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Essay title: Prehospital pain reduction: A comparison between the analgesic effects of ketamine, morphine and fentanyl in traumatic injuries

Word Count: 1490 words (*excluding reference list and title page*)

Clinical Scenario

Paramedics are called code one to a 67 year-old-female with an angulated femur fracture following a fall at home. Upon arrival paramedics find the patient lying supine on the floor, complaining of 9/10 pain to her right leg. The patient appears anxious and diaphoretic with a Glasgow Coma Score (GCS) of 14 (E-3, V-5, M-6). The patient is also tachypnoeic and tachycardic with weak, thready radial pulses. The paramedics are unsure of whether ketamine would be more effective than morphine or fentanyl in reducing the patient's pain severity.

PICO (Population – Intervention – Comparison – Outcome)

In patients with traumatic injuries in the prehospital setting, how do the analgesic effects of ketamine compare to morphine and fentanyl in reducing pain severity?

Search Strategy

A literature search was conducted using Medline Ovid, Embase, Cochrane Central Register of Controlled Trials (CENTRAL) and CINAHL Complete. The search date was refined to include literature published within the last 5 years (Week 1 August 2015 to Week 1 August 2020). The MeSH headings and keywords used in the search are outlined in Table 1. The reference lists of the retrieved articles were also examined to locate articles not initially found in the electronic database search. Articles were included if they compared the effectiveness of ketamine with morphine and/or fentanyl in decreasing pain severity in patients with traumatic injuries. Due to the lack of prehospital articles, the search was expanded to include articles conducted in the emergency department (ED). The search was limited to studies written in English that involved human participants. Articles that failed to

satisfy the PICO question or had an inferior level of evidence, determined by the Oxford Centre for Evidence-Based Medicine Level of Evidence, were also excluded.

Table 1. *The keywords and MeSH headings*

Population	Intervention	Comparison	Outcomes
Prehospital	Ketamine	Fentanyl	Pain reduction
Out of hospital		Morphine	Pain management
Ambulance			Pain score
Emergency medical services			Pain
Paramedic			
Trauma			
Severe injury			
Acute			
Emergency			

Study Results and Analysis

There were 83 studies located in the search. After application of inclusion and exclusion criteria, five studies were suitable for the critical appraisal. The detailed screening process is provided in Figure 1. Table 2 provides a brief summary and critique of the included articles.

Figure 1: Summary of inclusion /exclusion screening process

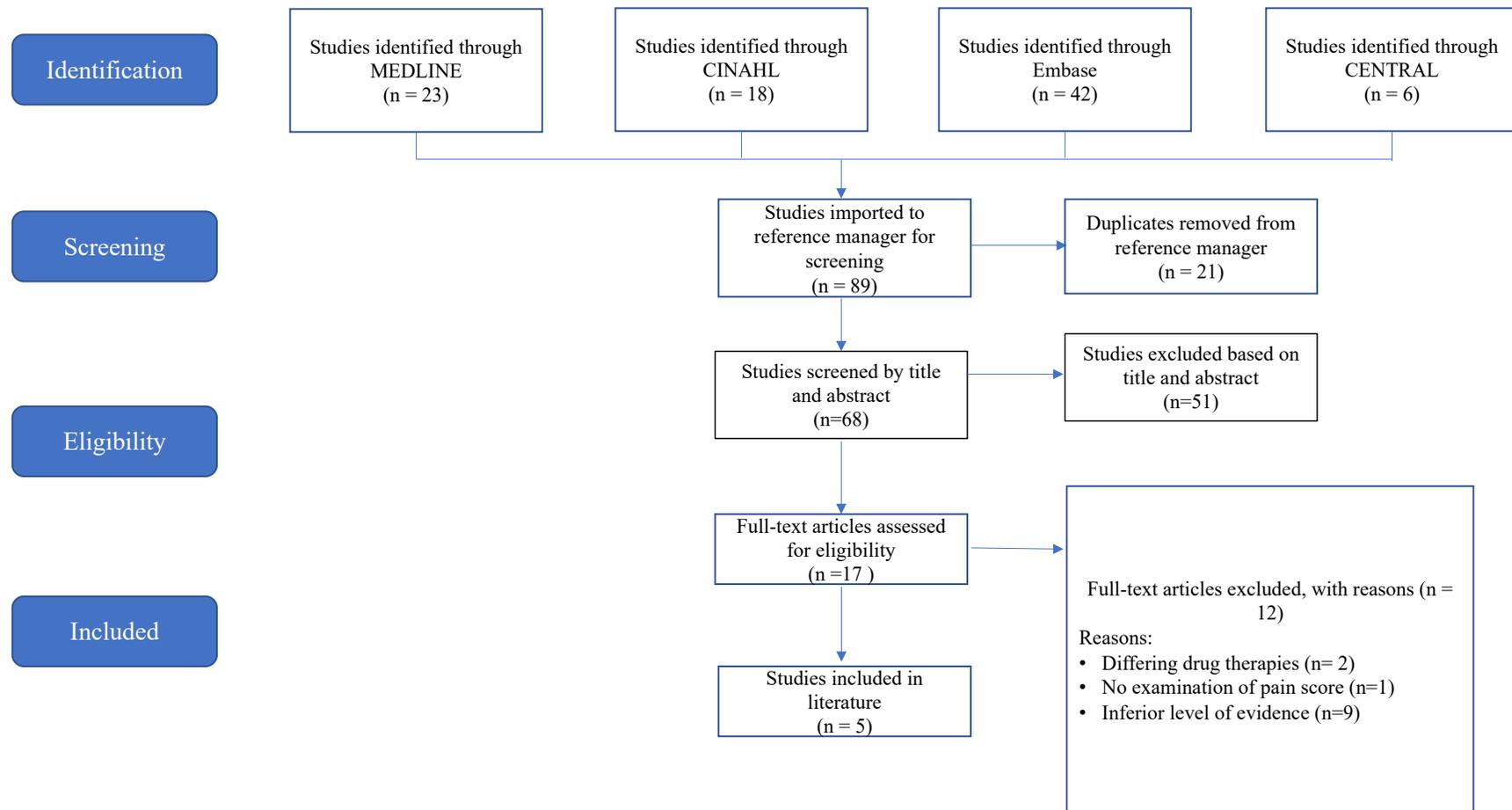


Table 2. Summary of included articles

Reference	Population: Sample Characteristics	Design	Outcomes	Results	Limitations, Strengths	OCEBM LOE, IF
(Bronsky et al., 2019)	200 adult patients (>17 years) who were transported to the ED of a Level 1 Trauma Centre by paramedics were included	Retrospective study	The primary outcome was to determine the analgesic effectiveness of intravenous ketamine and fentanyl, measured by change in pain score using the VAS	<p>-Patients receiving intravenous ketamine experienced a significantly larger decrease in pain than patients who received intravenous fentanyl</p> <p>-Ketamine reduced pain score by 5.5 and fentanyl reduced pain score by 2.5</p> <p>-Patients who received intravenous ketamine achieved at least a 50% reduction in pain</p>	<p>Strengths</p> <p>-A propensity matched analysis was undertaken to limit selection biases that may have favoured the administration of one drug over the other in the prehospital setting</p> <p>-Methodology was based on paramedic protocol guidelines, improving generalisability</p> <p>-Rigorous inclusion and exclusion criteria described and justified</p> <p>Limitations</p> <p>-The duration of prehospital analgesic effect is ambiguous as the pain scores were only recorded in a short timeframe</p> <p>-Retrospective, unblinded and non-randomised trial</p> <p>-Small sample size</p>	2b 2.690

Table 2 (continued)

(Frey et al., 2019)	90 children aged between 8 and 17 years, who presented to the ED of a level 1 Trauma Centre with moderate to severe pain as a result of traumatic limb injury were included	Double-blind, randomised, noninferiority clinical trial	The primary outcome was to compare the reduction in pain score between intranasal ketamine and intranasal fentanyl, measured by VAS	<p>-Both groups experienced statistically and clinically significant pain reductions</p> <p>-Ketamine was noninferior to fentanyl in pain reduction</p> <p>-Ketamine caused a reduction in pain score of 2.44 at 15 mins and 3.06 at 30 mins</p> <p>-Fentanyl caused a reduction in pain score of 2.53 at 15 mins and 3.19 at 30 mins</p>	<p>Strengths</p> <ul style="list-style-type: none"> -Randomised, double-blinded, contemporary literature -Methodological strategies outlined and justified -Homologous methodology when measuring pain score (VAS) -High impact factor <p>Limitations</p> <ul style="list-style-type: none"> - Poorly generalisable to the adult trauma population -Single centred, single provider -Small sample size -Trial wasn't powered to show a benefit (noninferiority study) - No standardisation in drug dosages 	1b 45.54
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Table 2 (continued)

(Jahanian et al., 2018)	<p>The study included 156 adult patients aged between 18 and 65 years who were referred to the ED with long bone fractures</p> <p>All participants had a VAS pain score of 7/10 or greater</p>	A randomised, double-blinded, clinical trial	The primary outcome was to compare intravenous morphine and low dose ketamine in pain management of patients with traumatic injuries, measured by the VAS	<p>-There was no significant difference between intravenous ketamine and morphine in reducing pain score after 30, 90, 120, 180 and 240 minutes</p> <p>-Morphine reduced pain score by 3.34 and 4.7 at 30mins and 60mins respectively</p> <p>-Ketamine reduced pain score by 3.65 and 4.81 at 30mins and 60mins respectively</p> <p>-There was a significant decrease in pain score in both groups</p> <p>-Ketamine had a higher need for rescue analgesic</p>	<p>Strengths</p> <ul style="list-style-type: none"> - Homologous methodology used to measure pain score (VAS) - Greater than 80% of the cohort study had follow-up -Randomised, double blinded, contemporary literature -Homologous statistical analysis -Rigorous inclusion and exclusion criteria described and justified <p>Limitations</p> <ul style="list-style-type: none"> -Single-centred, ED study which may compromise generalisability - No standardisation in dosages -Number of patients included in the study was limited -Low impact journal -Poorly generalisable to the paediatric trauma population 	1b 0.6
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Table 2 (continued)

(Mahshidfar et al., 2017)	<p>A total of 300 ED trauma patients aged 18 to 70 years with a pain score of 5/10 or more were included</p> <p>Pain score was measured by numeric rating scale</p>	A randomised, double-blinded clinical trial	The primary outcome was to compare the analgesic effect of low dose ketamine with intravenous morphine in reducing pain severity	<p>- Both groups had a statistically and clinically significant reduction in pain intensity at 15 minutes</p> <p>-Ketamine pain score reduced by 4 in 15 mins and 3.2 in 60 minutes</p> <p>-Morphine pain score reduced by 4.4 in 15 mins and 4.2 in 60 mins</p> <p>-There was no statistical difference between both groups</p>	<p>Strengths</p> <p>-Randomised, multicentred, double-blinded trial</p> <p>-Large number of participants (n=300)</p> <p>-Contemporary literature</p> <p>Limitations</p> <p>-Some adverse effects may interfere with blinding the study</p> <p>- Pain scores weren't recorded after 60 mins, compromising generalisability</p> <p>-Single-centred, ED study which may compromise generalisability</p> <p>- Heterogenous methodology in pain score measurement</p>	1b 2.707
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Table 2 (continued)

(Maleki Verki, Mozafari, Tirandaz, Motamed, & Khazaeli, 2019)	127 patients were included in the study who presented to the ED with severe pain secondary to a limb fracture Patients aged between 18 and 55 years of age were recruited	A double-blinded, randomised clinical trial	The primary outcome was to compare the VAS pain score following the administration of nebulised fentanyl and intravenous low dose ketamine for pain reduction in adult patients with long bone fractures	<p>-Ketamine effectively reduced the pain score in patients with limb fractures</p> <p>-Fentanyl was also effective in reducing pain of limb fractures</p> <p>-Fentanyl reduced pain score by 3.63 at 15 mins, 3.93 at 30 mins and 4.48 at 60 mins</p> <p>-Ketamine reduced pain score by 4.24 at 15mins, 5.24 at 30 mins and 5.05 at 60 mins</p> <p>-Ketamine reduced pain more effectively than fentanyl and required less additional treatments.</p>	<p>Strengths</p> <ul style="list-style-type: none"> -Double-blinded and randomised -Contemporary literature - Homologous methodology in pain score measurement <p>Limitations</p> <ul style="list-style-type: none"> -Short follow up period which precluded results -Limited sample size -Statistical analysis was heterogenous 	1b 1.3
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Abbreviations: ED, emergency department; GCS, Glasgow Coma Score; IF, impact factor; OCEBM LOE, Oxford Centre for Evidence-Based Medicine Level of Evidence; VAS, visual analogue score

Rationale

In the prehospital setting, the provision of analgesia in trauma is a vital aspect of patient management. As such, paramedics must comprehensively understand the efficacy and safety of these drugs to optimise patient care, reduce patient discomfort, and minimise adverse event frequency.

Consideration for practice

The reviewed literature suggests that ketamine, morphine, and fentanyl are effective analgesics that significantly reduce pain severity in patients with traumatic injuries. There was no statistically, or clinically significant difference found in the comparison of ketamine and morphine in reducing pain severity. Ketamine, however, was associated with a statistically larger decrease in pain severity compared to fentanyl.

There is limited evidence comparing the analgesic effectiveness of ketamine against morphine and/or fentanyl in the prehospital management of traumatic injuries. Therefore, additional prehospital randomised controlled trials are required to adequately determine which analgesic therapy is superior in reducing pain severity.

Clinical Bottom Line

When treating patients with traumatic injuries in the prehospital setting, ketamine and morphine both have equivalent analgesic abilities, and have been shown to significantly reduce pain severity. In contrast, fentanyl was not as effective compared to ketamine when discussing the same outcomes.

References

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