Real-World Preliminary Evaluation of Ketamine Infusions for Chronic Pain in Patients with Elevated Distress

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Introduction

- Ketamine, although off-label, has demonstrated efficacy for both chronic pain and psychiatric symptoms including for those who have not responded to prior treatments.
- Real-world effectiveness of ketamine infusions within chronic pain management settings remains needed.
- It is unclear whether patients with elevated pre-infusion distress experience similar changes in pain-related outcomes.

Results

- 22 (67%) had an elevated distress score before treatment.
- Elevated pre-treatment distress subjects had similar post-treatment distress levels as those with lower pre-treatment distress (63 [55;66] versus 59 [57;61], respectively; p = 0..56).
- Average distress and three versus four infusions were not significantly associated with post-treatment pain intensity (p = 0.35, p =0.40, respectively), PROMIS Physical Function (p = 0.81, p = 0.76, respectively), and PROMIS Pain Interference (p = 0.15, p = 0.98, respectively).
- Pre-treatment values were all significantly associated with post-treatment values, such that worse pre-treatment symptoms were associated with greater improvements (all p ≤ 0.001).

Discussion

- In a real-world setting, pre-treatment average distress was not associated with better post-treatment pain-related outcomes.
- Elevated pre-treatment distress subjects had similar post-treatment distress as their counterparts.
- Given the lack of differences between three and four sessions and clinically meaningful difference experienced by 44%, this study motivates the need for large pragmatic studies of ketamine therapy for chronic pain and the role of pre-treatment distress, as well as the mediating role of changes in distress.

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For chronic pain patients, **anxiety, depression, and anger** levels did **not** predict long-term response to **ketamine** treatment.

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Demographics	
Enrolled	35
Female	48%
Navy	82%
Age (IQR)	33 yrs (30-40)
Active Duty	94%
Black	9%
Native Hawaiian or Pacific Islander	18%
Latino	12%
White	54%
Other/Unk	6%

Table 1. Summary statistics of overall sample and by elevated distress group.

	Full Sample (N = 33)	Non-Elevated Distress (n = 11)	Elevated Distress (n = 22)	p-value
First to Last Treatment (Days)	63 [63;63]	63 [63;66]	63 [63;63]	0.50
First Treatment to Last Assessment (Days)	79 [71;99]	78 [72;104]	79 [71;94]	0.61
Pre-Treatment Average Pain Intensity	5 [5;6]	5 [4;6]	6 [5;7]	0.09
Pre-Treatment PROMIS Physical Function	36 [33;40]	40 [36;46]	35 [32;38]	0.009
Pre-Treatment PROMIS Pain Interference	66 [64;69]	62 [60;66]	68 [65;70]	0.03
Pre-Treatment Average Distress	61 [58;68]	57 [54;57]	67 [62;70]	<0.001
Pre-Post >= 30% Pain Intensity Decrease	5 (15%)	2 (18%)	3 (14%)	1.00
Post-Treatment Average Distress	59 [56;65]	59 [57;61]	63 [55;66]	0.56
Pre-Post >=5-Point Physical Function Increase	6 (22%)	0 (0%)	6 (32%)	0.14
Pre-Post >= 5-Point Pain Interference Decrease	10 (37%)	3 (33%)	7 (39%)	1.00

Note: PROMIS = Patient Reported Outcome Measurement Information System. Values are reported as frequencies (percentages) and medians [interquartile ranges].

Methods

This prospective, observational study received IRB approval from Naval Medical Center San Diego (NMCSD) IRB (#NMCSD.2019.0074).

Participants: Adult patients with chronic pain ages 24-52 years receiving 3-4 ketamine infusions, off-label for chronic pain, (dose = 0.5 mg per kg over 60 minutes) within 12 weeks.

Measures: Patients completed several Patient-Reported Outcomes Measurement Information System (PROMIS) scales and the Defense and Veterans Pain Rating Scale. Average distress was the average of PROMIS Anger, Anxiety, and Depression T-scores. Elevated distress was defined as pre-treatment average distress score >60.

Analyses: After completing descriptive statistics for the full sample, a generalized additive model (GAM) evaluated the primary outcome, post-treatment past 7-day pain intensity, while accounting for pre-treatment pain intensity, the number of sessions attended, days between first and last assessment, age, and average distress. The GAM was repeated for the secondary outcomes, PROMIS Physical Function and PROMIS Pain Interference. Significance was $p < 0.05$.