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Review Article

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Comparative Efficacy and Safety of Ketorolac and Ketamine in the Management of Traumatic Chest Pain: A Narrative Review

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Abstract

Traumatic chest pain, commonly resulting from rib fractures and blunt thoracic trauma, poses a significant analgesic challenge. Ketorolac (a nonsteroidal anti-inflammatory drug) and ketamine (an N-methyl-D-aspartate receptor antagonist) are widely used as opioid-sparing alternatives. This narrative review aimed to synthesize and critically appraise the literature comparing ketorolac and ketamine for pain management in traumatic chest injuries, focusing on efficacy, safety, and clinical applicability. Evidence suggests that ketamine provides faster and superior short-term analgesia, particularly among patients requiring chest tube insertion. At the same time, ketorolac is associated with reduced opioid consumption and lower pulmonary complication rates in rib fracture cohorts. Most findings were derived from indirect comparisons, with only one direct head-to-head randomized controlled trial (RCT) available. Both agents demonstrate favorable safety profiles, though ketamine may cause transient psychedelic effects, and ketorolac may cause bleeding or renal risks in high-risk populations. Given the limited direct comparative data, clinicians may consider ketamine for rapid analgesia and ketorolac for opioid-sparing benefits, tailoring choice to patient-specific factors. Future research should include well-designed RCTs comparing combination versus monotherapy, optimal dosing strategies, and long-term outcomes. Due to the paucity of direct comparative trials, conclusions rely primarily on indirect evidence and a single head-to-head study.

Keywords: Analgesics, Chest Pain, Ketorolac, Ketamine, Trauma

Introduction

Trauma remains a major global public health challenge, accounting for more than 5 million deaths annually worldwide, with thoracic trauma contributing to approximately 25% of trauma-related mortalities and substantial long-term morbidities (1, 2). Pain resulting from chest injuries—particularly rib fractures and chest tube insertion—is often severe and inadequately controlled, leading to impaired ventilation, an increased risk of pulmonary complications, such as atelectasis and pneumonia, and prolonged hospital stays (2). Despite its clinical importance, pain management in patients with trauma remains suboptimal, and oligoanalgesia continues to be widely reported in emergency departments (3).

Opioids have traditionally served as the cornerstone of acute trauma analgesia; however, their use is limited by well-recognized adverse effects, including respiratory depression, delirium, nausea, and dependence (4, 5). These concerns have driven increasing interest in opioid-sparing analgesic strategies, particularly in patients with chest trauma, where preservation of respiratory function is critical (4, 6). As a result, non-opioid agents, such as ketorolac and ketamine, have gained prominence as alternatives or adjuncts in multimodal trauma pain protocols.

Ketorolac, a parenteral nonsteroidal anti-inflammatory drug (NSAID), has been widely used in trauma and postoperative settings for its ability to reduce inflammation-mediated pain and decrease opioid requirements (7, 8). Observational studies and cohort analyses of rib fracture populations

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suggest that ketorolac may be associated with reduced opioid consumption and lower rates of pulmonary complications when used appropriately and for short durations (2, 8). Nevertheless, concerns regarding renal impairment, bleeding risk, and gastrointestinal toxicity have limited its use in certain trauma populations, particularly hypovolemic or elderly patients (9).

Ketamine, a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, has re-emerged as a valuable analgesic at sub-dissociative doses in emergencies and trauma care. Low-dose ketamine provides rapid analgesia while preserving airway reflexes and hemodynamic stability, making it particularly attractive for patients with severe chest pain or physiological instability (10, 11). Multiple randomized controlled trials (RCTs) and meta-analyses have demonstrated that ketamine is non-inferior or superior to opioids for acute traumatic pain, with a significant opioid-sparing effect and minimal risk of respiratory depression (4, 5, 12). However, transient neuropsychiatric adverse effects, such as dizziness and nausea, remain a concern (6, 10).

Despite the growing body of evidence supporting both agents individually, direct comparative data between ketorolac and ketamine in traumatic chest pain are extremely limited. To date, only one randomized double-blind clinical trial has directly compared intravenous ketamine with ketorolac specifically in patients with chest trauma, reporting superior short-term analgesia and reduced rescue opioid use with ketamine (6). The scarcity of head-to-head studies, along with heterogeneity in trauma populations and outcome measures, has hindered clear evidence-based recommendations regarding agent selection in this high-risk group.

Therefore, this narrative review aimed to compare the efficacy and safety of ketorolac and ketamine in the management of traumatic chest pain, with a particular focus on opioid-sparing potential and clinical applicability in emergency and trauma settings.

Methods

Study Design

This study was a narrative literature review. A non-systematic but structured literature search was performed to identify relevant studies evaluating the use of ketorolac and ketamine for pain management in patients with traumatic chest injuries. The methodology was designed to provide a comprehensive clinical overview rather than a quantitative synthesis.

Search Strategy

The literature search was conducted in the following electronic databases: PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. Articles published between January 2000 and September 2024 were considered. Only studies published in English were included.

The search strategy combined Medical Subject Headings terms and free-text keywords related to traumatic chest pain and analgesic interventions, including combinations of:

"traumatic chest pain," "rib fractures," "chest tube," "ketorolac," "ketamine," "analgesia," and "opioid-sparing."

Study Selection and Inclusion Criteria

Studies were selected based on their relevance to the clinical management of traumatic chest pain. The inclusion criteria included RCTs, observational studies, clinical reviews, guidelines, and relevant experimental or comparative studies.

Exclusion Criteria

Studies focusing on non-traumatic pain, pediatric populations only, or non-clinical outcomes were excluded. Given the narrative nature of this review, no formal screening protocol or duplicate reviewer process was applied.

Risk of Bias Assessment

Formal risk of bias assessment tools were not applied because this review was not intended to be a systematic review or meta-analysis. Instead, study quality and clinical relevance were considered descriptively when interpreting the evidence.

Data Extraction and Synthesis

Key information from the included studies—such as study design, patient population, intervention type, comparator, and main outcomes—was qualitatively extracted. Findings were synthesized narratively and organized thematically, focusing on analgesic efficacy, safety profile, and opioid-sparing potential.

Results

The literature search identified a broad range of

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studies evaluating ketorolac and ketamine for pain management in trauma settings. After screening for relevance to traumatic chest pain, studies focusing on rib fractures, blunt chest trauma, chest tube–related pain, and acute trauma analgesia were included. The final body of evidence consisted of RCTs, observational cohort studies, and relevant comparative trauma analgesia studies. Table 1 presents a summary of key studies included and their characteristics.

Table 1. Comparative Summary of Ketorolac vs. Ketamine in Traumatic Chest Pain: Evidence from Key Studies

Aspect	Ketorolac	Ketamine	Author, Year	Design
Primary mechanism of action	Cyclooxygenase inhibition leading to anti-inflammatory and analgesic effects	NMDA receptor antagonism produces dissociative analgesia with minimal respiratory depression	Radvinsky et al., 2013	Cohort; Review; RCT
Typical dosing in trauma studies	15–30 mg IV every 6 h (short-term) or single 30 mg IV bolus	0.2–0.3 mg/kg IV bolus ± infusion (0.1–0.3 mg/kg/h)	Motov et al., 2015	RCT; Review
Main studied populations	Rib fractures, blunt chest trauma, polytrauma	Prehospital trauma, ED acute pain, severe trauma, chest trauma	Walters et al., 2018	Cohort; RCT
Direct head-to-head comparison in chest trauma	Higher pain scores and greater rescue opioid use	Lower pain scores at 30–60 min and reduced opioid use	Majidinejad et al., 2020	Double-blind RCT
Short-term pain relief (0–60 min)	Less effective than ketamine in direct comparison	Superior pain reduction at early time points	Majidinejad et al., 2020	RCT
Comparison with opioids	Opioid-sparing; reduced morphine equivalents	Non-inferior or superior to opioids; marked opioid-sparing	Motov et al., 2015	RCT; Cohort
Onset of analgesia	Gradual onset related to anti-inflammatory action	Rapid onset, often within minutes	Motov et al., 2015	RCT
Pulmonary outcomes	Reduced pneumonia and improved ventilator-free days in rib fracture cohorts	Preserves respiratory drive; no increase in pulmonary complications	Radvinsky et al., 2013	Cohort
Adverse effects reported	Rare with short-term use; minimal bleeding or renal events	Transient psychoperceptual effects; no respiratory depression	Motov et al., 2015	RCT; Cohort
Hemodynamic profile	Generally stable; caution in hypovolemia	Favorable; suitable in shock or unstable patients	Sin et al., 2017	Review; RCT
Long-term outcomes assessed	Reduced opioid exposure; no increased non-union	Limited long-term chest-trauma–specific data	Walters et al., 2018	Cohort; Review
Evidence specific to chest trauma pain	Moderate (mostly indirect rib-fracture cohorts)	Moderate (one direct RCT plus supportive trauma trials)	Majidinejad et al., 2020	RCT; Cohort

Abbreviations: RCTs, randomized controlled trials; NMDA, N-methyl-D-aspartate; ED, emergency department; IV, intravenous.

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Efficacy: Pain Reduction

Across the reviewed studies, both ketorolac and ketamine demonstrated clinically meaningful pain reduction in patients with traumatic chest injuries. Ketorolac was consistently associated with improved pain control in patients with rib fractures, particularly when used as part of a multimodal analgesic regimen (13, 14). Ketamine, administered at sub-dissociative doses, showed rapid and significant pain reduction, with superior short-term analgesia compared with ketorolac in the only direct head-to-head randomized controlled trial [Majidinejad et al., 2020] (Table 1).

Opioid-Sparing Effects

Opioid-sparing effects were consistent across studies for both agents. Ketorolac use was associated with reduced opioid requirements and lower cumulative morphine equivalents in patients with rib fractures (13, 14). Ketamine demonstrated marked opioid-sparing properties in both emergency department and prehospital trauma settings and was non-inferior or superior to opioids for acute pain control (10, 12). These findings are summarized comparatively in Table 1.

Safety and Adverse Events

The short-term use of ketorolac in trauma populations was generally well tolerated, with low rates of clinically significant bleeding, renal dysfunction, or gastrointestinal complications reported in the included studies (13, 14). Ketamine was associated primarily with transient psychoperceptual adverse effects, such as dizziness or nystagmus, without evidence of respiratory depression or clinically significant hemodynamic instability (6, 12). Table 1 presents the safety profiles for both agents.

Special Populations and Clinical Contexts

Evidence suggests that ketamine may be particularly advantageous in patients with severe pain, opioid tolerance, or hemodynamic instability, where opioid minimization and preservation of respiratory drive are priorities (6, 15). Ketorolac appeared most beneficial in hemodynamically stable patients with isolated rib fractures, where its anti-inflammatory effects may contribute to improved pulmonary outcomes (13, 14). Data on elderly patients and those with significant comorbidities remain limited.

Integration of Evidence

Overall, the findings from the reviewed studies indicate that ketorolac and ketamine provide effective, opioid-sparing analgesia for traumatic chest pain, with different strengths depending on the clinical context. The comparative characteristics and key outcomes of included studies are systematically summarized in Table 1, with all data points directly referenced to their sources.

Discussion

This narrative review synthesized the available evidence on the use of ketorolac and ketamine for managing traumatic chest pain. Overall, the reviewed studies suggest that both agents are effective analgesic options with opioid-sparing potential (1, 3). Ketorolac has consistently demonstrated efficacy in reducing pain scores and opioid requirements in patients with rib fractures, particularly in hemodynamically stable individuals (13, 14). Ketamine, administered at sub-dissociative doses, was associated with effective analgesia and reduced opioid consumption, especially in patients with severe pain or opioid tolerance (10, 12).

These findings highlight that the choice between ketorolac and ketamine should be guided by patient characteristics, clinical setting, and safety considerations (16). Ketorolac may be preferable for stable trauma patients without contraindications to nonsteroidal anti-inflammatory drugs, given its ease of administration and favorable analgesic profile (13, 17). In contrast, ketamine may offer advantages in patients with severe pain, opioid tolerance, or respiratory compromise, where opioid minimization is critical (12, 15). In the context of traumatic chest injuries—where adequate pain control is essential to prevent pulmonary complications—both agents may play complementary roles within multimodal analgesic strategies (8, 18).

The findings of this review are generally consistent with prior literature emphasizing multimodal, opioid-sparing analgesia in trauma care (18, 19). Previous reviews have reported the benefits of NSAIDs in rib fracture–related pain and the emerging role of low-dose ketamine in acute trauma settings (6, 11, 14). However, compared with earlier reviews that focused predominantly on either NSAIDs or ketamine individually, this review provides a focused comparative synthesis within the specific context of traumatic chest pain. Notably, inconsistencies across studies—particularly regarding the magnitude of opioid-sparing effects—likely reflect differences in study design, dosing

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regimens, and outcome measures (20, 21).

This study has several limitations. First, the available evidence is limited by a small number of RCTs, particularly for ketamine in traumatic chest pain (4, 12). Second, heterogeneity across studies in terms of patient populations, injury severity, analgesic dosing, and outcome assessment limits direct comparability (20). Third, as a narrative review, this study did not apply a systematic search strategy or formal risk-of-bias assessment, raising the possibility of publication bias and selective reporting (22). These limitations should be considered when interpreting these findings.

Future research should focus on well-designed RCTs directly comparing ketorolac and ketamine in patients with traumatic chest injuries (4, 23). Studies evaluating combination therapy versus monotherapy within multimodal analgesic protocols would be particularly valuable (9). Additionally, standardized outcome measures—including pulmonary complications, functional recovery, and patient-reported outcomes—are needed to better inform clinical decision-making (24). Research addressing optimal dosing strategies and safety profiles in high-risk populations, such as older adults and patients with comorbidities, is warranted (17, 25).

Conclusions

In summary, both ketorolac and ketamine are effective opioid-sparing analgesic options for traumatic chest pain, with distinct advantages depending on the clinical context. Integrating these agents into tailored, multimodal pain management strategies may improve pain control while minimizing opioid-related adverse effects. Further high-quality comparative research is needed to define the optimal roles of these biomarkers in trauma care pathways.

Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Data Availability Statement

The datasets utilized or analyzed in the present study are accessible upon reasonable request from the corresponding author.

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Author's Contribution

FH independently reviewed and interpreted the studies retrieved from the databases, extracted data from the eligible articles, and drafted the manuscript. He also reviewed and approved the final manuscript.

Conflict of Interest

The author declared no conflicts of interest.

Declaration of Generative Artificial Intelligence in Scientific Writing

The researcher did not use artificial intelligence to generate content at any stage of this study. Grammarly software was used to check the text grammar and spelling.

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