Comparative Effectiveness of Intravenous Ketamine and Intranasal Esketamine in Real-World Setting Among Patient's With Treatment Refractory Depression

Balwinder Singh MD MS,[1] Simon Kung MD,[1] Kathryn M. Schak MD,[1]
William V. Bobo MD MPH,[2] Mark A. Frye MD[1] Jennifer L. Vande Voort MD,[1]
Department of Psychiatry & Psychology; Mayo Clinic, [1]Rochester, Minnesota, and [2]Jacksonville, Florida, USA

Background

- Ketamine, an N methyl-D-aspartate receptor antagonist, has been "repurposed" as a rapid-acting antidepressant for treatment-resistant depression (TRD).
- The s-enantiomer of ketamine, "esketamine," was FDA approved for TRD and depressive symptoms in adults with major depressive disorder with suicidal ideations/behaviors. Intravenous (IV) ketamine, although financially less expensive, is often not covered by insurance; and intranasal (IN) esketamine, although covered by insurance can be expensive.
- There is a paucity of literature on efficacy data comparing subanesthetic IV ketamine and IN esketamine for TRD in a real-world scenario. Thus, we conducted this study comparing the efficacy and the number of treatments required to achieve remission/response with repeated use of subanesthetic IV ketamine vs IN esketamine among TRD patients.

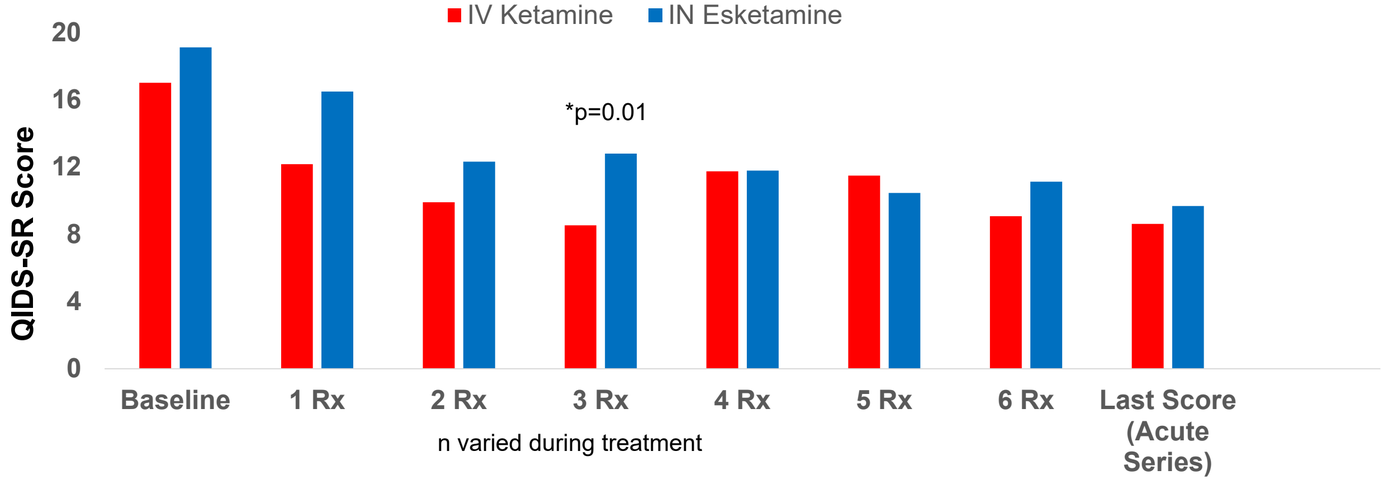
Methods

- Design: Observational study
- Eligibility: Adults (18-65 yrs) with TRD who provided consent and had received up to 6 IV ketamine infusions (0.5 mg/kg, infused over 40 minutes) or up to 8 IN esketamine (56/84 mg) treatments for TRD at the Mayo Clinic Depression Center.
- Depression symptoms were measured utilizing the self-report 16-Item Quick Inventory of Depressive Symptomatology (QIDS-SR) scale before and 24 hours after ketamine/esketamine treatment.
- Remission and response defined as QIDS-SR score ≤5 and ≥50% change in QIDS-SR 16 score, respectively. Number of treatments to remission/response were calculated.
- Continuous variables reported as means ±SD and categorical variables as counts and percentages.
- The unpaired Student's-t test or Mann-Whitney U test are used to compare continuous variables. Chi-square and Fisher's exact tests were used to compare categorical variables.

Results

- N=63 (60 MDD, 3 Bipolar disorder)
- Mean age 47.0±12.1 years; 65% Female
- 75% IV Ketamine (n=47); 25% IN esketamine (n=16)
- Baseline mean±SD QIDS-SR score 17.6 ±3.7
  - Mean (SE) change in QIDS-SR 16 score at end of acute phase -8.7±0.7 (p<0.001)
- Remission rate 36.5%
- Response rate 55.6%
- The mean number of treatments received to achieve response (2.5±1.6 vs 4.4±2.1) and remission (2.4±1.3 vs 6.3±2.4) were ***significantly lower among patients who received IV ketamine*** vs IN esketamine (p=0.008).
- Both treatments were well tolerated by most patients.

Intravenous Ketamine vs Intranasal Esketamine



	Intravenous Ketamine n=47	Intranasal Esketamine n=16	P-value
Age, mean (SD)	45.83 (11.62)	50.46 (13.04)	0.19
Female	33 (70.2%)	8 (50.0%)	0.15
Baseline QIDS-SR, mean (SD)	17.02 (4.05)	19.13 (1.82)	0.05
Post-1st treatment, mean (SD)	13.18 (5.65)	16.50 (4.72)	0.06
Post-2nd treatment, mean (SD)	9.91 (5.72)	12.33 (4.89)	0.20
Post-3rd treatment, mean (SD)	8.54 (5.58)	12.80 (4.41)	0.01
Acute Phase, mean difference (SE)	-8.40 (0.84)	-9.44 (1.11)	0.52
Response rate	26 (55.3%)	9 (56.2%)	0.95
Remission	19 (40.4%)	4 (25%)	0.27

Intravenous Ketamine.
0.5 mg/kg, 40-100 min 3x//week, up to 6 infusions.

Intranasal Esketamine.
Weeks 1-4: Administer 2x/week, day 1 starting dose 56 mg; subsequent doses 56 mg or 84 mg.

Limitations

- Observational study design
- Small sample size

Conclusions

- Intravenous ketamine and intranasal esketamine showed similar response/ remission in TRD patients.
- The number of treatments required to achieve response/ remission was significantly lower with IV ketamine vs IN esketamine.
- These findings need to be investigated in a randomized control trial comparing these two treatment interventions.

References

1. Vande Voort JL, Morgan RJ, Kung S, et al. Continuation phase intravenous ketamine in adults with treatment-resistant depression. J Affect Disord. 2016;206:300-304.
2. Singh B, Bobo WV, Rasmussen KG, et al. The association between body mass index and remission rates in patients with treatment-resistant depression who received intravenous ketamine. J Clin Psychiatry. 2019;80(6):19l12852.
3. Joseph B, Parsaik AK, Ahmed AT, Erwin PJ, Singh B. A systematic review on the efficacy of intravenous racemic ketamine for bipolar depression. J Clin Psychopharmacol. 2021;41(1):71-75.