



## OUT-OF-HOSPITAL KETAMINE USE BY INDIANA EMS PROVIDER AGENCIES: A RETROSPECTIVE ANALYSIS

### BACKGROUND

Ketamine is a unique drug with multiple medical indications and uses. Originally developed for veterinary medicine and pediatric sedation, ketamine has been used safely and effectively in the medical field for more than five decades.<sup>1</sup> First synthesized in 1962<sup>5</sup>, this drug has seen a recent increase in interest due to its unique properties of being both a potent analgesic and sedative agent with multiple indications for patient use.

Ketamine is classified as a Schedule III controlled substance by the Drug Enforcement Administration (DEA) in the United States. When administered at sedative and anesthetic doses, ketamine causes a dissociated state unique to this specific drug. The patient often is not unarousable as seen with medications like etomidate and midazolam, but unlike other agents, their consciousness also is disconnected from their sensory input.<sup>2</sup> Patients have been noted to speak or have occasional movement with this medication; however, they remain unaware of their surroundings. Patients often will have non-purposeful eye movements including various patterns of nystagmus.<sup>2</sup> The effectiveness of ketamine comes from its ability to render a patient sedated and unresponsive to painful stimuli, while also providing amnesia and analgesia.<sup>2</sup> Unlike other sedative and analgesic agents, ketamine is ideal for out-of-hospital use due to its limited depression of the respiratory drive. Likewise, ketamine causes fewer negative hemodynamic effects (less drop in blood pressure or cardiac output) when compared to other medications used to achieve similar states.

Because of increased use and interest, along with the sensationalism of recent public and social-justice cases in the media, increasing volumes of literature and publications have attempted to describe the use of ketamine across multiple treatment domains.<sup>3</sup> Overwhelmingly, the majority of ketamine is administered in emergency department and inpatient settings. However, ketamine use has seen growth in the out-of-hospital setting by emergency medical services (EMS).<sup>4</sup> An analysis of this medication and summary of EMS use and administration in the state of Indiana is useful for the field provider, medical directors and emergency physicians who receive EMS patients and provide direction and oversight of those agencies. This analysis is the first of its kind from the Indiana Department of Homeland Security (IDHS) in an attempt to better understand ketamine use by Indiana licensed EMS professionals.

## METHODS

This was a retrospective analysis using data pulled from the Indiana EMS Data Registry which houses patient care data from Indiana EMS provider agencies. From this database, data from 28,639 EMS runs from Dec. 16, 2016 through April 8, 2021 mentioning ketamine administration were obtained. Specifically, data from the following fields were analyzed:

- Response type
- Date of service
- Incident complaint reported by dispatch
- EMS disposition
- Mode of transportation
- Patient demographics of age, race and gender
- Ketamine dose
- Route of administration
- Reported complications after ketamine administration
- Initial and post-administration pain score
- Initial and final respiratory rates
- Initial and final heart rate
- Initial and final pulse oximetry reading
- Patient Successful Procedure Descriptions List (performed interventions)
- Destination

Of the 28,639 administrations on record, it was evident that some patients received more than one dose, with 9,722 unique patient administrations.

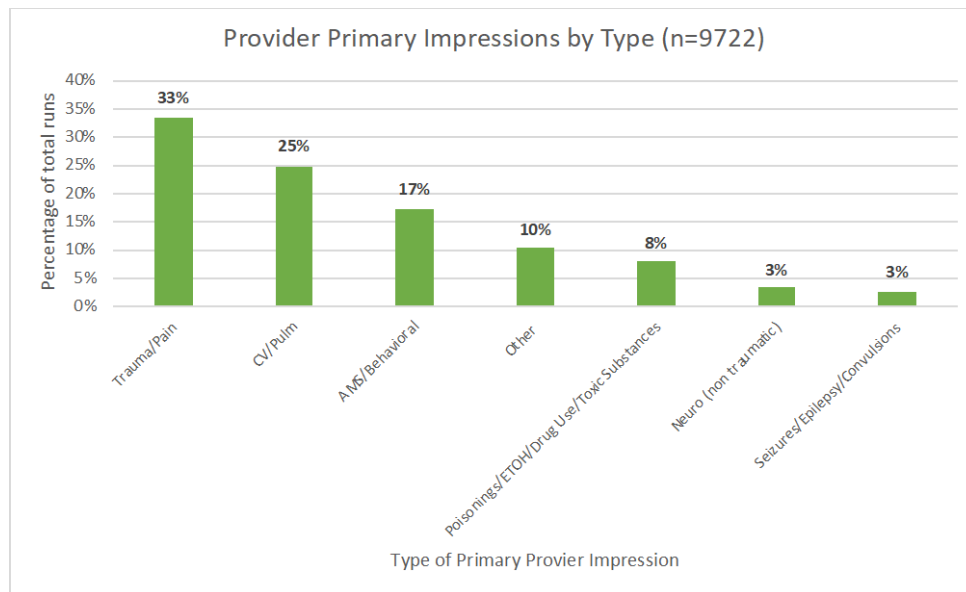
## DATA

Ketamine was administered a total of 28,639 times to 9,722 unique patients in the pre-hospital setting in the state of Indiana from Dec. 16, 2016 through April 8, 2021. Analyses of the data fields obtained from state EMS records were performed.

### PROVIDER PRIMARY IMPRESSION

Analysis of provider primary impressions reported by EMS providers revealed the top categories to be trauma/pain (33%), CV/pulmonary (25%) and AMS/behavioral (17%).

Figure 1: Provider Primary Impressions by Type



## INCIDENT COMPLAINT REPORTED BY DISPATCH

The unique categories of incident complaint reported by dispatch are compiled in decreasing order in Figure 2.

*Figure 2: Incident Complaint Reported by Dispatch*

Dispatch Complaint	n	Percentage of N
Transfer/Interfacility/Palliative Care	1526	16%
Traumatic Injury	1031	11%
Breathing Problem	969	10%
Sick Person	705	7%
Traffic/Transportation Incident	636	7%
Falls	619	6%
Unconscious/Fainting/Near-Fainting	492	5%
Overdose/Poisoning/Ingestion	477	5%
Psychiatric Problem/Abnormal Behavior/Suicide Attempt	466	5%
Airmedical Transport	387	4%
Other	374	4%
Convulsions/Seizure	348	4%
Cardiac Arrest/Death	318	3%
Unknown Problem/Person Down	272	3%
No Other Appropriate Choice	217	2%
Burns/Explosion	156	2%
Stroke/CVA	142	1%
Stab/Gunshot Wound/Penetrating Trauma	127	1%
Abdominal Pain/Problems	109	1%
Heart Problems/AICD	103	1%
Back Pain (Non-Traumatic)	98	1%
Chest Pain (Non-Traumatic)	86	1%

## PATIENT DEMOGRAPHICS

74.33% of unique patients who received ketamine had a documented race of “white,” 8.79% as “Black or African American” and 1.51% as “Hispanic or Latino.” In 14.54% of runs, the race was undocumented. The remaining percentages of patients (0.83%) were documented in other categories as seen in Figure 3. Of all unique ketamine administrations, males made up 59.5% of those who received ketamine while females made up 39.4% as seen in Figure 4. Documented patient ages from each unique run where ketamine was administered were divided into the noted intervals and quantified to produce Figure 5.

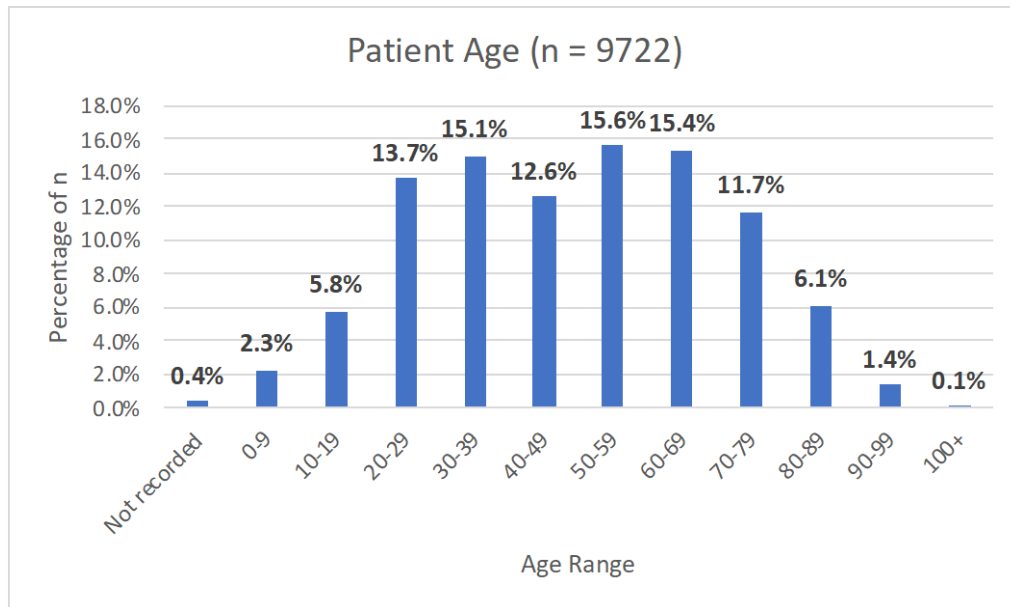
Figure 3: Patient Race by Number and Percentage

Race	n	percentage of N (N=9722)
White	7226	74.33%
<b>Left Blank</b>	<b>1414</b>	<b>14.54%</b>
Black or African American	855	8.79%
<b>Hispanic or Latino</b>	<b>147</b>	<b>1.51%</b>
Asian American/Pacific Islander	37	0.38%
<b>Other Race</b>	<b>27</b>	<b>0.28%</b>
American Indian or Alaska Native	6	0.06%
<b>Hispanic or Latino, White</b>	<b>4</b>	<b>0.04%</b>
Black or African American, Hispanic or Latino	3	0.03%
<b>Hispanic or Latino, Black or African American</b>	<b>3</b>	<b>0.03%</b>

Figure 4: Patient Gender by Percentage

Patient gender	percentage of N (N=9722)
Male	59.55%
<b>Female</b>	<b>39.44%</b>
Unknown (Unable to Determine)	0.59%
<b>Not Recorded</b>	<b>0.40%</b>
Not Applicable	0.03%

Figure 5: Patient Age by Percentage of Total Unique Patients



## ROUTES OF ADMINISTRATION

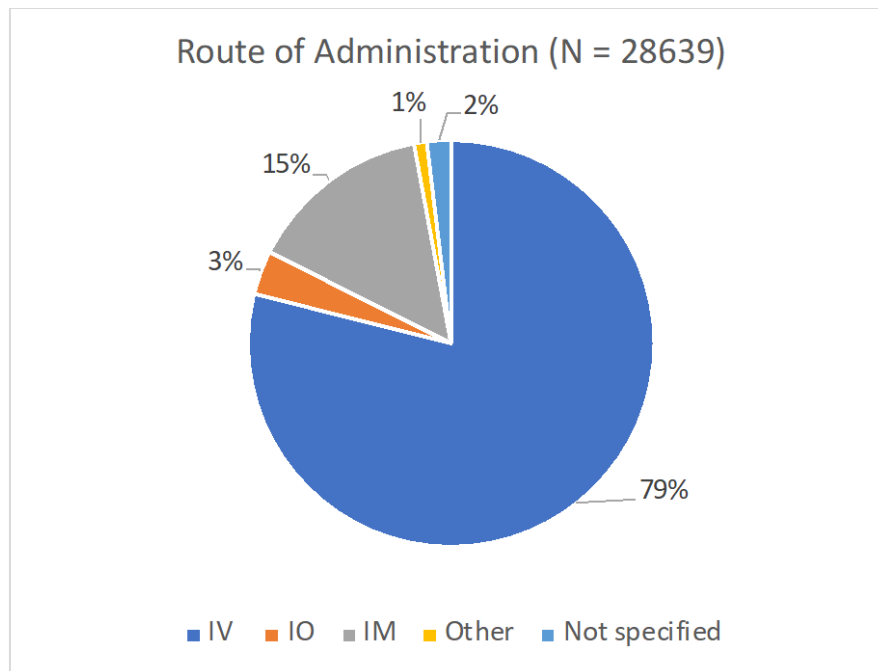
A total of 28,639 administrations were documented in the EMS Data Registry in Indiana between the dates Dec. 16, 2016 through April 8, 2021. The figure below displays all the routes of administration documented.

Figure 6: Routes of Administration

Endotracheal*	Blow-by*
Intraarterial*	Other/miscellaneous*
Portacath*	IV Push <sup>1</sup>
Slow IV push <sup>1</sup>	Intranasal*
Left blank/not recorded	Intramuscular (IM)
IV pump <sup>1</sup>	Intraosseous (IO)
Intravenous (IV) <sup>1</sup>	

Note: routes listed with an asterisk (\*) denote routes that were compiled to comprise “other” in Figure 7. Routes listed with a superscript “1” denotes routes that were combined to be listed as “IV” in Figure 7. This figure details the percentage of administrations documented as each type. Most notably, 79% of doses were documented as being administered via IV.

Figure 7: Route of Administration



## DOSING

There were a total of 619 different ways that EMS providers documented doses of ketamine. Dosing was recorded in a variety of units. Some providers used units (ex: milligrams), weight-based units (ex: milligrams per kilogram) and units/weight/time-based units (ex: milligrams per kilogram per minute).

## INTRAVENOUS

EMS providers most commonly recorded dosing of ketamine in milligrams when they administered ketamine via an intravenous dose. The lowest recorded value was 0 milligrams while the highest recorded dose was 25 grams (n=2). Upon further investigation of the run where 0 milligrams were documented as given, the narrative stated that EMS provider drew up Ketamine, but ended up wasting it as the situation no longer warranted the administration of the medication. Upon further investigation into the run in which 25 grams was documented, the written narrative stated, "25 mg of ketamine SIVP for pain control". Thus, the highest documented dose likely was due to an error in documentation. The next largest dose given was 1000 milligrams, given to a motor vehicle collision victim, and this correlated with what was documented in the narrative section of the patient care record. This dose was due to an error in dosing made by EMS personnel in the field. This was also documented in and described in the narrative section of the patient care record.

A table listing the most frequently administered IV doses of ketamine is shown below. While some narratives listed estimated patient weights and expected dosing based upon those rates, this was not common in the records that were analyzed.

*Figure 8: Most Frequent Intravenous Doses*

Intravenous dose	Number of administrations
100 Milligrams (mg)	4539
50 Milligrams (mg)	2399
200 Milligrams (mg)	2187
150 Milligrams (mg)	1447
25 Milligrams (mg)	1433
10 Milligrams (mg)	1146
20 Milligrams (mg)	1128
75 Milligrams (mg)	740
30 Milligrams (mg)	535
15 Milligrams (mg)	458
80 Milligrams (mg)	436
250 Milligrams (mg)	398
300 Milligrams (mg)	381
70 Milligrams (mg)	374
60 Milligrams (mg)	328
120 Milligrams (mg)	266
40 Milligrams (mg)	244
90 Milligrams (mg)	216
<b>Total number of IV administrations</b>	<b>22601</b>

## INTRAOSSEOUS

A total of 1000 doses of ketamine were documented as intraosseous (IO) administrations. The lowest recorded dose was 0 milligrams, and the highest recorded dose was 500 milligrams (n=1) and was given to an unconscious patient. Upon further investigation of the run where 0 milligrams were documented as given, the narrative stated that EMS provider drew up Ketamine, but ended up wasting it as the situation no longer warranted the administration of the medication. Figure 9 is a table listing the most frequently administered IO doses of ketamine. There was a total of 65 unique documented doses. 200 milligrams and 100 milligrams were the most frequently documented IO doses of ketamine.



Figure 9: Most Frequent Intraosseous Doses

Intraosseous dose	Number of administrations
200 Milligrams (mg)	235
<b>100 Milligrams (mg)</b>	<b>232</b>
150 Milligrams (mg)	86
<b>300 Milligrams (mg)</b>	<b>31</b>
50 Milligrams (mg)	28
<b>250 Milligrams (mg)</b>	<b>23</b>
70 Milligrams (mg)	25
<b>140 Milligrams (mg)</b>	<b>21</b>
80 Milligrams (mg)	17
<b>160 Milligrams (mg)</b>	<b>16</b>
10 Milligrams (mg)	15
<b>125 Milligrams (mg)</b>	<b>15</b>
100 Micrograms (mcg)	14
<b>75 Milligrams (mg)</b>	<b>14</b>
120 Milligrams (mg)	13
<b>180 Milligrams (mg)</b>	<b>11</b>
400 Milligrams (mg)	11
<b>280 Milligrams (mg)</b>	<b>10</b>
60 Milligrams (mg)	9
<b>Total number of IO administrations</b>	<b>1000</b>

## INTRAMUSCULAR

A total of 4197 doses of ketamine was documented as intramuscular (IM) administrations. The lowest recorded dose was 0 milligrams, and the highest recorded dose was 1112 milligrams (n=1). Upon further investigation of the run where 0 milligrams were documented as given, the narrative stated that EMS provider drew up Ketamine, but ended up wasting it as the situation no longer warranted the administration of the medication. Upon further investigation of run where 1112 milligrams were documented, the narrative reported that the patient received “three IM doses of 250 mg,” so this dose is not the single largest IM dose given. The highest dose documented appropriately in the narrative was 1000 milligrams (n=3). Figure 10 is a table showing the most frequent doses.

Figure 10: Most Frequent Intramuscular Doses

Intramuscular dose	Number of administrations
300 Milligrams (mg)	2078
<b>150 Milligrams (mg)</b>	<b>410</b>
100 Milligrams (mg)	376
<b>200 Milligrams (mg)</b>	<b>319</b>
50 Milligrams (mg)	154
<b>250 Milligrams (mg)</b>	<b>116</b>
400 Milligrams (mg)	96
<b>500 Milligrams (mg)</b>	<b>69</b>
25 Milligrams (mg)	68
<b>75 Milligrams (mg)</b>	<b>55</b>
20 Milligrams (mg)	34
<b>30 Milligrams (mg)</b>	<b>24</b>
10 Milligrams (mg)	22
<b>Total number of IM administrations</b>	<b>4197</b>

## OTHER ROUTES

Other routes of administration included endotracheal (n=8), blow-by (n=1), intraarterial (n=1), other/miscellaneous (n=3), portacath (n=2), intranasal (n=274), and undocumented routes (n=552) were also found in the data set, but doses given in these routes only contribute to ~3% (n=841) of the total doses. Some of these documented routes and units were likely documentation error. For example, it would be inappropriate to administer any drug via the intra-arterial route in the prehospital setting. Upon further investigation, all the endotracheal doses (n=8), which were recorded in a dosage unit of “drops,” were found to be documentation errors and were given by other routes. There was one dose recorded as being given intra-arterially, but the narrative stated that this was given via central line during a patient transport.

## DOCUMENTED MEDICAL COMPLICATIONS

Documented medication complications from each unique run where ketamine was administered were summed, categorized and tabulated to produce Figure 11. Of all unique administrations, 97.36% had no documented medical complication associated with ketamine usage. The most common documented medication complication was altered mental status (AMS) which had a prevalence of 1.25%. While this is listed as a complication, altered mental status is in many circumstances the desired effect of ketamine administration. Likewise, other symptoms such as tachycardia or hypertension are known side effects of ketamine.

Figure 11: Documented Medical Complications

Documented Complication	n	Percentage of N (N=9722)
None	9465	97.36%
<b>AMS</b>	<b>122</b>	<b>1.25%</b>
Other	60	0.62%
<b>Hypotension</b>	<b>17</b>	<b>0.17%</b>
Apnea	15	0.15%
<b>Nausea or Vomiting</b>	<b>11</b>	<b>0.11%</b>
Hypoxia	8	0.08%
<b>Hypertension</b>	<b>8</b>	<b>0.08%</b>
Respiratory Distress	7	0.07%
<b>Bradypnea</b>	<b>1</b>	<b>0.01%</b>

## OXYGEN SATURATION TRENDS

Oxygen saturation trends (SpO<sub>2</sub>) captured by pulse oximeter can be summarized in the following figure.

Figure 12: Oxygen Saturation Trends

Parameter	n	Percentage of N (N=9722)
Final SpO <sub>2</sub> was equal to or greater than initial value	7205	74%
<b>No initial or final SpO<sub>2</sub> recorded</b>	<b>1070</b>	<b>11%</b>
Drop in SpO <sub>2</sub> >5% but less than <10%	592	6%
<b>Drop in SpO<sub>2</sub> &gt; 10%</b>	<b>0</b>	<b>0%</b>

To note, 74% of the patients had no recorded change in SpO<sub>2</sub> and zero patients out of 9722 unique patients experienced a drop in SpO<sub>2</sub> greater than 10% of their originally recorded value.

## END TIDAL CO<sub>2</sub> MONITORING

Of the 9722 unique runs where ketamine was administered, only 14 of these had documented end tidal CO<sub>2</sub> (ETCO<sub>2</sub>). Thus, no large-scale comparisons can be made regarding this metric.

## PATIENT SUCCESSFUL PROCEDURE DESCRIPTIONS LIST

Of 9,722 unique runs, 1,529 had no procedures documented under the “Patient Successful Procedure Descriptions List” field. In most of these cases where no procedures were documented, EMS providers elected to mention procedures within the narrative. The 8,193 runs with documented procedures had a variety of procedures documented. Figure 13 highlights how many runs included documentation of selected procedures. Figure 13 contains redundancies since the data lists the documented procedures in a list format. For example, the data for a single run may have included “Ventilator care and management, extremity vein catherization, cardiac monitoring”. This singular run would have been included in the total for ventilator management and cardiac monitoring as it references both procedures.

*Figure 13: Patient Successful Procedure Descriptions List*

Documented Procedure	Number of runs including documented procedure
EKG obtained	2630
<b>Ventilator management</b>	<b>400</b>
ETCO2 monitoring	480
<b>Advanced airway</b>	<b>2632</b>
Bagged ventilations	1018
Cardiac monitoring	1730

“Advanced airway” from Figure 13 consists of supraglottic airways, combitubes, endotracheal intubations, rapid-sequence intubations, orotracheal intubations, nasopharyngeal airway insertion and oropharyngeal airway insertion. “Bagged ventilations” includes runs that documented bagged ventilations via tube and mask.

## CONCLUSIONS

Ketamine is used by EMS professionals for a variety of patient indications in the out-of-hospital setting. Analysis of the Indiana EMS Registry data revealed more than 9000 patients received ketamine over a nearly five-year period by Indiana EMS providers with the most common indications for use being trauma or pain.

Overall, ketamine proved to be a very safe drug in the vast majority of patients to whom it was administered in this pre-hospital use analysis with few documented complications. Having said that, there is room for improvement in documentation of administration route and dosing, as well as improvement in institution of monitoring parameters, such as end-tidal CO<sub>2</sub> and cardiac monitoring. Appropriate documentation has been a common pain point for EMS providers and their medical directors and continues to be an opportunity for improvement as it applies to ketamine administration. Careful attention to these elements certainly could lead to greater quality improvement opportunities.

An additional area of concern, identified in this analysis, is the lack of patient weight documentation along with the apparent lack of weight-based dosing for ketamine administration. EMS medical directors are urged to pay particular attention to these details when creating ketamine administration guidelines. While not studied in this analysis, it is also recommended that cardiac monitoring be done on all patients receiving ketamine during their clinical care.

## REFERENCES:

1. Mion G, Villeveille T. Ketamine pharmacology: an update (pharmacodynamics and molecular aspects, recent findings). *CNS Neurosci Ther.* 2013; 19(6): 370- 380.
2. Zanos P, Moaddel R, Morris PJ, et al. Ketamine and ketamine metabolite pharmacology: insights into therapeutic mechanisms. *Pharmacol Rev.* 2018; 70(3): 621- 660.
3. White PF, Way WL, Trevor AJ. Ketamine—its pharmacology and therapeutic uses. *Anesthesiology.* 1982; 56(2): 119- 136.
4. Jennings PA, Cameron P, Bernard S. Ketamine as an analgesic in the pre-hospital setting: a systematic review. *Acta Anaesthesiol Scand.* 2011; 55(6): 638- 643.
5. <https://www.restorativehealthprimarycare.com/about/published-articles/history-of-ketamine>
6. [Br J Pharmacol.](#) 2015 Sep; 172(17): 4254–4276.