Is Fentanyl better than Morphine better than Ketamine for the management of pain in burn patients By Jasmin Perry

Topic Overview

One of the most basic rights in every patient is the administration of rapid and effective pain relief, considered a humanistic action (Sommerville, 1995). Burn-induced pain is one of the most severe forms of trauma and involves damage to peripheral sensory neurons and, initiation of inflammatory processes exacerbates this acute response and can result in the development of chronic pain (Morgan et al., 2018). Analgesic agents commonly used in clinical practice, such as ketamine, morphine and fentanyl, for the treatment of pain and, less commonly, sedation, offer a better quality of life for patients experiencing acute and chronic pain, hence potentially reducing outcomes associated with severe pain (Pathan & Williams, 2012).

Clinical Scenario

You arrive on scene to a patient with significant facial and abdominal burns after they were caught in a burning building two stories high. The patient is in significant pain, with a pain severity of nine out of ten. Pain relief is required for this patient; however, he has already been unresponsive to the morphine and fentanyl you have given him. You and your partner decide that ketamine would be appropriate for this patient. Your CCP backup arrives and administers 8mg of ketamine, diluted with sodium chloride, intravenously.

PICO (Population – Intervention – Comparison – Outcome) Question

In a burn's patient, is fentanyl, morphine or ketamine more effective in the management of acute pain?

Search Strategy

A literature search using electronic databases such as Ovid MEDLINE, CINAHL, EMBASE and Scopus was conducted. References of the included articles were also reviewed to retrieve any articles missed during the initial search process. Relevant articles were found using MeSH terms and keywords both independently and in combination; morphine, opioid, opiate, fentanyl, ketamine, burns patient, pain, burns victim, wound care, analgesic and hyperalgesia.

Studies that met the inclusion criteria included articles that compared the efficacy of morphine, fentanyl or ketamine in treating burns victims, both adults and paediatrics. Articles were excluded if they were not written in English, were not recently published, focused on animals in the study or did not compare two or more of the drugs outlined (morphine, fentanyl or ketamine).

Search Outcome

The search located 88 articles, with 3 articles meeting the inclusion criteria (Figure 1).

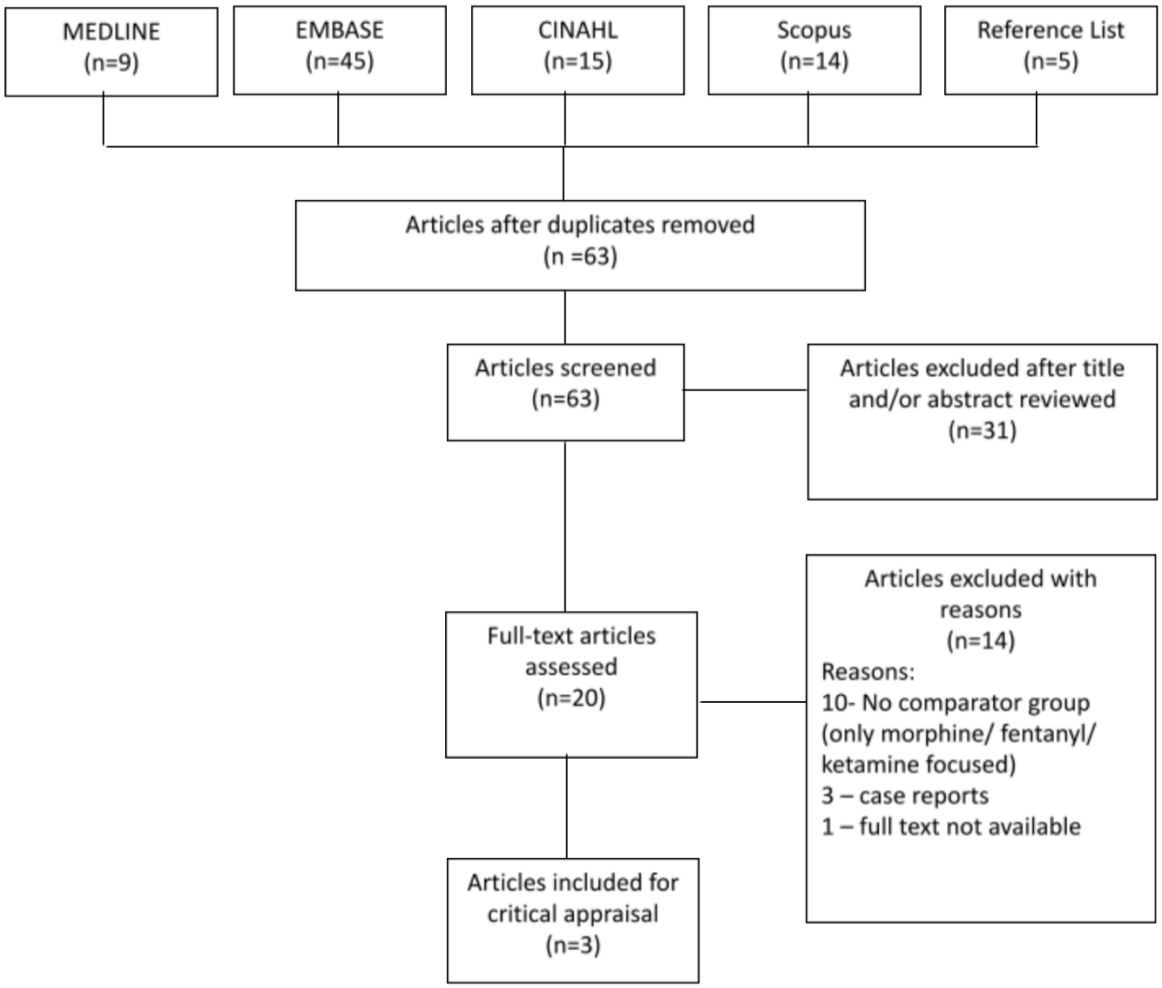

Figure 1: Search flow diagram

Table 1: Data Extraction

Author, Date	**Population: Sample Characteristics**	**Design and Level of Evidence (LOE)** (See Appendix A)	**Results**	**Strengths and Weaknesses**
Borland et al., 2005	24 paediatric patients requiring daily dressing with oral opiate analgesia due to burns covering more than 10% of their body. Patients were split into two groups, group A (N=14) and group B (N=10). Both groups received oral morphine and intranasal placebo on one of the two days and oral placebo and intranasal fentanyl on the following day.	Randomized Control Trial LOE 1	Pain ratings tended to be slightly higher with intranasal fentanyl than with oral morphine at -1.5 to 0.5 respectively, with the negative signs indicating a worse pain score. After adjustment for a potential period effect, the mean pain difference scores were virtually identical. The time to fluid intake after wound dressing was 108 minutes with oral morphine compared to intranasal fentanyl's 140 minutes.	**Strengths** • The study used pain scores that didn't exclude younger children, which constitutes a large percentage of the burn's patient population • Patient enrolment was done randomized, based on the desire to demonstrate equivalent efficacy on the primary outcome **Weaknesses** • 63% of patients experienced side effects such as nausea, vomiting and drowsiness with both fentanyl and morphine • The difference between treatments at the patient level is potentially biased by a period effect, a period by treatment interaction or carry-over • The study may be advantageous in select cases as indicated by the small sample size of the study • The study was based in the ED, and hence these results may not be generalizable for Paramedics
Tosun et al., 2008	32 paediatric patients receiving analgesia hospitalised for	Randomized Control Trial	Ketamine was associated with a significantly high	**Strengths** • Demonstrates how ketamine could be beneficial in comparison to fentanyl for

	second degree burns on a total surface area of 5% to 25%. 17 of the patients (53%) received 1mg/kg of ketamine and 1.2mg/kg of propofol, and 15 of the 32 patients (47%) received 1ug/kg of fentanyl and 1.2mg/kg of propofol.	LOE 1	respiratory rate compared to baseline observations. Both ketamine and fentanyl were associated with high sedation scores after induction and similarly reduced pain scores. Restlessness during the procedure was seen in patients who had received Fentanyl and as such, ketamine was seen as more efficient. One patient in each group experienced hypotension with a decrease in systolic blood pressure of more than 30 mmHg	analgesia in burns patients due to a decreased associated with restlessness **Weaknesses** • The small sample size of the study meant that evaluation of moderate and major burn patients was categorized the same • The study was based in a hospital and so the results are not comparable for Paramedics • Retrospective documentation of patient vital signs and outcomes were involved in the findings of this study and hence may be prone to recall errors or bias.
Warncke et al., 1997	12 adult patients with a first degree burn injury covering the medial aspect of their calf precipitated by the authors. The subjects received morphine hydrochloride, ketamine hydrochloride or placebo intravenously on three separate days.	Randomized Control Trial LOE 1	Secondary hyperalgesia (to stimuli applied) and wind-up-like pain were both significantly reduced by ketamine. Morphine failed to have an effect on secondary hyperalgesia and wind-up-like pain. Thermal thresholds in primary or secondary hyperalgesia were not affected by either ketamine or morphine.	**Strengths** • Use of combined drug therapy prevented the production of central hyperexcitability • Demonstrates effectively how ketamine is superior to morphine in the management of pain in burns patients **Weaknesses** • No analgesia comparator group • small sample size • The findings were not performed in a pre-hospital setting, hence not directly relevant for the review

Comments

Zero articles directly compared the efficacy of morphine, fentanyl and ketamine in treating burns patients in the one article, majority compared two of the three.

There is a paucity of studies that specifically denote a superior opioid between morphine and fentanyl. All studies found by the author alluded that both morphine and fentanyl had the same outcome on hyperalgesia.

Ketamine in a burn's patient with acute pain may be safe and advantageous when compared to morphine and fentanyl

All articles directly answered the PICO question, indicating that Ketamine is the most efficacious analgesic medication for the treatment of burns patients, both adult and paediatric.

Consider

Ketamine may be the most effective analgesic medication in comparison to morphine and fentanyl, for the management of pain in both adult and paediatric burns patients. However, the proposed value of ketamine originates from a limited amount studies, generalization is limited by a small sample size and study designs were prone to confounding variables. Therefore, caution should be taken when interpreting these results.

Clinical Bottom Line

There is not enough high-quality evidence to show that ketamine is superior to morphine and fentanyl in the burn's patient experiencing pain. Current evidence pertains to the advantages that ketamine presents that is not offered in morphine or fentanyl, however further controlled studies in the prehospital setting should occur before paramedics interpret this research.

References

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Appendix A

Figure 1: The Oxford Levels of Evidence (OCEBM Levels of Evidence Working Group).

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning