Study Title: A Multi-Center Prospective Evaluation of Pre-Hospital Ketamine Administration and ED Disposition in the Trauma Patient

Study background and Significance

Ketamine is a dissociative anesthetic that has proven to be versatile in the hospital setting. Its rapid onset, sedative, and analgesic properties are effective for pain management and as an adjunct to sedation for combative or agitated patients.[12,3,4] In addition to intravenous (IV) administration, ketamine can be administered intranasally and intramuscularly which make it adaptable in emergent situations where IV access is unable to be established. These factors have made its use appealing in the pre-hospital setting to be administered by emergency medical service (EMS) providers. Use of pre-hospital ketamine in trauma patients is limited but benefit has been shown for agitation and pain. A prospective randomized control trial of 135 trauma patients in the pre-hospital patients found better pain control with IV ketamine when compared to IV morphine with mean pain score change of -5.6 vs. -3.2, respectively.[2] A retrospective pre-hospital case series of 11 combative trauma patients found prehospital IV ketamine to effectively sedate agitated patients when used alone or in combination with IV midazolam.[3]

Adverse effects of ketamine in the pre-hospital setting have predominantly centered around its increased rate of hypoxia and need for intubation with higher doses as demonstrated by Burnett et al.[4] Sound and efficacious treatment of the trauma patient depends on a proper initial workup and an organized transition from the pre-hospital setting to emergency department arrival to disposition. It is, therefore, important to establish a protocol allowing proper evaluation and triage of trauma patients receiving ketamine in the pre-hospital setting

The objective of this study is to determine how pre-hospital administration of ketamine affects disposition of the trauma patient and the appropriate dose that balances the challenges of pre-hospital transport of a trauma patient with appropriate disposition of a patient arriving at a trauma center.

- Aim #1: To identify prehospital practice patterns for the management of trauma patients with agitation
- Aim #2: To determine the effects of pre-hospital ketamine administration on trauma patient ED disposition
- Aim #3: To develop a standardized protocol for prehospital ketamine administration for trauma patients

2. Subject Population

We will prospectively enroll trauma patients presenting to our Level 1 trauma center at University Medical Center in New Orleans (UMCNO) and Our Lady of the Lake Regional Medical Center (OLOLRMC) in Baton Rouge, a Level 2 trauma center, from September 1, 2021-August 31, 2024. The PI and sub-PIs will have access to the information from the trauma registry. This time span reflects the years that include the beginning of ketamine administration by EMS.

The patients will not be contacted as part of this study. The study population will include all adult trauma patients (age 18 and older) who presented to UMCNO & OLOLRMC having received ketamine by EMS prior to admission. Patients less than 18 years old, those who did not receive ketamine in the pre-hospital setting, and members of vulnerable populations (children, pregnant women, and prisoners) will be excluded. We anticipate reviewing 5000 charts.

Working in coordination with EMS administrators, we will obtain pre-hospital information on trauma patients who received pre-hospital ketamine and presented to our facility. This pre-hospital information will be cross-referenced with information in the patient's medical record and our trauma registry. Transport of trauma patients to these hospitals is provided by the two major EMS providers in the metropolitan areas of New Orleans and Baton Rouge. New Orleans EMS is a provider of EMS services within the city of New Orleans and falls under the operations of the New Orleans Office of Homeland Security and Emergency Preparedness (headquarters: 2929 Earhart Blvd. New Orleans, LA 70125). Acadian Ambulance Service is a private ambulance service providing ambulance services by ground transport, helicopter, or fixed wing throughout Louisiana, Mississippi, Texas, and Tennessee (headquarters: 130 E. Kaliste Saloom Road. Lafayette, LA 70508). Both of these sites have provided letters of collaboration.

This is a chart review only and involves no therapeutic intervention.

3. Study Procedures

Study Design

This is a prospective multi-center study involving trauma patients at participating sites. For trauma patients who have received ketamine, ED or trauma team staff will document in their admission H&P or consult note ketamine administration to include dose, route, indication, and the patient identification number used by that EMS provider. Working with trauma research coordinators utilizing the trauma registry, data will be collected on those patients that have received ketamine every 3 months.

Working in coordination with representatives from each EMS organization, we will obtain pre-hospital information on trauma patients who received pre-hospital ketamine and

presented to participating facilities. Information will include EMS patient identification number, ketamine dose, route of administration, ketamine indication, additional opioid or sedative medications given, transport time, pre-hospital initial Glasgow Coma Scale (GCS), pre-hospital vitals, occurrence of pre-hospital procedures, use of restraints, event association with substance abuse, air vs ground transport, and transport priority.

This pre-hospital information will be combined with the information in the patient's medical record from the trauma registry at each participating hospital utilizing the EMS identification number cross-referenced to the admission MRN. Information of particular importance after arrival contained within the hospital's trauma registry database will include age, gender, race, height, weight, trauma type, ISS, admission GCS, admission vitals, occurrence of ED intubation, indication for ED intubation TBI, rib fractures, pulmonary contusion, diaphragm injury, etoh positive, urine toxicology positive, duration of mechanical ventilation, positive head CT findings, OR procedure, hospital and ICU LOS, discharge disposition, tracheostomy, ARDS, PE, DVT, AKI, VAP, unplanned intubation, cardiac arrest, hypoxic event, and mortality.

The appointed trauma staff at each participating site will have access to patient data at their respective facility as an attending Critical Care/Trauma surgeon. Using our provided data collection tool, research coordinators will input the provided data into the collection tool after it has been de-identified. This will be sent to data organizers and reviewed in coordinated meetings between trauma staff representatives from each participating institution. Patients will not be contacted to obtain information and will have no time commitment. To minimize the risk of privacy loss to subjects, patient data will only be shared between researchers using HIPAA protected email sending encrypted files only to those granted access to the trauma registry. Only the PI and other members of the research team that have been granted access will have access to the database.

Data Collection:

Working in conjunction with EMS providers, they will provide the trauma research team at each participating facility a data set of patient information on trauma transports of patients administered ketamine on scene or in route to the hospital. This pre-hospital data from EMS will include patient name, DOB, EMS patient identification number, ketamine dose, route of administration, ketamine indication, additional opioid or sedative medications given, transport time, pre-hospital initial Glasgow Coma Scale (GCS), pre-hospital vitals, occurrence of pre-hospital procedures, use of restraints, event association with substance abuse, air vs ground transport, and transport priority. This patient information will be obtained from each participating institution after completing a data use agreement. With this information, the research team will cross reference this EMS data with data in their facility's trauma registry aligning EMS identification number with MRN. Name, DOB, and transport date can also be

cross-reference as a backup for confirmation. This will identify in the trauma registry the patients who received ketamine and provide further pre-hospital information that does not exist in the trauma registry. This EMS data and trauma registry data will be combined in a new data set which will be inputted into the data collection tool provided by the study organizers. The information will then be uploaded to a REDCAP database. An additional data set of 200 trauma patients from the same time period who did not receive ketamine will be collected. This group of patients will serve as a control group that will be matched for age, gender, ISS, mean initial GCS, and trauma type at each institution. All patients will be assigned a subject code number to de-identify data to ensure that the risk for privacy loss of subjects is minimized. All files will be password protected. The master list of code numbers assigned to each subject will be stored in a separate database only accessible to the PI. Data collection documents will be available to the principal investigator or key subject personnel on the research team. The data collection tool will not contain patient identifiers. De-identified data will be archived in the PI's office computer as a password-protected file for 3 years.

Outcomes Measured: The primary outcome measured will be intubation after arrival in the Emergency Department. Secondary outcomes will include: duration of mechanical ventilation, OR procedure, hospital and ICU LOS, discharge disposition, tracheostomy, ARDS, PE, DVT, AKI, VAP, unplanned intubation, cardiac arrest, hypoxic event, and mortality.

Variables Collected:

1. Age
2. DOB
3. Gender
4. Race
5. Height
6. Weight
7. BMI
8. Chief complaint
9. Mechanism of Injury--blunt vs penetrating
10. Association with intoxication/substance abuse
11. Admission date
12. EMS transport company
13. EMS transport time
14. Type of EMS transport--ALS vs BLS, air vs ground
15. Transport time
16. Ketamine indication
17. Ketamine dose
18. Ketamine route
19. Additional pre-hospital sedation
20. Additional pre-hospital opioids

21. Use of restraints
22. Prehospital fluid administration
23. Prehospital blood product administration
24. Prehospital vitals (HR, BP, RR, SPO2)
25. Prehospital procedures performed
26. Prehospital GCS
27. Mechanism of injury
28. Presence of TBI
29. Presence of Rib fractures
30. Presence of pulmonary contusions
31. Presence of Diaphragmatic injury
32. ISS (injury severity score)
33. AIS (abbreviated injury score)
34. Discharge date
35. ICU step-down date
36. Admission vitals (HR, BP, RR, SPO2)
37. GCS on admission
38. Blood alcohol positivity
39. Drug screen
40. Intubation
41. Indication for intubation
42. Date and time of intubation
43. Date and time of extubation
44. Re-intubation
45. Normal head CT
46. “Pan scan” performed (CT head, chest, abd/pelvis)
47. MV days
48. ICU LOS
49. Hospital LOS
50. Dispo at discharge
51. Tracheostomy
52. ARDS
53. PE
54. DVT
55. AKI
56. VAP
57. Mortality
58. Procedures performed
59. OR procedure
60. Cardiac arrest

61. Hypoxic events

Statistical Analysis:

Effect of pre-hospital ketamine administration of emergency department intubation will be assessed using chi square and logistical regression statistical methods. The patients will be divided based on those who received pre-hospital ketamine and those who did not. Continuous variables will be compared using Student's t-test and the Mann Whitney U test. The Chi-squared tests or Fisher's exact test will be used to compare categorical variables. All variables with a p value <0.2 on univariate analysis will be entered into a multivariable logistic regression analysis to identify independent risk factors for increased length of stay. Data will be reported as adjusted odds ratios with 95% confidence intervals. Statistical significance will be set at $p<0.05$.

An *a priori* power analysis was conducted using retrospective data from our institution. A total of 660 patients (330 patients/group) will give the study an adequate power of 80%.

4. Risks

As this study is a chart review, the risks posed to subjects is minimal. The main risk to patients is loss of privacy due to the data collection as the patient's MRN will be reviewed. We will take the appropriate steps to minimize these risks. The PI is not requesting access to any additional information that is not included as part of the Trauma Registry or provided EMS info.
All files will be stored electronically as password protected files only accessible to research personnel. All subjects included in the chart review will be assigned a coded subject ID number and kept in a password protected folder on the PI's office computer that is only accessible to the PI. Key research personnel and the PI will have access to the database and data collection sheet which will include de-identified data using an assigned subject ID number. Files will be archived in the PI's office computer for a period of 3 years as a password protected file. Data will be permanently deleted at the completion of 3 years post-study completion.

5. Benefits

There will be no direct benefits to subjects for participating in this research. However, the knowledge gained from the study may benefit society in general. The effect of pre-hospital ketamine administration on rates of emergency department intubation has not been demonstrated. The results from this single-center study could help to further elucidate data to help improve existing protocols on this important topic.

6**. Remuneration**

There will be no payment for participation in this research study.

7. Academic or Extra Credit

None

8. Costs

There will be no costs to the subject for participating in this research study.

9. Alternatives

This does not apply.

10. Consent process and documentation

As this study is a chart review, the risks posed to subjects is minimal. The main risk to patients is loss of privacy due to the data collection. This is a chart review of pre-existing data from patient medical records and the UMCNO/OLOLRMC trauma registries. We have applied for expedited research given that the research poses no more than minimal risk, that the prospective study will not impact the care of the subjects involved, and that the research could not be carried out without the waiver of consent given that it would be impractical to contact the majority of the large patient pool involved. Data will be recorded on a data sheet and transferred to a secured database that is devoid of patient identifiers. Due to difficulty with patient follow up in the Trauma population and the minimal risk nature of this study, it would not be feasible to contact study participants, a waiver of consent will be requested.

11. References

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