

Background

- Complex regional pain syndrome (CRPS) is a painful and debilitating condition characterized by abnormal sensory, motor, sudomotor, vasomotor, edema, and/or trophic findings seemingly disproportionate in time or degree to an initial trauma.
- Many patients progress from an acute phase of peripheral nervous system inflammation to a chronic phase of central nervous sensitization involving activation and proliferation of NMDA receptors.
- Ketamine is an NMDA-receptor antagonist that has been used with increasing frequency over the past two decades to treat chronic pain.
- There is moderate evidence supporting serial ketamine infusions at a sub-anesthetic level over a 10-day induction period to provide reductions in pain for up to 12 weeks in CRPS patients.

Purpose

- The goal of this pilot study was to observe and evaluate the results of induction and maintenance ketamine infusions at sub-anesthetic doses on the long-term treatment and symptom experience of CRPS patients.

Study Design

- This was a single-center, retrospective, observational chart review.
- We used descriptive analysis to evaluate all information in this study.

Methods and Materials

- Inclusion criteria:
 - ✓ primary diagnosis of CRPS
 - ✓ received ketamine infusions between July 2014 and December 2019
 - ✓ completed CSS17 at baseline and one year later
- Induction consisted of 10 daily treatments in 2 consecutive weeks, starting at 80 mg over 4 hrs and increasing by increments of 5mg, as tolerated, to a therapeutic level up to 400 mg.
- Maintenance infusions occurred with decreasing frequency as tolerated.

- The CRPS Severity Score (CSS17) survey is a quantitative index with two parts:



- a subjective patient-reported section indicating presence or absence of common signs and symptoms of CRPS
- an observed provider-reported section indicating presence or absence assessment of CRPS signs

- A secondary outcome was patient-reported lowest, highest, and average pain scores over the last 7 days.

Results

- 16 patients met inclusion criteria.
- Patients received an average of 79 (SD = 42.05, range = 34 to 188) infusions over about one year.
- 11 patients (69%) rated their pain intensity as low-to-moderate at baseline and 5 patients (31%) rated their pain as high at baseline
 - There was no significant difference between the two groups in number of infusions received.
- Number of ketamine infusions was positively correlated with reduction in both CSS observed scores ($r = 0.543, p = 0.03$) and CSS total scores ($r = 0.646, p = 0.007$) from baseline to one-year follow-up.
 - Similarly, number of ketamine infusions was positively correlated with reduction in CSS subjective scores ($r = 0.314$), but this finding was not significant.
- Greater number of ketamine infusions was associated with lower average pain at follow-up ($r = -0.311$) and a greater reduction in average pain from baseline to follow-up ($r = 0.344$); however, these findings were not significant.



Table 1	Mean	SD	Min	Max
Age at 1 st infusion	47.8	15.7	23	73
Symptom duration at 1 st infusion (years)	9.0	7.0	1	27
Total number of infusions	79.0	42.1	34	188
			% of patients	
Race	White			50
	Other			43.75
	Asian			6.25
Ethnicity	Non Hispanic or Latino			81.25
	Hispanic or Latino			12.5
	Pt refuses or does not know			6.25

Conclusions

- The results of this pilot study suggest that long-term ketamine infusions at sub-anesthetic doses may be effective at significantly reducing observed signs of CRPS.
- This study did not reveal a significant change in subjective symptoms or pain reported by patients.
- The follow-up appointment was chosen to be as close as possible to one year but was not exact.
- Vitaly, this study was limited by an extremely small sample size at a single outpatient infusion center.
- Thus these conclusions should be viewed as suggestions to direct further research rather than as broadly generalizable findings.

Future Directions

- Further studies are needed with a larger sample size and across multiple treatment centers to determine whether ketamine is an effective therapeutic modality for CRPS.
- Considerations should include the significant financial and time costs associated with long-term ketamine treatment and the need to achieve patient-perceived improvement in symptoms.