UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

THE TABLET: PALLIATIVE CARE PHARMACY TIPS

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Palliative Care Pharmacy Team:

Special thanks to student pharmacist research team:

Lana Callaghan and Sadora (Sadie) Franklin

Clinical Pharmacy Specialist:

Maria Felton Lowry, PharmD, BCPS, BCGP
Assistant Professor
University of Pittsburgh School of Pharmacy, Department of Pharmacy and Therapeutics
Palliative Care Clinical Pharmacy Specialist
UPMC Palliative and Supportive Institute

Cell: 412-627-8473
Office: 412-864-2899
Email: lowrymf@upmc.edu

If you have a topic you would like the pharmacy team to answer, please send your suggestions to: lowrymf@upmc.edu

TODAY'S TOPIC:

UPMC Research: Description of the use of ketamine for opioid-refractory pain in an inpatient palliative care population

Lana Callaghan, Sadora Franklin, Kendall Downer MD, Kathy Wunderle MD, Maria Felton Lowry, PharmD, BCPS, BCGP

Results presented at American Society of Health-System Pharmacists (ASHP) Midyear Meeting 2024

Background:

- Intravenous (IV) ketamine is used off-label in the palliative care setting to target opioid-refractory pain
- There are no standard guidelines for dosing regimens, titration parameters, or duration of use for ketamine in the palliative care setting

Importance:

IV ketamine is being used by our palliative care teams for opioid-refractory pain. It is important to review our internal prescribing practices, efficacy and safety to compare to other palliative care (limited) evidence.

The Research:

Primary Objective: To describe the prescribing practices of ketamine in an inpatient palliative care population, including: the initial rate of infusion, duration of infusion, and average rate of ketamine infusion.

Secondary Objectives: Describe efficacy and safety outcomes of ketamine infusion: change in oral morphine equivalents (OMEs) from pre-ketamine infusion to post-ketamine infusion, reported pain scores using the Modified Edmonton Symptom Assessment Scale (ESAS), incidence of hallucinations, and cardiovascular adverse events.

Methods:

- IRB-approved retrospective chart review for patients who received a ketamine infusion for opioid-refractory pain from August 31, 2021 to May 31, 2024
- **Inclusion Criteria:** Adult patients (>18 years old) hospitalized at UPMC Shadyside who received IV ketamine during inpatient admission with palliative care consult with a documented ESAS pain score >0 immediately preceding ketamine order
- **Exclusion Criteria:** Ketamine administration within peri-operative period (less than 48 hours before or following a surgical procedure) or died while receiving ketamine infusion
- Descriptive statistics utilized to analyze prescribing practices; Wilcoxon-Signed Rank Test for pre- and post-data

Results:

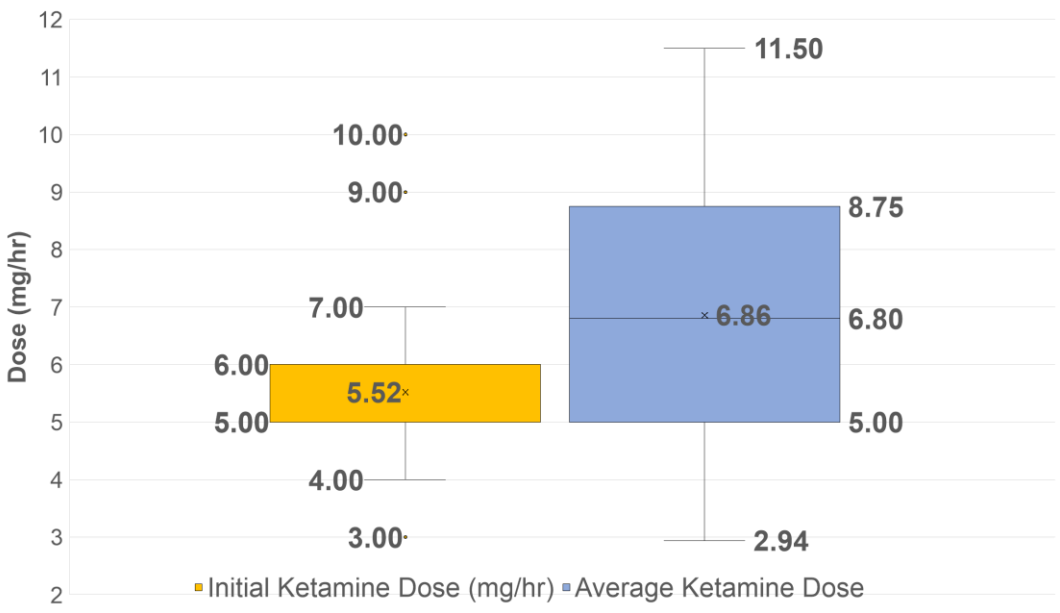
- N=19 patients included, mean (SD) age 54.5 (15.9), 57.9% male, mean (SD) weight: 73.1 (21.3)
- Charlson Comorbidity Index mean (SD): 8.8 (3.2)
- 89.5% patients died during admission
- 21.1% transitioned to inpatient hospice unit (GIP)

Table 1. Prescribing Practices of Ketamine Administration

Ketamine Administration	N=19
Initial Rate (mg/kg/hr)	
Mean (SD)	0.079 (0.032)
Median [Min, Max]	0.07 [0.04, 0.16]
Duration of Infusion (hr)	
Mean (SD)	111.3* (122.2)
Median [Min, Max]	76 [14, 504]
Average Rate (mg/hr)	
Mean (SD)	6.86 (2.55)
Median [Min, Max]	6.8 [2.9, 11.5]

*one patient received ketamine for 504 hours

Figure 1: Initial Ketamine Dose vs. Average Ketamine Dose



CONCLUSION: Prescribers opted to initiate ketamine at ~0.1mg/kg/hr and minimally titrated the dose before discontinuation after approximately 3 days of treatment.

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Figure 2: Average Difference of ESAS Pain Score Before and After Ketamine Infusion

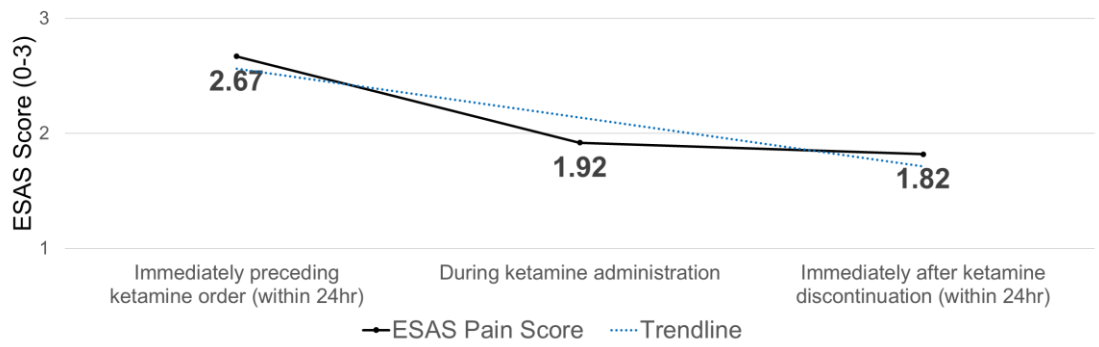


Figure 3: Analgesics Trialed Before Ketamine

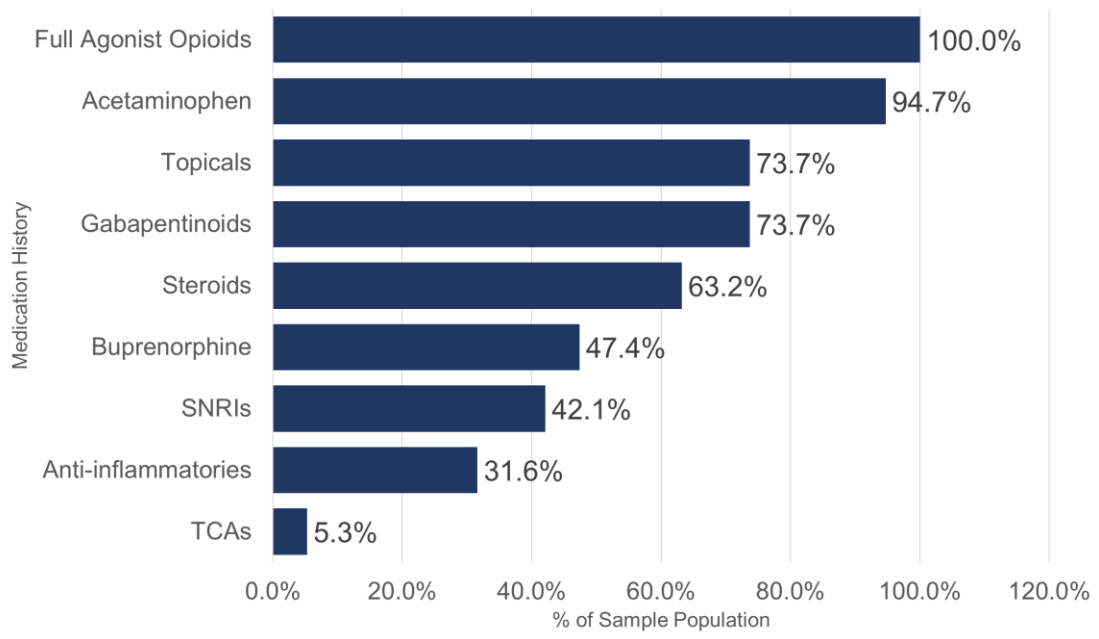
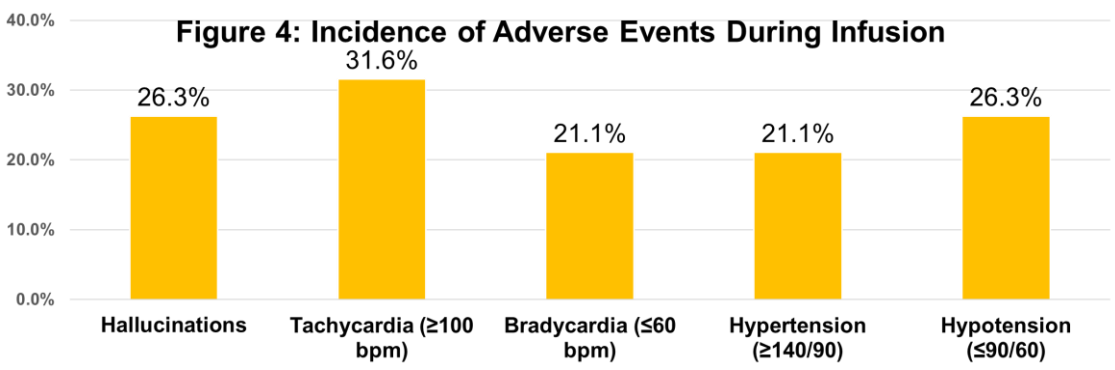


Table 3: Change in oral morphine equivalence, values taken 24 hours pre- and post-ketamine infusion

Change in OMEs (% reduction)	N=19	P value
Mean (SD)	14.9% (39.2%)	0.2247
Median [Min, Max]	25.1% [-76.2%, 70.4%]	



*No patients discontinued treatment due to hallucinations or adverse events per documentation in clinical notes

Discussion:

- This data suggests that IV ketamine infusions may reduce pain ratings in opioid refractory pain in a palliative care population as ESAS scores did reduce by almost a full point (from pre to post ketamine infusion) on a 4-point scale, which seems clinically relevant
- Despite the prevalence of adverse effects, we are unable to determine if they were related to ketamine infusion alone given retrospective nature of chart reviews
- The data suggests it is not necessary to pre-emptively reduce opioids before ketamine administration and ketamine was not shown to be significantly opioid-sparing in our population
- Prescribing practices in this population were consistent with our institution's Injectable Ketamine Safe Practice Guidelines (starting dose: 0.1mg/kg/h) and similar to anesthesia guidelines for post-operative pain
- Many analgesics were trialed before ketamine in our population, emphasizing the role ketamine has in “refractory” pain management at our institution
- It is possible that we are not titrating ketamine infusions, given similarities between mean starting doses (5.5 mg/h) and mean doses overall (6.9 mg/h). We may have more room to increase to improve analgesic response. This of course, would not come without increased risk of possible side effects.
- **Limitations**:
  - Recall and observer bias, as this retrospective review depended heavily on documentation of subjective data outcomes
  - Confounding variables of complicated medical histories that may have contributed to patient outcomes
  - Small sample size, one patient received ketamine for 504 hours, likely skewing the mean duration of infusion, as seen by lower median

References:

1. Jiao J, Fan J, Zhang Y, Chen L. Efficacy and safety of ketamine to treat cancer pain in adult patients: a systematic review. *J Pain Symptom Manage*. 2024;67(3):e185-3210.
2. Loveday BA, Sindt J. Ketamine protocol for palliative care in cancer patients with refractory pain. *J Adv Pract Oncol*. 2015;6(6):555–561.

CONCLUSION: Prescribers opted to initiate ketamine at ~0.1mg/kg/hr and minimally titrated the dose before discontinuation after approximately 3 days of treatment.