Treatment With (Es)ketamine in Catatonia:

A Systematic Review of Case Reports

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Catatonia remains a subject of ongoing debate, whether it represents a purely motoric syndrome, a separate distinct neuropsychiatric entity, or a symptom cluster within broader psychiatric conditions, characterized by features such as stupor, mutism, and negativism. The pathophysiology remains poorly understood, but multiple neurotransmitter systems seem to be involved in catatonia, including γ-aminobutyric acid (GABA) and glutamate.[1] First-line treatment is the $GABA_A$ agonist lorazepam, with response rates varying between 66% and 100%, and second-line treatment is electroconvulsive therapy (ECT).[2] Patients nonresponsive to treatment remain challenging. Recent evidence suggests that *N*-methyl-D-aspartate (NMDA) receptor antagonists, such as (es)ketamine, may offer benefit. We conducted a systematic review to evaluate the efficacy and safety of (es)ketamine for catatonia.

Methods

We searched 14 databases (eg, PubMed) through February 26, 2025, using terms related to "ketamine" and "catatonia." All abstracts and titles were independently screened by 2 authors (P.B.v.d.M. and S.V.), who also independently reviewed the full-text manuscripts for inclusion in the systematic review when deemed relevant. Inclusion criteria required adults (≥18 years); diagnosed with catatonia (using *Diagnostic and Statistical Manual of Mental Disorders* [*DSM*] or *International Classification of Diseases* [*ICD*] criteria or validated rating scales); treated with racemic ketamine, arketamine, or esketamine; an outcome assessing severity of catatonia; and manuscript language of English, Spanish, Portuguese, Dutch, German, or French. Nonhuman studies, reviews, and reports on anesthetic/recreational ketamine use were excluded. Quality assessment of case reports was done with the Joanna Briggs Institute critical appraisal checklist consisting of 8 aspects.

Results

A total of 998 unique records were identified, of which 24 full-text articles were screened, and 9 articles reporting 10 unique patient cases were included. Patient characteristics are shown in Table 1. Most patients were female (n = 9), were aged 23–81 years, and had a mood disorder, most commonly major depressive disorder (n = 5). Catatonic symptoms frequently included mutism (n = 7), stupor (n = 7), and withdrawal (n = 8). Most patients had failed lorazepam treatment (n = 6), while ECT was attempted in only 3 patients.

Interventions varied: 9 patients received intravenous, sublingual, or intramuscular racemic ketamine (10–40 mg), while 2 received intranasal esketamine (56–84 mg). Symptom improvement was observed in all patients, often within hours to days after administration. In 6 patients, the Bush–Francis Catatonia Rating Scale was used: 4 patients (of 6) achieved response (≥50% symptom reduction) within 1 week; 1 in the second week; and 1 at discharge. Remission (no symptoms of catatonia) was achieved in 2 patients (of 6) within 2 weeks, and in 2 later during follow-up. Most aspects were relatively well reported by the authors (eg, demographics, patient's history), except for diagnostic tests and adverse events, which were reported on by less than half of the authors.

Discussion

These findings align with earlier work on NMDA antagonists (eg, amantadine) as third-line options after lorazepam and ECT or as second-line options, especially if ECT is unavailable or severe somatic complications will complicate ECT.[12] Notably, (es)ketamine offers diverse administration routes, useful in severely withdrawn or stuporous patients unable to take oral medications. Given its rapid efficacy and tolerability, especially in major depressive disorder, the most common underlying diagnosis, (es)ketamine may offer a dual therapeutic benefit. Importantly, concerns that (es)ketamine may exacerbate mania or psychosis in bipolar or schizophrenia spectrum patients were not supported in a recent systematic review and cohort studies.[13–15] This suggests that use of (es)ketamine may be safe in catatonia patients nonresponsive to lorazepam and/or ECT. Nevertheless, limitations include variable dosing, heterogeneity in catatonia severity and etiology, and potential publication bias. While randomized controlled trials are unlikely due to catatonia's rarity, systematic synthesis of case reports remains vital in guiding treatment for this life-threatening condition.

Table 1.

Studies Evaluating the Efficacy of (Es)ketamine in Catatonia

Reference and country	Age, sex, and diagnosis	Previous treatments for catatonia during current episode	Intervention	Outcome after initiation of (es)ketamine	Adverse events	Reason (es)ketamine was administered
Gómez-Revuelta et al,[3] Santander, Spain	55 y, female, major depressive disorder	Intravenous diazepam 60 mg/day; ECT 12 sessions (bilateral)	Intranasal esketamine 56 mg 3 times weekly in weeks 1 and 2, 84 mg 3 times weekly in week 3, then 84 mg once a week in weeks 4–7, then 84 mg once in 2 weeks in weeks 8–78	BFRS scores: response in week 2 (score decreased from 20 to 5); remission in weeks 3–78	Mild concentration and memory problems	A month prior to development of catatonia, the patient discontinued oral antidepressant medications due to adverse events. Oral route of administration was not an option; therefore, intranasal esketamine was started
Laurin et al,[4] Nantes, France	65 y, female, major depressive disorder with psychotic symptoms	None	Intravenous ketamine 17 mg per session once weekly in weeks 1 and 2, then 19 mg once weekly in weeks 3–8, then 19 mg 3 times in 2 weeks in week 9 to end of treatment (not reported when)	BFRS scores: response in week 1 (score decreased from 38 to 1); remission in week 8 to end of treatment	No adverse effects reported	Limited access to ECT due to COVID-19 pandemic
Trejos Orozco et al,[5] Pereira, Colombia	63 y, female, major depressive disorder with psychotic symptoms	Lorazepam (dosage not reported)	Intravenous ketamine 0.5 mg/kg (dosage not reported)	Improved in week 1 (no scores reported, "no catatonic features")	No adverse effects reported	ECT was not possible due to the patient's cardiovascular disease and anticoagulation medicine
Kobayashi et al,[6] Irvine, US	44 y, female, major depressive disorder	Intravenous lorazepam 2 mg/day	Intravenous ketamine 0.2 mg/kg (10 mg)	Improved in weeks 1–12, relapse of catatonia in week 12	No adverse effects reported	She did not show improvement on lorazepam and had been hospitalized many times with similar presentations; therefore, the treatment team decided to initiate ketamine
Olazabal Eizaguirre et al,[7] Bilbao, Spain	56 y, female, major depressive disorder	Benzodiazepines (not further specified), ECT 39 sessions (not reported uni- or bilateral)	Intravenous ketamine 0.5 mg/kg (dosage not reported) per session ~3 times weekly in weeks 1–4	BFRS scores: Response (score decreased from 25 to 9) at discharge (number of weeks not reported)	Nausea, vomiting, and dissociation	She was refractory to ECT, and other treatment options were considered; ketamine was eventually chosen
Gregor and Zheng,[8] Morgantown, US	63 y, female, schizoaffective disorder	Lorazepam and diazepam (dosage not reported), diazepam (dosage not reported)	Sublingual ketamine and after 1–2 mo switched to esketamine, which was later changed to both ketamine and esketamine (dosage not reported). During this time, paliperidone was changed to lumateperone	BFRS scores: response in week 1 (score decreased from 12 to 2), but was thereafter readmitted in the hospital due to relapse of catatonia, which showed improvement in 11 days and later she was clinically stable (undefined)	No adverse effects reported	Not reported
Sarma et al,[9] Gold Coast, Australia	81 y, female, bipolar disorder	Lorazepam 3 mg/day	Intravenous ketamine 0.5 mg/kg (40 mg) per session twice weekly in weeks 1–6	BFRS scores: response in week 1 (score decreased from 18 to 3); remission in weeks 2–26	No adverse effects reported	As an alternative to ECT treatment with ketamine was commenced as she was deemed high risk for ECT due to severe cardiomyopathy

(continued)

Table 1 (continued).

Reference and country	Age, sex, and diagnosis	Previous treatments for catatonia during current episode	Intervention	Outcome after initiation of (es)ketamine	Adverse events	Reason (es)ketamine was administered
Sarma et al,[9] Gold Coast, Australia	76 years, female, bipolar disorder	Lorazepam (dosage not reported), ECT 1 session (not reported uni- or bilateral)	Intravenous ketamine 0.5 mg/kg (dosage not reported) per session twice weekly in weeks 1 and 2	BFRS scores: response in week 1 (score decreased from 9 to 1); remission in weeks 2–52	Dissociative symptoms	Due to her pulmonary history and fluctuating oxygen saturation, it was unlikely that treating the pulmonary embolism would provide a timely response to restart ECT. Ketamine was started because treating the patient's catatonic depressive symptoms was priority
Iserson and Durga,[10] Tucson, US	23 y, male, no diagnosis	None	Intravenous ketamine 0.17 mg/kg (12.5 mg) once	Improved in week 1–3 (no scores reported "resolved catatonia")	No adverse effects reported	Catatonia treatment lorazepam was not available in the resource-limited setting
Siddiqui,[11] Houston, US	77 y, female, schizophrenia	Lorazepam 8 mg/day	Intravenous ketamine 0.5 mg/kg (30 mg) once	Improved in week 1 (no scores reported "started communicating verbally with resolution of immobility") to 8	No adverse effects reported	Limited access to ECT due to COVID-19 pandemic

Abbreviations: BFRS = Bush–Francis Rating Scale, ECT = electroconvulsive therapy.

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