Safety and efficacy of perioperative intravenous ketamine in a retrospective study of patients undergoing amputation

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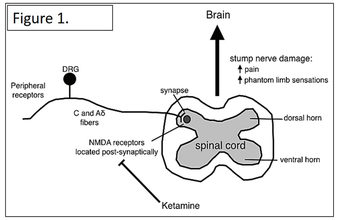
Introduction

The incidence of persistent post-operative pain, specifically phantom limb pain following amputation has been reported in 4-83% of patients. [1] NMDA receptor antagonists, such as ketamine have been purported to minimize central sensitization at the spinal cord level and may decrease the neuropathic pain that develops following amputation (Figure 1). [2-4] Literature reports that adverse events of ketamine include psychomimetic and cardiovascular effects usually seen as higher anesthetic doses and not with the lower doses. However, there is conflicting information in the literature regarding information on using ketamine infusions to treat acute post-amputation pain or chronic phantom limb pain. [5-8] The intent of this retrospective review is to identify amputation patients who have received ketamine infusion for inpatient acute pain management and examine safety and efficacy of the treatment.

Figure 1.

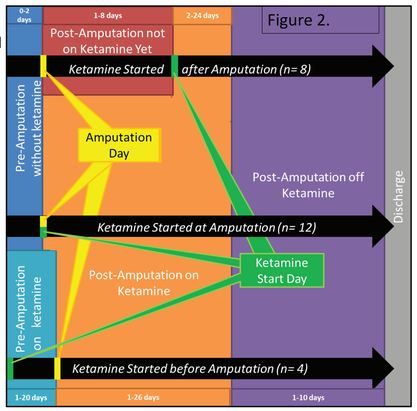


Study Design & Methods

Study Design: Retrospective and observational review of patients who underwent limb amputation and received ketamine treatment during hospitalization.

Participants At Thomas Jefferson University Hospitals (TJUH) all ketamine treatment on medical floors is administered via the Acute Pain Medicine Services and all ketamine related consults were screened for individuals that underwent amputation during that hospitalization. Currently the study has included 24 individuals (16 with full chart review completed) that received limb amputation and a consult to the Acute Pain Medicine Services at TJU Hospital for ketamine treatment from January 2009 through October 2015. An age, gender, and pathology-matched control group, consisting of patients who underwent limb amputation without perioperative ketamine, was recently approved for study inclusion and future comparative statistical analysis. The ketamine course relative to amputation for each participant is summarized in Figure 2.

Figure 2.



Data collection: Pain characterization and intensity over time, duration and dosage of ketamine, adjuvant analgesic usage, and side effect occurrences were abstracted from the EMR record of each patient's hospitalization. Study data were collected and managed using REDCap electronic data capture tools.

Results

Table 1.

Demographics:		Mean SD
Age at Admission	(years old)	48 14 (22 to 70 yo)
		% (n)
Gender	Male	60% (15)
	Female	40% (10)
Race	African American	33.3% (8))
	Caucasian	54.2% (13)
	Hispanic	4.2% (1)
	Unknown/Other	8.3% (2)
Marital Status	Single/Unknown	60% (15)
	Married	24% (6)
	Divorced	4% (1)
	Widowed	12% (3)
Opioid Tolerant prior to Hospitalization	No	24% (6)
	Unknown	8% (2)
	Yes	68% (17)
	Outpatient 24-hour Morphine Equivalent Dose	310 282 (50 to 784)

Figure 3.

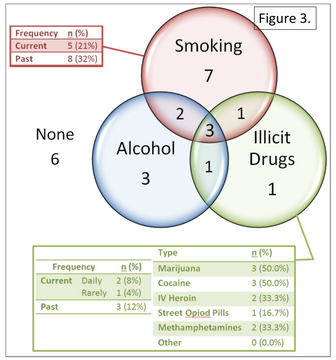


Figure 4.

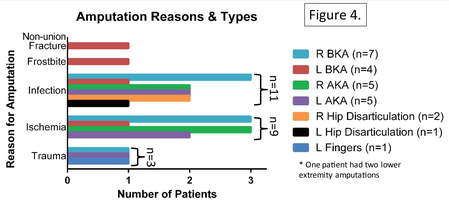
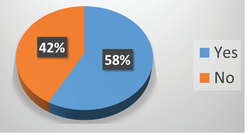


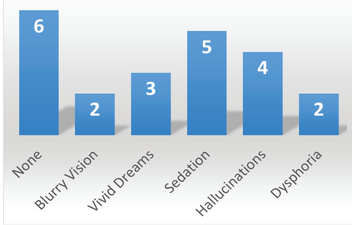
Figure 5. Intraoperative Ketamine Used During Amputation



- Indications for amputation were predominantly infection (41.7%) and ischemia secondary to peripheral vascular disease (33.3%), followed by trauma (16.7%) and one case each of vasopressor induced ischemia and frostbite (Figure 2).
- There were nine cases each of below or above the knee amputations, 3 hip dysarticulations, a transmetatarsal amputation, multiple finger or bilateral lower extremity and forearm amputations (Figure 3.)
- Intraoperative ketamine was utilized in 58.3% with the rest of subjects being initiated on ketamine no longer than 8 days from their procedure (Figure 5 and 1).
- Length of treatment varied from 1-26 days with doses of ketamine infusion most frequently between 10-25mg/hr, ranging from 5-75mg/hr.

Results

Figure 6. Frequency of Side Effects



- Ketamine dose did not correlate with side effect presentation or severity although the rate of dose escalation and use of 10mg ketamine boluses was the inciting event for some side effects.
- Preliminary data demonstrated that 54% displayed an absence of or mild self-limited side effects on that were well tolerated, including one night of vivid dreams, blurry vision, or mild dizziness and disorientation. Moderate to severe psychoactive side effects occurred in four individuals including hallucinations, dissociative feelings, and confusion. Only one patient required immediate ketamine discontinuation while a decreased dose was tolerated and justified due to the reported pain reduction benefit. (Figure 6.)
- Of note there were no cardiovascular disturbances or hepatic-related lab abnormalities; nor was there any neurological deficits or loss of consciousness in any patient.
- All side effects resolved without complications within 12-24 hours.

Future Directions

- Further pain score analysis, opioid utilization, and comparison with non-ketamine treated patients is ongoing.
- Perioperative ketamine warrants further prospective research to investigate its potential role in acute pain management protocols following amputation.

References

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