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Effects of Ketamine Versus Morphine in the Treatment of Acute Pain in the Emergency Department

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ABSTRACT

Objective: To compare the effects of treatment of acute pain in the emergency department using intravenous ketamine or intravenous morphine. **Methods:** A search was conducted in PubMed using the terms ("low dose ketamine" OR "sub-dissociative dose ketamine") AND "morphine" AND ("emergency department" OR "ED"). The results were filtered for relevancy to our research question. **Results:** All three studies demonstrated similar effectiveness between morphine and ketamine in the first 30 minutes with similarly significant pain score reductions. However, the analgesic effects of morphine consistently lasted longer than ketamine, and less people in the morphine group required additional doses of medication. Adverse drug events occurred at similar rates between the groups; although, different side effect profiles were observed between the drugs, as expected. **Conclusion:** Ketamine does not appear to be a replacement for morphine; however, ketamine shows potential to be a safe and effective alternative option for treating acute pain in the ED. Further research is warranted to study the safety and efficacy low-dose ketamine at higher doses infused over a longer duration or as usage as an adjunct to morphine.

INTRODUCTION

Acute pain is the most common cause of emergency department (ED) visits in the United States.[1] Patients presenting to the ED with moderate to severe pain are commonly treated with intravenous (IV) opioids. Morphine is mostly commonly used; however, a current shortage is creating a demand for other options.[2,3] Other IV opioids available for treating acute pain, such as fentanyl and hydromorphone, are also in shortage according to the Food and Drug Administration (FDA).[3]

Ketamine is a noncompetitive antagonist of N-methyl-D-aspartate receptors in the central nervous system and at higher doses may also bind to opioid mu and sigma receptors.[4] Ketamine has been used as a dissociative general anesthetic for procedural sedation and intubation since the 1970s.[5] Positive attributes of ketamine for acute pain management include a very large therapeutic window, rapid onset, and an adverse effect profile that is different from opioids.[6,7] Most importantly, ketamine has an absence of significant respiratory complications; however, elevated pulse and blood pressure, hallucinations, and dysphoria are common adverse effects.[7]

Low-dose IV ketamine is a potential candidate for safe and effective treatment of acute pain management in the ED. Using ketamine will help increase medication diversity, which will help prevent drug shortages by lessening the dependence on IV opioids. Using ketamine also gives an additional benefit of providing a non-opioid option for patients. This study aims to investigate ketamine as a safe and effective alternative to morphine for treatment of acute pain in the ED.

PICO

Population: Adult hospitalized patients with acute pain
Intervention: IV Ketamine
Comparison: IV Morphine
Outcome: self-reported pain control and the occurrence of adverse reactions

CLINICAL QUESTION

Can ketamine be used as a safe and effective alternative to morphine for the treatment of acute pain in the ED?

METHODS

As outlined in Figure 1, an initial search of PubMed was performed using the search terms ("low dose ketamine" OR "sub-dissociative dose ketamine") AND "morphine" AND ("emergency department" OR "ED"). This database search yielded 27 articles, none of which were duplicates. We further screened these articles based on relevance to our study. For example, if the article did not mention the use of ketamine for managing acute pain it was excluded, which left us with 19 eligible articles. We then analyzed the remaining full-text articles to ensure they were an appropriate match for our study. Articles were excluded if they did not compare ketamine to morphine, if they focused on a single etiology of pain, or if they were meta-analyses. Ultimately, three randomized controlled trials were chosen to include in this study. These articles were chosen based on their comparison of morphine vs ketamine for treating acute pain, and their use of numeric rating scale (NRS) pain scales to measure outcomes (Appendix 1).

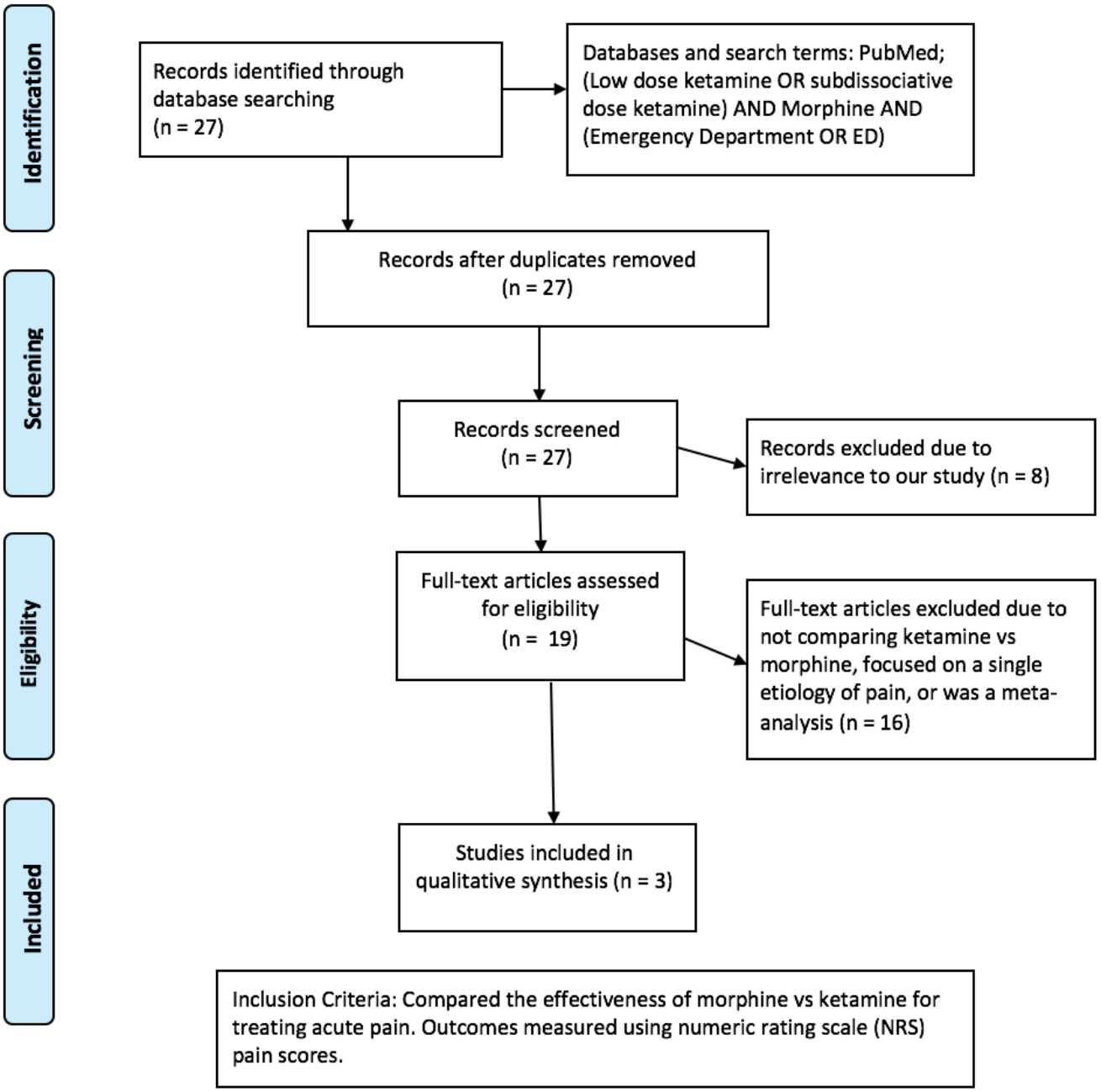

Figure 1. PRISMA flow diagram summarizing the article search process.

RESULTS

Study 1

Low dose ketamine vs morphine for acute pain in the ED: A randomized controlled trial. Miller et al.[6]

Objective

To compare the maximum change in NRS pain scores in patients receiving IV low-dose ketamine (LDK) or IV morphine (MOR) for acute pain in the emergency department.

Study Design

The study was conducted in a tertiary, level one trauma center ED at San Antonio Military Medical Center, with a patient population of uniformed military personnel (20%) and civilians (80%). A convenience sample was obtained using standard enrollment protocol and patients were selected based on criteria defined in Table 1.

Forty-five subjects were enrolled from March to November 2012 with similar demographic variables, vital signs, and baseline NRS (7.1) pain scores. Patients were randomly assigned to receive an initial dose of 0.3 mg/kg IV LDK (n=24) or 0.1 mg/kg IV MOR (n=21) infused over 5 minutes. After 20 minutes, the patient was asked if another dose was needed. This question was repeated every 20 minutes until 120 minutes had elapsed. Protocol allowed for a second, equal dosage to be given as early as 20 minutes post-initial dose. Data collection was stopped if the patient requested a third dose, underwent procedural sedations, or was discharged from the ED. Midazolam treatment was allowed for agitation or emergence reactions, and naloxone treatment was allowed for evidence of opioid overdose. Any other medication reactions were treated per the provider's discretion.

The primary outcome measurement was the maximum change on the verbal NRS pain score as compared to the baseline score. Clinically meaningful change in the NRS score from baseline was deemed to be 2 points between the treatment groups. The pain score was obtained prior to drug administration and after administration at 5, 10, 20 minutes and then every 20 minutes thereafter up to 120 minutes. Secondary outcomes included levels of agitation or sedation as measured by the Richmond Agitation-Sedation Scale (RASS), vital signs, adverse events, and need for repeat dosing. Providers and nurses were surveyed after the patient encounter to rate their satisfaction with the medication on a scale of 1 (very dissatisfied) to 5 (very satisfied). The outcomes were recorded and entered into a secured electronic database by a blinded research nurse.

Table 1. Inclusion and exclusion criteria for participation in study 1.

Inclusion Criteria	Exclusion criteria
18 to 59 years Acute abdominal, flank, low back, or extremity pain that the ED provider felt warranted IV opioid treatment	Oxygen saturation < 95% Systolic blood pressure < 90 mmHg or > 180 mmHg Pulse rate < 50 or > 120 beats/min Respiratory rate < 10 or > 30 respirations/min AMS Intoxication Fibromyalgia or other chronic pain condition requiring the use of opioids or tramadol as outpatient Ischemic heart disease, heart failure, or unstable dysrhythmias Use of an opioid or tramadol within 4 hours prior to enrollment Allergy to morphine or ketamine Required pain medication immediately Pregnant or breastfeeding History of chronic oxygen-dependent pulmonary disease Hepatic cirrhosis Dialysis-dependent Presence of intracranial mass History of psychosis Weight < 45 kg or > 115 kg Presence of acute ocular or head trauma

Study Results

The maximum change in NRS pain score from baseline in the MOR group was 5 at 100 minutes and 4.9 in the LDK group at 5 minutes. In the LDK group, there was an initial decrease in pain scores followed by a rapid increase within the first 20 minutes, whereas the MOR group experienced a steady trend of reduced pain over time (Table 2). A second dose was administered in 54% of the ketamine group and only 38% in the morphine group. A third dose was requested in 25% of the ketamine group and 14% in the morphine arm.

Secondary outcomes were similar between the groups. RASS scores varied within the first 20 minutes after drug administration in both groups, but subsequent variation from baseline was minimal. Ketamine caused a statistically significant increase in systolic blood pressure at 5 and 10 minutes from the morphine group, but no other differences were observed in vital signs. Most notably, patients in the MOR group experienced more headache, drowsiness, and decreased oxygen saturation, whereas the LDK group experienced more dysphoria and hallucinations.

However, adverse event rates were similar across treatment groups. Neither Midazolam nor naloxone was administered during the study and there were no dissociation or emergency reactions.

The median provider satisfaction score was 4 (somewhat satisfied) for both LDK and MOR groups, whereas the median nursing satisfaction score was 4 (somewhat satisfied) for LDK and 5 (very satisfied) for the MOR group.

Table 2. Pain scores overtime in study 1.

Time	Morphine (95% CI)	Low-dose ketamine (95% CI)
T5	− 3 (− 3.9, − 2.1)	− 4.9 (− 5.8, − 4)
T10	− 3.4 (− 4.4, − 2.5)	− 4.3 (− 5.5, − 3.1)
T20	− 3.3 (− 4.4, − 2.2)	− 3.2 (− 4.4, − 2.1)
T40	− 4.5 (− 5.6, − 3.5)	− 3.7 (− 5.2, − 2.3)
T60	− 4.8 (− 5.8, − 3.8)	− 3.5 (− 5.4, − 1.6)
T80	− 4.4 (− 5.9, − 2.9)	− 3.9 (− 6.1, − 1.6)
T100	− 5 (− 6.6, − 3.5)	− 4.1 (− 6.8, − 1.5)
T120	− 5 (− 7.1, − 2.9)	− 3.6 (− 6.1, − 1)

Study Critique

Strengths include the study design and similar group characteristics. The study directly compared morphine to ketamine for analgesia with a prospective, double-blinded randomized control trial. The sample population had similar demographic variables, vital signs, and baseline NRS pain scores, so confounding variables were limited.

The study had many limitations, such as small sample size with a possible generalizability limitation, a non-standardized dose of ketamine for analgesia, and the use of RASS in a non-validated setting. The sample size was approximately 20 patients per treatment group enrolled at a military medical center. Results of the study may not be generalizable due to the study location at a military medical center and sampling bias due to a convenience sample. Due to the small sample, statistical analysis had to detect a two-point difference in maximum change in NRS scores from baseline between the groups. Other authors have reported 1.3 as a statistically significant change in NRS scores, so a greater difference in clinical effect between the groups may be observed in a larger sample.[8] A standardized dose of ketamine for analgesia is not available, so the authors extrapolated data from other studies that suggested 0.3 mg/kg dosing for adequate pain control without adverse neurologic effects.[9] The RASS was used to measure sedation and agitation. RASS is standardly used in the setting of the intensive care unit but not in the ED, so the reliability and validity of this scale has not been established in the sample population of this study.

Study 2

Acute pain management in emergency department, low dose ketamine versus morphine, a randomized clinical trial. Mahshidfar et al.[7]

Objective

To compare analgesic effects of low dose ketamine versus morphine in trauma patients presenting to the ED.

Study Design

A double-blinded randomized clinical trial was conducted in two university teaching hospital EDs in Tehran, Iran. Participants in this study were trauma patients aged 18 to 70 years old who were referred to the ED with a musculoskeletal pain score of at least 5 on a standard NRS. Other inclusion and exclusion criteria are summarized in Table 3.

From September 2014 to September 2015, 332 eligible participants were enrolled, but 32 patients were excluded from analysis due to study refusal, patient requesting morphine or ketamine only, incomplete data, or disrespect to the study protocol. There was minimal difference between the groups' demographic characteristics, vital signs, or baseline pain scores. Participants were randomly assigned into IV LDK (0.2 mg/kg) or IV MOR (0.1 mg/kg) treatment groups equally using block randomization. Pain score, vital signs, and side effects were measured at 0, 15, 30, 45, and 60 minutes after the drug was administered. Adequate pain reduction was defined as a decrease in NRS pain score equal to 3 or more. If there was insufficient pain reduction, 3 mg of IV morphine was injected every 5 minutes as a rescue analgesic. Patient satisfaction was asked one hour after drug injection on a 5-point scale; a response of 4 or 5 were defined as reaching proper analgesic effect.

The primary outcome measured in this study was change in NRS pain score as compared to baseline over time. Other outcomes measured were changes in vital signs, development of adverse effects, and patient satisfaction. The medication was administered by a blinded nurse, but the study did not clearly state the outcome recorder.

Table 3. Inclusion and exclusion criteria for participation in study 2.

Inclusion Criteria	Exclusion Criteria
18 to 70 years old Trauma patients presenting to ED Rated pain at 5 or more on standard 0-10 NRS	Unstable vital signs Head trauma Glasgow coma scale < 15 Opiate user Psychiatric or cardiac problem Hypersensitivity to ketamine or morphine Pregnancy Breastfeeding Renal or hepatic insufficiency Upper respiratory infection Patient requesting morphine or ketamine only

Study Results

The average baseline NRS pain score was 8.1 in the ketamine group and 8.4 in the morphine group. There was a statistically significant reduction in pain scores at 15 minutes in both groups with no significant difference between the groups. Subsequently at 30, 45, and 60 minutes, the morphine group had statistically significant lower pain scores than the ketamine group (Table 4).

No life-threatening adverse effects were observed in either group. The morphine group experienced a statistically significant higher incidence of flushing and decreased oxygen

saturation below 90%. Other minor adverse effects were observed with equal incidence between the groups such as nausea, dizziness, and mood changes. A higher score rate of patient satisfaction was reported in the morphine group one hour after administration.

Table 4. Pain trends overtime in study 2.

Time (min)	Group		P Value
	Ketamine	Morphine	
0	8.1±1.1	8.4±0.9	0.15
15	4.1±2.8	4.0±2.5	0.23
30	4.5±3.1	3.8±3.0	0.01*
45	4.8±3.2	3.4±3.1	< 0.001*
60	4.9±3.3	3.2±2.9	< 0.001*

*P Values with statistical significance.

Study Critique

Strengths include the design, large sample size, and similar group demographics. The study directly compared morphine to ketamine for analgesia with a double-blinded, randomized controlled trial. This study has a large sample size since patients were enrolled from two large teaching hospitals. Confounding variables were reduced due to similar patient demographics between the groups.

Alternatively, limitations of the study were a potential for unblinding and limited generalizability. There was a potential for unblinding due to the specific adverse reactions associated with each medication. Extrapolation of the results to patients in the United States may be problematic due to cultural or medical practice differences in Iran.

Study 3

Intravenous subdissociative-dose ketamine versus morphine for analgesia in the emergency department: A randomized controlled trial. Motov et al.[10]

Objective

To compare the analgesic efficacy and safety of IV subdissociative-dose ketamine versus morphine for acute pain in ED patients.

Study Design

The study was conducted in a 711-bed community teaching hospital as a prospective, double-blinded, randomized control trial. Participants were 18 to 55 years old who presented to the ED with acute abdominal, flank, back, or musculoskeletal pain rated at least 5 on a standard NRS. Other inclusion and exclusion criteria are summarized in Table 5.

Between June 2013 to May 2014, 90 participants were enrolled through convenience sampling. The groups were similar regarding demographic characteristics, baseline vital signs, pain scores, and chief complaint. Block randomization was utilized to equally divide participants into treatment groups IV MOR (0.1 mg/kg) or IV LDK (0.3 mg/kg). Pain scores, vital signs, and adverse effects were recorded at 15, 30, 60, 90, and 120 minutes after drug administration. If the patient reported a pain NRS score of 5 or more and requested additional pain relief, 1 μg/kg of fentanyl was utilized for rescue analgesia.

The primary outcome was comparative NRS pain score reduction after 30 minutes between the treatment groups. Clinically meaningful change in the NRS score of acute pain in the ED was deemed to be 1.3 between the treatment groups as evidenced by other studies.[8] Other outcomes analyzed were fentanyl rescue at 30 or 60 minutes, vital signs, and adverse reactions. Outcomes were measured by a blinded provider then recorded by the blinded data-collection team. The ED pharmacist, research manager, and statistician were not blinded.

Table 5. Inclusion and exclusion criteria for participation in study 3.

Inclusion Criteria	Exclusion Criteria
18 to 55 years old Presenting to Ed with acute (onset within 7 days) abdominal, back, flank, or musculoskeletal pain Rated pain a score of 5 or more on standard 0-10 NRS Attending physician determined opioid analgesia is needed	Pregnancy Breastfeeding Altered mental status Allergy to morphine or ketamine Weight < 46 kg or > 115 kg Systolic blood pressure < 90 or > 180 mmHg Heart rate < 50 or > 150 bpm Respiratory rate < 10 or > 30 bpm History of acute head or eye injury History of seizure History of intracranial hypertension History of chronic pain History of hepatic or renal insufficiency History of alcohol or drug abuse History of psychiatric illness Opioid use within last 4 hours

Study Results

Patients in both groups showed significant reductions in NRS pain scores at 15 minutes (-1.0) and 30 minutes (0.2), but no statistically significant difference was detected between the groups. The changes in NRS pain scores for each group from baseline to 30 minutes showed a

similar pattern of decline. More patients in the ketamine group experienced a complete resolution of pain (NRS=0) at 15 minutes than patients in the morphine group; however, the difference had dissipated at the 30-minute mark (Table 6). There was no statistically significant difference in the use of rescue fentanyl at 30 and 60 minutes between the groups, but the ketamine group required significantly more rescue fentanyl at the 120-minute mark.

No serious or life-threatening adverse events occurred with either medication. More patients in the ketamine group reported minor adverse effects immediately after medication administration and at the 15-minute mark when compared to the morphine group, but the difference equalized at the 30 minutes. The most common minor adverse effects reported in both groups were dizziness and nausea. Neither group experienced any significant change to vital signs that were concerning or required intervention.

Table 6. Pain trends overtime in study 3.[10]

Time Interval*	Group		Difference (95% CI)
	Ketamine	Morphine	
Pain NRS, mean (SD)			
Baseline	8.6 (1.5)	8.5 (1.5)	0.1 (−0.46 to 0.77)
15	3.2 (3.5)	4.2 (2.9)	−1.0 (−2.40 to 0.31)
30	4.1 (3.2)	3.9 (3.1)	0.2 (−1.19 to 1.46)†
60	4.8 (3.2)	3.4 (3.0)	1.4 (0.13 to 2.75)
90	4.8 (3.1)	3.9 (3.1)	0.9 (−0.37 to 2.28)
120	3.9 (2.9)	3.7 (2.9)	0.2 (−1.09 to 1.46)
Complete resolution of pain, No. (%)			
15	20 (44)	6 (13)	31 (13.1 to 49.2)
30	12 (27)	11 (24)	3 (−16.3 to 20.7)
60	9 (21)	12 (27)	−6 (−25.6 to 11.6)
90	7 (16)	9 (21)	−5 (−21.5 to 12.2)
120	9 (22)	9 (21)	1 (−17.7 to 18.8)
Reduction of 3+ NRS, No. (%)			
15	34 (75)	31 (69)	6 (−12.3 to 25.6)
30	33 (73)	31 (69)	4 (−14.7 to 23.6)
60	25 (58)	33 (77)	−19 (−38.5 to 1.3)
90	23 (54)	33 (77)	−23 (−43.3 to –3.2)
120	29 (71)	33 (79)	−8 (−27.0 to 11.3)
Fentanyl rescue incidence, No. (%)			
15	0	0	0
30	4 (9)	1 (2)	7 (−2.9 to 16.3)
60	4 (9)	6 (14)	−5 (−18.1 to 9.0)
90	5 (11)	5 (12)	−1 (−13.1 to 14.1)
120	12 (29)	5 (12)	17 (0.8 to 34.2)

NRS, Numeric rating scale.

* Minutes from time of medication injection.

† 95% CI –0.77 to 1.05 is based on the SD from the mixed-model regression.

Study Critique

Strengths include design, study location, and similar group demographics. The study directly compared morphine to ketamine for analgesia with a double-blinded, randomized control trial. The sample population was selected at a large community teaching hospital with a highly utilized ED, so the sample is potentially diverse. Confounding variables were reduced since the groups were similar regarding demographic characteristics and baseline vital signs, pain scores, and chief complaint.

Alternatively, some weaknesses were small sample size, the use of convenience sampling, and participant inclusion was partially subjective. The use of convenience sampling can allow for sampling bias, so the sample may not be representative of the entire population. Inclusion was determined in part by the on-duty, attending physician's subjective opinion on the patient's need for opioid analgesia.

DISCUSSION

Acute, moderate to severe pain in the ED is most commonly managed with IV opioids. However, a current shortage of IV opioids is creating a demand for other options. Ketamine has been used as a dissociative general anesthetic since the 1970s and current research has been focused on ketamine utilization for safe and effective acute pain management.

An overview of the three studies is provided (Table 7). The Miller et al and Motov et al studies are similar with small sample populations, similar pain characteristics, and the same drug dosage. Mahshidfar et al had the advantage of a large population size, although the patient population was trauma patients outside of the United States. All three studies used the NRS for quantifying pain scores and utilized double-blinding procedure.

Table 7. Overview of studies

	Miller, et al	Mahshidfar, et al	Motov, et al
Patients, n	45	332	90
Population	18-59 year olds Acute abdominal, flank, low back, or extremity pain	18-70 year olds Trauma patients	18-55 year olds Acute abdominal, back, flank, or musculoskeletal pain
Location	Military level 1 trauma center ED. Uniformed military (20%) and civilians (80%)	2 university teaching hospital EDs in Tehran, Iran	711-bed community teaching hospital ED
Primary interest	Maximum change in NRS pain score as compared to baseline	Change in NRS pain scores from baseline over time	NRS pain score reduction after 30 minutes
Dosages	0.3 mg/kg LDK, IV 0.1 mg/kg MOR, IV	0.2 mg/kg LDK, IV 0.1 mg/kg MOR, IV	0.3 mg/kg LDK, IV 0.1 mg/kg MOR, IV
Blinding	Yes	Yes	Yes
Other outcomes measured	Adverse events, vital signs, & provider satisfaction	Adverse events, vital signs, & patient satisfaction	Adverse events, vital signs, & fentanyl rescue

The primary outcome of the studies was pain reduction in ketamine versus morphine. All three studies showed effective pain relief in the first 20 minutes without a statistically significant difference between the treatment groups. The LDK group demonstrated an initial decrease in pain scores followed by an increase after 30 minutes, whereas the MOR group showed a steady decline in pain scores over time (Table 8). Specifically, in the Miller et al study, the maximum reduction in pain score for the LDK group was seen immediately after infusion completion and was sustained for only 5 to 10 minutes. In the MOR group, a steady decline in pain scores was seen with a maximum reduction reached at 100 minutes post-infusion.

The short duration of ketamine's analgesic effect likely led to the increased rate of subsequent doses in the Miller et al and Mahshidfar et al studies and increased rescue fentanyl use at 120 minutes in the Motov et al study. Miller et al observed repeat dosing for LDK (54%) versus MOR (38%) although the difference was not statistically significant. In the ketamine group, 25% of the patients did not complete the entire 120 minutes of data collection due to requesting a third dose versus the 14% of patients excluded in the morphine arm due to requesting a third dose. Mahshidfar et al study revealed a statistically significant difference between the groups requesting an additional dose of analgesia, 34% in the ketamine group and 10% in the MOR group. Motov et al showed no statistically significant difference in the use of rescue fentanyl at 30 and 60 minutes between the groups, but the ketamine group required significantly more rescue fentanyl at the 120-minute mark (17% difference).

Table 8. Overview of pain scores over time

	Baseline	T5	T10	T15	T20	T30	T60	T100	T120
Miller et al									
Ketamine	7.13	2.23	2.83	-	3.93	-	3.63	3.03	3.53
Morphine	7.14	4.14	3.74	-	3.84	-	2.34	2.14	2.14
Mahshidfar et al									
Ketamine	8.1	-	-	4.1	-	4.5	4.9	-	-
Morphine	8.4	-	-	4.0	-	3.8	3.2	-	-
Motov et al									
Ketamine	8.6	-	-	3.2	-	4.1	4.8	-	3.9
Morphine	8.5	-	-	4.2	-	3.9	3.4	-	3.7

- Indicates that pain scores were not recorded at this time.

Secondary outcomes measured included adverse drug events, vital signs, and provider or patient satisfaction. No serious or life-threatening side effects were observed in any of the studies. All three studies showed no significant difference between the groups in the rate of minor adverse events, such as nausea and dizziness (Table 9). Miller et al and Mahshidfar et al showed the MOR group experienced a statistically significant decrease in oxygen saturation. Miller et al also revealed the LDK group experienced more dysphoria and hallucinations. Motov et al observed a statistically significant increase in adverse effects immediately post-injection and at the 15-minute mark in the LDK group, but the difference between the groups equalized at 30 minutes.

Miller et al found both drugs scored similarly with providers and nurses. The median nursing satisfaction score was 4 (somewhat satisfied) for LDK and 5 (very satisfied) for MOR,

but the difference was not statistically significant. Mahshidfar et al showed a greater patient satisfaction score in the morphine group one-hour post-injection.

Table 9. Overview of adverse drug event rates

	Decrease in oxygen saturation	Dysphoria	Hallucinations	Flushing	Nausea	Dizziness
Miller et al						
Ketamine	0	16%	13%	-	13%	8%
Morphine	5%	0	0	-	10%	5%
Mahshidfar et al						
Ketamine	4%	4%	-	0	16%	34%
Morphine	18%	2%	-	36%	17%	32%
Motov et al						
Ketamine	-	2%	-	-	13%	18%
Morphine	-	0	-	-	20%	13%

- Indicates that the adverse drug reaction was not analyzed.

CONCLUSION

In the treatment of acute pain, IV ketamine and IV morphine have a significant short-term (15-30 minutes) reduction in pain scores; however, the effects of ketamine are unsustainable without repeat dosing after 30 minutes. Morphine maintains a longer duration of action without repeat dosing. Based on these results, ketamine does not appear to be an adequate replacement for morphine in the management of acute pain in the ED.

Ketamine is still a promising alternative due to its similar short-term efficacy and safety profile. It may be utilized in opioid-tolerant patients and in areas of IV opioid shortage. Since ketamine is unable to sustain pain relief over the normal course of an ED stay, further research is warranted for either higher doses of low-dose ketamine infused over a longer duration or the use of adjunctive medications for ED management of acute pain.

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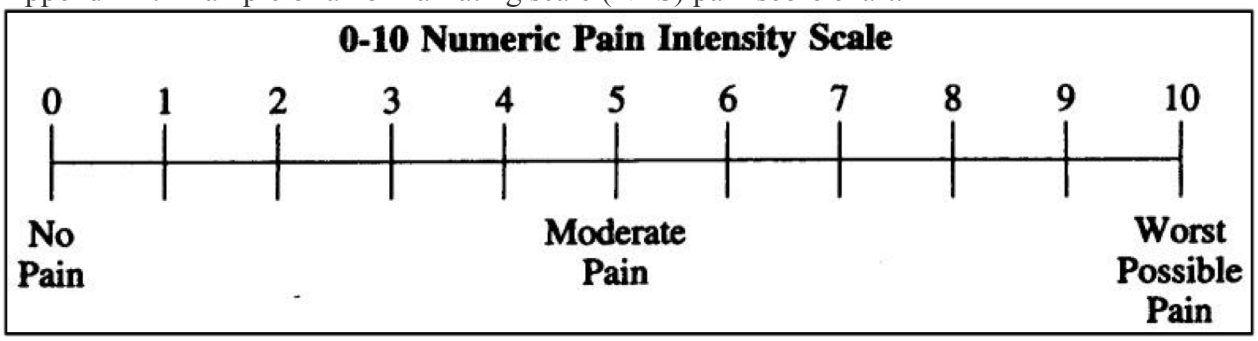
APPENDICES

Appendix 1: Example of a normal rating scale (NRS) pain score chart.[11]



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