Comparative Effectiveness of Intravenous Ketamine and Intranasal Esketamine in Real-World Setting Among Patients with Treatment Refractory Depression

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Abstract
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/IN esketamine among TRD patients.

Methods. This was an observational study where we included adults (≥18 years) with TRD who provided consent and had received up to 40 minutes) or up to 8 intranasal (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 were defined as QIDS-SR 16 score ≤5 and ≥50% change in QIDS-SR 16, respectively. Continuous variables are reported as means ± SD and categorical variables as counts and percentages. The Wilcoxon rank-sum test was used to compare continuous variables. Chi-square and Fisher’s exact tests were used to compare categorical variables. The number of treatments to remission/response was calculated.

Results. Sixty-three adults with TRD, middle-aged (47.0 ± 12.1 years), predominantly female (65%), of which 76% (n = 48) and 24% (n = 15) received IV ketamine and IN esketamine, respectively. Mean (SE) change in QIDS-SR 16 score was −8.7 ± 0.7 (P < .001), a significant reduction (improvement) from baseline (mean ± SD = 17.6 ± 3.7). Overall remission and response rates were 36.5% and 55.6%, respectively in the acute phase. Response (56.3% vs 53.3%) and remission rates (39.6% vs 26.7%) were similar among patients who received IV ketamine or IN esketamine, respectively (P > .05). The mean number of treatments received to achieve response (2.5 ± 1.6 vs 4.6 ± 2.1) and remission (2.4 ± 1.3 vs 6.3 ± 2.4) were significantly lower among patients who received IV ketamine compared to IN esketamine (P < .005). Most patients tolerated both treatments well.

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

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Opioid Prescription Dispensing Patterns in Patients with Bipolar Disorder: Real-World Evidence from the IBM Market Scan Research Databases

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Abstract
Objective. Prescription opioid dispensing patterns over time were assessed for individuals with bipolar disorder (BD) vs matched controls.

103 and glucose) and the lack of bacterial growth on gram stain. Inasmuch, antibiotic therapy was not initiated. Empiric acyclovir 1000 mg IV every 8 hours was initiated as viral meningitis had not been eliminated, due to the lack of viral meningeal PCR testing. By HD-3, the CSF culture resulted without growth and the patient was alert and oriented. By HD-4 the patient was discharged, having received 6 doses of IV acyclovir, with 7 more days of oral therapy.

Discussion. In 2018, McDonald et al documented the first case of probable levetiracetam-related antiepileptic induced meningitis (AEIM). The mainstay of treatment is discontinuing the offending agent. Resolution of symptoms is typically 2 to 3 days after drug discontinuation as seen in this patient case report. Symptomatic resolution within days of stopping the suspected offending drug has been observed in all reported cases of AEIM where 1 to 2 weeks is generally seen with viral meningitis. Applying the Naranjo Scale yields a score of 4, which indicates possible levetiracetam-induced meningitis in this adult patient. Providers should be cognizant when prescribing antiepileptics to assess and monitor for aseptic meningitis that may appear with atypical symptoms.

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neurosyphilis. Bacterial meningitis was ruled out based on the CSF analysis (WBC 144 × 103 and glucose) and the lack of bacterial growth on gram stain. Inasmuch, antibiotic therapy was not initiated. Empiric acyclovir 1000 mg IV every 8 hours was initiated as viral meningitis had not been eliminated, due to the lack of viral meningeal PCR testing. By HD-3, the CSF culture resulted without growth and the patient was alert and oriented. By HD-4 the patient was discharged, having received 6 doses of IV acyclovir, with 7 more days of oral therapy.

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