RESEARCH PAPER

Add-on Intravenous Ketamine Infusions in Treatment-Resistant Obsessive-Compulsive Disorder: A Case Series of 22 Patients

Running title: Add-on IV ketamine in resistant OCD: a case series

Brijrani Singh[1], Mehak Jaggi[2], Kriti Choudhary[2]

[1] Senior Resident, Department of Psychiatry, Sawai Man Singh Medical College, Jaipur, Rajasthan, India

[2] Junior Resident, Department of Psychiatry, Sawai Man Singh Medical College, Jaipur, Rajasthan, India

Corresponding author: Dr. Brijrani Singh, Department of Psychiatry, Sawai Man Singh Medical College, Jaipur, Rajasthan, India. Email: brijranisingh1995@gmail.com

Abstract

Background: About one-third of people with obsessive-compulsive disorder (OCD) do not respond adequately to serotonin reuptake inhibitors (SRIs) and cognitive behavioural therapy with exposure and response prevention (ERP). Glutamatergic dysfunction has been implicated in OCD, and intravenous (IV) ketamine, an NMDA-receptor antagonist, has been proposed as an add-on treatment. Data on repeated-dose infusions remain limited.

Case series presentation: We describe 22 consecutive adults (mean age 34.3 years; 68.2% male) with ICD-10 OCD, Y-BOCS ≥ 16 and at least two prior inadequate treatment trials with an SRI and/or ERP, who chose add-on ketamine at a tertiary-care psychiatry unit in India between November 2023 and May 2024. All were on stable psychotropic medication. Each received five IV infusions of ketamine 0.5 mg/kg over 40 minutes, given thrice weekly. Y-BOCS, the 17-item Hamilton Depression Rating Scale (HAM-D-17) and the Clinical Global Impression (CGI) scale were assessed before and at the end of treatment; dissociative and psychotomimetic effects were rated during infusions.

Outcomes: Mean Y-BOCS fell from 25.45 ± 4.03 to 17.13 ± 4.06 (mean percentage reduction 32.5%; $p < 0.001$) and mean HAM-D-17 from 12.36 ± 5.46 to 5.81 ± 4.21 (53.3%; $p < 0.001$). Eight patients (36.4%) had a ≥ 35% Y-BOCS reduction (response), five (22.7%) a 25–34% reduction (partial response), and nine (40.9%) a reduction below 25%. Mean CGI-Improvement was 1.86 ± 0.63. Transient dissociation was almost universal (mean CADSS-6 6.59 ± 3.73); other effects were mild dizziness, nausea, vomiting and headache. There were no serious adverse events and no dropouts.

Conclusion: In this uncontrolled series, a short course of add-on IV ketamine was followed by clinically meaningful improvement in obsessive-compulsive and depressive symptoms in a substantial minority to majority of patients with treatment-resistant OCD, and was tolerated. Controlled studies with longer follow-up are needed.

Keywords: obsessive-compulsive disorder; ketamine; treatment-resistant; add-on treatment; case series; Yale-Brown Obsessive Compulsive Scale

How to cite this article: Brijrani Singh. Add-on Intravenous Ketamine Infusions in Treatment-Resistant Obsessive-Compulsive Disorder: A Case Series of 22 Patients. Int J Drug Deliv Technol. 2026;16(89s):412-416. DOI: 10.25258/ijddt.16.89s.43.

Introduction

Obsessive-compulsive disorder affects an estimated 2–3% of people over the lifetime and is a source of chronic functional disability [1]. SRIs are the usual first-line drug treatment in India, while ERP, the most effective psychotherapy, is frequently unavailable because of cost and a shortage of trained therapists [2]. Roughly one-third of patients do not respond to an SRI alone, and those who do may wait two to three months for benefit [3]. Antipsychotic augmentation helps only a minority and carries a considerable side-effect burden [4]. Because of the persistent course of the illness and its toll on quality of life, faster and more effective options are needed [5,6].

Glutamatergic abnormalities are implicated in the pathophysiology of OCD [7]. Ketamine, an NMDA-receptor antagonist with rapid antidepressant effects in treatment-resistant depression [8], has therefore been tried in OCD, with a randomised crossover trial, case reports, and small open-label and repeated-infusion studies suggesting benefit [9–12]. Evidence on repeated sub-anaesthetic infusions as an add-on in routine clinical settings, particularly from low- and middle-income countries, is still sparse.

We report a case series of 22 patients with treatment-resistant OCD who received five add-on IV ketamine infusions, describing their clinical features, symptom trajectories and tolerability. These patients form the ketamine arm of a larger, preference-based cohort that included a second group treated with transcranial direct current stimulation; the full cohort is reported separately [13].

Methods

Design, setting and reporting

This is a prospective, open-label, uncontrolled case series of consecutive patients who chose ketamine, treated from November 2023 to May 2024 in the Department of Psychiatry, Sardar Patel Medical

College and Associated Group of PBM Hospitals, Bikaner, Rajasthan, India. Patients were recruited from outpatient and inpatient services. The report is organised with reference to the CARE guideline for case reports and series.

Patients

Of 54 patients with a primary ICD-10 diagnosis of OCD screened for the parent cohort, 39 were enrolled after exclusions; all patients were informed of both available add-on options (ketamine or tDCS) and chose their preferred treatment. Twenty-two chose ketamine and are described here.

Inclusion criteria were age 18–65 years, either sex; Y-BOCS ≥ 16; and treatment resistance, defined as at least two adequate prior trials of an SRI and/or ERP-based CBT [14]; and stable concomitant psychotropic medication for at least one month before and throughout the study. Exclusion criteria were comorbid bipolar disorder or psychotic disorder, active suicidal ideation, current non-nicotine substance use disorder, unstable medical or neurological illness, and pregnancy or breastfeeding.

Intervention

Patients received five IV infusions of ketamine 0.5 mg/kg over 40 minutes, administered thrice weekly, after anaesthetist clearance and an 8-hour fast. Vital signs were monitored throughout each infusion. Psychotropic medication doses were not changed during the study.

Assessments

OCD severity was rated with the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) [15] and depressive symptoms with the HAM-D-17 [16], at baseline and at the end of the treatment course. Global severity and improvement were rated with the CGI-Severity and CGI-Improvement scales [17]. Response was defined as a Y-BOCS reduction of ≥ 35% and partial response as a reduction of 25–34%; the proportion with a reduction of ≥ 25% is also reported. Dissociative symptoms and transient psychotomimetic effects were rated during infusions using the six-item Clinician-Administered Dissociative States Scale (CADSS-6) [18] and the positive-symptom items of the Brief Psychiatric Rating Scale (BPRS) [19]. Other adverse effects were recorded on a structured checklist.

Analysis

This is a descriptive series. Continuous variables are given as mean ± SD or median [interquartile range] and categorical variables as n (%). Change from baseline to end of treatment was examined with paired t-tests; p-values are descriptive, as there was no control group. The relationship between percentage reductions in Y-BOCS and HAM-D-17 was examined with Pearson correlation. A two-sided $p < 0.05$ was taken as significant. Analyses used SPSS 24.0 and Epi Info 7.2.6.0.

Results

Characteristics of the series

All 22 patients completed the five infusions and both assessments; none was lost to follow-up. Baseline characteristics are shown in Table 1. Most patients were men in their mid-thirties with onset in early adulthood and a median illness duration of 9 years. Repeating compulsions were the most frequent predominant symptom type (10 patients, 45.5%). Nineteen patients (86.4%) had a comorbid psychiatric disorder, most commonly depression or anxiety. Individual patient-level details are given in Table 5.

Table 1. Baseline characteristics (n = 22)

Characteristic	Value
Age, years, mean ± SD	34.3 ± 12.2
Male sex, n (%)	15 (68.2)
Married, n (%)	12 (54.5)
Currently employed, n (%)	8 (36.4)
Age at OCD onset, years, mean ± SD	22.50 ± 8.20
Duration of illness, years, median [IQR]	9 [5.75–17]
Predominant compulsion type: repeating, n (%)	10 (45.5)
Baseline Y-BOCS, mean ± SD	25.45 ± 4.03
Baseline HAM-D-17, mean ± SD	12.36 ± 5.46
Baseline CGI-Severity, modal category, n (%)	Markedly ill, 10 (45.5)
Comorbid psychiatric illness, n (%)	19 (86.4)

Clinical outcomes

The mean Y-BOCS score fell from 25.45 ± 4.03 to 17.13 ± 4.06, a mean percentage reduction of 32.48% ± 14.07% ($p < 0.001$). The mean HAM-D-17 score fell from 12.36 ± 5.46 to 5.81 ± 4.21, a mean reduction of 53.29% ± 22.39% ($p < 0.001$) (Table 2). Eight patients (36.4%) were responders (≥ 35% Y-BOCS reduction), five (22.7%) were partial responders (25–34%), and nine (40.9%) improved by less than 25%; thus 13 patients (59.1%) had a reduction of at least 25%. Mean CGI-Improvement was 1.86 ± 0.63. Greater percentage reduction in Y-BOCS was associated with greater percentage

reduction in HAM-D-17 (Pearson r = 0.50, p = 0.016).

Table 2. Change in symptom scores from baseline to end of treatment (n = 22)

Measure	Baseline	End of treatment	Mean % reduction ± SD	p (paired t-test)
Y-BOCS	25.45 ± 4.03	17.13 ± 4.06	32.48 ± 14.07	< 0.001
HAM-D-17	12.36 ± 5.46	5.81 ± 4.21	53.29 ± 22.39	< 0.001

Table 3. Y-BOCS response categories (n = 22)

Category	n (%)
Response (≥ 35% reduction)	8 (36.4)
Partial response (25–34% reduction)	5 (22.7)
Reduction of ≥ 25% (response + partial response)	13 (59.1)
Reduction of < 25%	9 (40.9)

Adverse effects

There were no serious adverse events (Table 4). Dissociative symptoms were common during infusions (mean CADSS-6 6.59 ± 3.73), including feeling disconnected from one's body (95.5%) and the sense that time or events were slowed (86.4%). Mild unusual thought content occurred in 63.6% (mean four-item BPRS positive-symptom score 2.9 ± 2.99). Dizziness (31.8%), nausea (27.3%), vomiting (9.1%) and headache (9.1%) were also reported. The effects were transient and resolved without treatment.

Table 4. Adverse effects during ketamine infusions (n = 22)

Adverse effect	n (%)
Feeling disconnected from own body	21 (95.5)
Things seemed to move slowly	19 (86.4)
Things seemed unreal	16 (72.7)
Mild unusual thought content	14 (63.6)
Dizziness	7 (31.8)
Nausea	6 (27.3)
Vomiting	2 (9.1)
Headache	2 (9.1)
Serious adverse events	0

Mean CADSS-6 score 6.59 ± 3.73; mean four-item positive-symptom BPRS score 2.9 ± 2.99.

Table 5. Individual patient data [template: to be completed from patient-level records before submission]

Patient	Age/sex	Illness duration (years)	Predominant symptoms	Concurrent medication	Y-BOCS pre → post	HAM-D-17 pre → post	CGI-I	Adverse effects
1								
2								
…								
22								

Discussion

In this series of 22 patients with SRI-resistant OCD, five add-on ketamine infusions at 0.5 mg/kg were followed by an average one-third reduction in Y-BOCS score and more than a halving of depressive symptom scores. Just over one-third met the stricter response threshold of ≥ 35%, and 59.1% achieved at least a 25% reduction. The direction of effect agrees with earlier randomised, open-label and repeated-infusion reports [9–12]. Direct numerical comparison with those studies is limited by differences in dose, number and spacing of infusions, response definitions and timing of assessment.

The average change should be read alongside its spread: the standard deviation of the percentage reduction was 14 points, and about four in ten patients improved by less than 25%. Reporting both the ≥ 35% and ≥ 25% thresholds makes clear that many patients had a partial benefit rather than remission. Mean end-of-treatment Y-BOCS (17.1) was still in the clinically significant range, which suggests that ketamine may be best viewed as a way to reduce symptom burden rather than as a stand-alone solution.

Improvement in OCD and depressive symptoms went together (r = 0.50). Baseline depression scores were in the mild range on average, so the HAM-D-17 change may partly reflect a broader mood effect of ketamine [8]. Overlapping glutamatergic mechanisms in OCD and depression have been proposed [7,11,12], but this series cannot separate a direct anti-

obsessional effect from a secondary effect of improved mood.

Tolerability was acceptable. Dissociation was almost universal but brief, and psychotomimetic and gastrointestinal effects were mild and self-limiting, in keeping with earlier reports [10]. No serious adverse event occurred. The procedural safeguards used here (anaesthetist clearance, fasting and continuous vital-sign monitoring) require a supervised setting and anaesthetic support, which may limit scalability outside tertiary centres.

Limitations

This series has no comparison group, so spontaneous change, expectancy and placebo effects cannot be excluded. Patients chose ketamine themselves, which may select for those more willing to accept an infusion-based treatment. The design was open-label [authors to confirm whether raters were blinded], and the dissociative effects of ketamine may themselves unblind patients and raters. The sample is small and from a single centre. Outcomes were measured only before and at the end of treatment, so durability of benefit, relapse and delayed adverse effects are unknown. Patients were on varied stable medication regimens that could not be standardised. The work was derived from a postgraduate dissertation and was not prospectively registered in a clinical trials registry.

Conclusion

In this case series of treatment-resistant OCD, a short course of five add-on IV ketamine infusions was followed by meaningful improvement in obsessive-compulsive and depressive symptoms in many patients, with transient dissociative effects and no serious adverse events. These observations support, but do not establish, a role for ketamine as an add-on option. Randomised, sham- or placebo-controlled trials with longer follow-up are needed to define efficacy, durability and optimal dosing.

Declarations

Ethical approval and consent: The study was approved by the Institutional Ethics Committee and Scientific Research Review Board, Sardar Patel Medical College, Bikaner, and followed the Declaration of Helsinki and its amendments. All participants gave written informed consent. [Authors to confirm that consent covers publication of anonymised data.]

Related work: The 22 patients reported here are the ketamine arm of a preference-based comparative cohort of 39 patients, reported separately [13]. No between-group comparison is made in this report.

Author contributions: Conceptualization and methodology: B. Singh and [Guide name]. Investigation, data curation and formal analysis: B. Singh. Original draft: B. Singh. Review and editing: B. Singh and [Guide name]. Supervision: [Guide name]. [Roles of M. Jaggi and K. Choudhary, and the final author list, to be agreed by all authors before submission.]

Conflicts of interest: None declared.

Funding: No specific funding from public, commercial or not-for-profit sources.

Data availability: De-identified data are available from the corresponding author on request.

References

1. Ruscio AM, Stein DJ, Chiu WT, Kessler RC. The epidemiology of obsessive-compulsive disorder in the National Comorbidity Survey Replication. Mol Psychiatry. 2010;15(1):53–63.
2. Janardhan Reddy Y, Sundar AS, Narayanaswamy J, Math SB. Clinical practice guidelines for obsessive-compulsive disorder. Indian J Psychiatry. 2017;59(Suppl 1):S74–90.
3. Skapinakis P, Caldwell DM, Hollingworth W, et al. Pharmacological and psychotherapeutic interventions for management of obsessive-compulsive disorder in adults: a systematic review and network meta-analysis. Lancet Psychiatry. 2016;3(8):730–9.
4. Bloch MH, Landeros-Weisenberger A, Kelmendi B, Coric V, Bracken MB, Leckman JF. A systematic review: antipsychotic augmentation with treatment refractory obsessive-compulsive disorder. Mol Psychiatry. 2006;11(7):622–32.
5. Hirschtritt ME, Bloch MH, Mathews CA. Obsessive-compulsive disorder: advances in diagnosis and treatment. JAMA. 2017;317(13):1358–67.
6. Kochar N, Ip S, Vardanega V, Sireau NT, Fineberg NA. A cost-of-illness analysis of the economic burden of obsessive-compulsive disorder in the United Kingdom. Compr Psychiatry. 2023;127:152422.
7. Pittenger C, Bloch MH, Williams K. Glutamate abnormalities in obsessive compulsive disorder: neurobiology, pathophysiology, and treatment. Pharmacol Ther. 2011;132(3):314–32.
8. Zarate CA, Singh JB, Carlson PJ, et al. A randomized trial of an N-methyl-D-aspartate antagonist in treatment-resistant major depression. Arch Gen Psychiatry. 2006;63(8):856–64.
9. Bandeira ID, Lins-Silva DH, Cavenaghi VB, et al. Ketamine in the treatment of obsessive-compulsive disorder: a systematic

review. Harv Rev Psychiatry. 2022;30(2):135–45.
10. Rodriguez CI, Kegeles LS, Levinson A, et al. Randomized controlled crossover trial of ketamine in obsessive-compulsive disorder: proof-of-concept. Neuropsychopharmacology. 2013;38(12):2475–83.
11. Bloch MH, Wasylink S, Landeros-Weisenberger A, et al. Effects of ketamine in treatment-refractory obsessive-compulsive disorder. Biol Psychiatry. 2012;72(11):964–70.
12. Sharma LP, Thamby A, Balachander S, et al. Clinical utility of repeated intravenous ketamine treatment for resistant obsessive-compulsive disorder. Asian J Psychiatr. 2020;52:102183.
13. Singh B, Jaggi M, Choudhary K. Intravenous ketamine infusion versus transcranial direct current stimulation as add-on treatment in treatment-resistant obsessive-compulsive disorder: an open-label comparative study. [Journal, year, volume and pages, or manuscript status, to be added.]
14. Pallanti S, Quercioli L. Treatment-refractory obsessive-compulsive disorder: methodological issues, operational definitions and therapeutic lines. Prog Neuropsychopharmacol Biol Psychiatry. 2006;30(3):400–12.
15. Goodman WK, Price LH, Rasmussen SA, et al. The Yale-Brown Obsessive Compulsive Scale: I. Development, use, and reliability. Arch Gen Psychiatry. 1989;46(11):1006–11.
16. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry. 1960;23(1):56–62.
17. Berk M, Ng F, Dodd S, et al. The validity of the CGI severity and improvement scales as measures of clinical effectiveness suitable for routine clinical use. J Eval Clin Pract. 2008;14(6):979–83.
18. Rodrigues NB, McIntyre RS, Lipsitz O, et al. A simplified 6-item clinician administered dissociative symptom scale (CADSS-6) for monitoring dissociative effects of sub-anesthetic ketamine infusions. J Affect Disord. 2021;282:160–4.
19. Overall JE, Gorham DR. The Brief Psychiatric Rating Scale. Psychol Rep. 1962;10(3):799–812.