subjective. The relatively small sample size may have reduced the statistical power to detect modest between-group differences, particularly for secondary outcomes, such as adverse effects and rescue analgesia requirements. Consequently, the possibility of type II error cannot be excluded, and these findings should therefore be interpreted with caution. Furthermore, while we focused on acute limb trauma, a formal injury severity scoring system (e.g., Injury Severity Score) was not utilized to categorize the extent of tissue damage. Although we attempted to standardize the population by excluding unstable patients, the lack of control for specific injury severity remains a limitation that may have influenced baseline pain levels and individual responses to analgesia.

Future studies with extended follow-up periods (e.g., 1–6 hours or longer) are recommended to better compare the full pharmacodynamic profiles of these agents. Further research with larger multicenter studies and extended follow-up is recommended to evaluate long-term outcomes, cost-effectiveness, and combination therapy approaches. Future studies should also investigate multimodal analgesic strategies combining intravenous acetaminophen with lower opioid doses, as well as evaluate efficacy and safety in specific patient populations, such as elderly trauma patients, patients with multiple comorbidities, and hemodynamically vulnerable individuals.

Conclusion

This randomized double-blind clinical trial demonstrated that intravenous acetaminophen achieved pain reduction comparable to intravenous morphine during the early management of acute limb trauma in the emergency department, while showing a lower frequency of adverse effects and maintaining hemodynamic stability. These results support the use of intravenous acetaminophen as an effective opioid-sparing alternative in emergency pain management. Incorporating non-opioid analgesics into standard emergency protocols may enhance patient safety, improve tolerability, and optimize overall trauma care. Further research with larger, multicenter studies and extended follow-up is recommended to evaluate long-term outcomes, cost-effectiveness, and combination therapy approaches.

Consent for Publication

None.

Data Availability Statement

The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Author's Contribution

Conceptualization, methodology, investigation, writing of the original draft: F.H;

Data curation, formal analysis, writing, review and editing: F.H;

Supervision, validation, writing, review and editing: F.H.

All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work.

Conflict of Interest

The authors declared no conflicts of interest.

Declaration of Generative Artificial Intelligence in Scientific Writing

During the preparation of this manuscript, the authors used large language model tools (ChatGPT) to assist with language editing and grammar checking to improve readability and clarity. Following its use, the authors carefully reviewed and revised the content and assumed full responsibility for the final published version of the manuscript. No generative AI was used for data analysis, scientific interpretation, or core scientific tasks.

References

1. Zanza C, Romenskaya T, Zuliani M, Piccolella F, Bottinelli M, Caputo G, et al. Acute traumatic pain in the emergency department. Diseases. 2023;11(1):45. [DOI: 10.3390/diseases11010045]
2. Fabbri A, Voza A. The pain management of trauma patients in the emergency department. J Clin Med. 2023;12(9). [DOI: 10.3390/jcm12093289]
3. Gompels B, McCarron L, Jovanovic L, Molloy T, Ahmed V, Gargan M, et al. Just the facts: assessing and managing soft tissue knee injuries in the emergency department. Cjem. 2024;26(11):778-80. [DOI: 10.1007/s43678-024-00761-w]
4. Blanco-Barrio A, Moreno-Pastor A, Lozano-Ros M. Fractures of the limbs: basic concepts for the emergency department. Radiologia. 2023;65:S42-52. [DOI: 10.1016/j.rxeng.2022.09.009]
5. Craig M, Jeavons R, Probert J, Benger J. Randomised comparison of intravenous paracetamol and intravenous morphine for acute traumatic limb pain in the emergency department. Emerg Med J. 2012;29(1):37-9. [DOI: 10.1136/emj.2010.104687]
6. Arnold MJ. Management of acute pain from non–low back musculoskeletal injuries: guidelines from AAFP and ACP. Am Fam Physician. 2020;102(11):697-8. [URL: https://www.proquest.com/openview/7f79ff27c7d01ded633e8ec63f0d3d30/1?pq-origsite=gscholar&cbl=35707]
7. Foroughian M, et al. Effectiveness of intravenous lidocaine versus intravenous morphine in reducing acute extremity trauma-induced pain: A triple-blind randomized clinical trial. Koomesh. 2020;22(3):411-8. [URL: https://brieflands.com/journals/koomesh/articles/153196]
8. Pan Z, Qi Y, Wen Y, Chen L. Intravenous morphine titration vs. oral hydrocodone/acetaminophen for adults with lower extremity displaced fracture in an emergency department setting: A randomized controlled trial. Exp Ther Med. 2018;16(4):3674-9. [DOI: 10.3892/etm.2018.6606]

9. Fu Y, Liu Q, Nie H. Efficacy of opioids for traumatic pain in the emergency department: a systematic review and Bayesian network meta-analysis. Fron Pharmacol. 2023;14:1209131. [DOI: 10.3389/fphar.2023.1209131]
10. Rech MA, Griggs C, Lovett S, Motov S. Acute pain management in the Emergency Department: Use of multimodal and non-opioid analgesic treatment strategies. Am J Emerg Med. 2022;58:57-65. [DOI: 10.1016/j.ajem.2022.05.022]
11. Kaczorowski J, Bilodeau J. Emergency department-initiated interventions for patients with opioid use disorder: a systematic review. Acad Emerg Med. 2020;27(11):1173-82. [DOI: 10.1111/acem.14054]
12. Bijur PE, Friedman BW. 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(8):717-24. [DOI: 10.1111/acem.13947]
13. Tompkins DM, DiPasquale A, Segovia M, Cohn SM. Review of Intravenous Acetaminophen for Analgesia in the Postoperative Setting. Am Surg. 2021;87(11):1809-22. [DOI: 10.1177/0003134821989056]
14. Mollaei M, Esmailian, M., & Heydari, F. Comparing the effect of intravenous acetaminophen (Apotel®) and intravenous morphine in controlling the pain of forearm and leg fractures in adults. J Isfahan Med School. 2016;34(376):293-8. [URL: https://jims.mui.ac.ir/article_14910_en.html?lang=fa]
15. Esmailian M, Moshiri R, Zamani M. Comparison of the analgesic effect of intravenous acetaminophen and morphine sulfate in rib fracture; a randomized double-blind clinical trial. Emerg (Tehran, Iran). 2015;3(3):99-102. [URL: https://pmc.ncbi.nlm.nih.gov/articles/PMC4608332/]
16. Jalili M, Mozaffarpour Noori A, Sedaghat M, Safaie A. Efficacy of intravenous paracetamol versus intravenous morphine in acute limb trauma. Trauma Mon. 2016;21(1):e19649. [DOI: 10.5812/traumamon.19649]
17. Minotti B, Mansella G, Sieber R, Ott A, Nickel CH, Bingisser R. Intravenous acetaminophen does not reduce morphine use for pain relief in emergency department patients: A multicenter, randomized, double-blind, placebo-controlled trial. Acad Emerg Med. 2022;29(8):954-62. [DOI: 10.1111/acem.14517]
18. Delgado DA, Lambert BS, Boutris N, McCulloch PC, Robbins AB, Moreno MR, et al. Validation of Digital Visual Analog Scale Pain Scoring With a Traditional Paper-based Visual Analog Scale in Adults. J Am Acad Orthop Surg Glob Res Rev. 2018;2(3):e088. [DOI: 10.5435/jaaosglobal-d-17-00088]
19. Serinken M, Eken C, Turkcuer I, Elicabuk H, Uyanik E, Schultz CH. Intravenous paracetamol versus morphine for renal colic in the emergency department: a randomised double-blind controlled trial. Emerg Med J. 2012;29(11):902-5. [DOI: 10.1136/emermed-2011-200165]
20. 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(4):822-31. [DOI: 10.1097/00000542-200504000-00019]
21. Lvovschi V, Aubrun F, Bonnet P, Bouchara A, Bendahou M, Humbert B, et al. Intravenous morphine titration to treat severe pain in the ED. Am J Emerg Med. 2008;26(6):676-82. [DOI: 10.1016/j.ajem.2007.10.025]
22. Authors, Brett K, Severn M. CADTH Health Technology Review. IV Acetaminophen for Acute Pain in Emergency Departments: CADTH Health Technology Review. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health. 2023. [URL: https://canjhealthtechnol.ca/index.php/cjht/article/download/RC1508/1587?inline=1]
23. Mallet C, Desmeules J. An updated review on the metabolite (am404)-mediated central mechanism of action of paracetamol (acetaminophen): experimental evidence and potential clinical impact. J Pain Res. 2023;16:1081-94. [DOI: 10.2147/jpr.s393809]
24. Le Cornec C, Le Pottier M, Broch H, Marguinaud Tixier A, Rousseau E, Laribi S, et al. Ketamine compared with morphine for out-of-hospital analgesia for patients with traumatic pain: a randomized clinical trial. JAMA Netw Open. 2024;7(1):e2352844. [DOI: 10.1001/jamanetworkopen.2023.52844]
25. Maxwell EN, Johnson B, Cammilleri J, Ferreira JA. Intravenous acetaminophen-induced hypotension: a review of the current literature. Ann pharmacother. 2019;53(10):1033-41. [DOI: 10.1177/1060028019849716]
26. Motov S, Strayer R, Hayes BD, Reiter M, Rosenbaum S, Richman M, et al. The treatment of acute pain in the emergency department: a white paper position statement prepared for the american academy of emergency medicine. J Emerg Med. 2018;54(5):731-6. [DOI: 10.1016/j.jemermed.2018.01.020]
27. Elsarrag M, Soldozy S, Patel P, Norat P, Sokolowski JD, Park MS, et al. Enhanced recovery

after spine surgery: a systematic review. Neurosurg Focus. 2019;46(4):E3. [DOI: 10.3171/2019.1.focus18700]
28. Sobieraj DM, Martinez BK, Miao B. Comparative Effectiveness of Analgesics to Reduce Acute Pain in the Prehospital Setting. Prehosp Emerg Care. 2020;24(2):163-74. [DOI: 10.1080/10903127.2019.1657213]