STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN

A Prospective Observational Study of Suicidal Ideation, Dissociative Symptoms, and Treatment Response in Psychiatric Patients Receiving Electroconvulsive Therapy

NCT Number: Not yet assigned

Study Site: Pamukkale University Hospital, Department of Mental Health and Diseases

Principal Investigator: Res. Asst. Dr. Nurdan Sağbaş

Study Type: Non-Interventional, Prospective Observational Study

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1. Rationale and Aim of the Study

Major Depressive Disorder (MDD) is one of the most prevalent psychiatric disorders worldwide, affecting 16–20% of the population. According to DSM-5, MDD is diagnosed when at least five characteristic symptoms — including depressed mood, loss of interest or pleasure, sleep and appetite disturbances, psychomotor changes, fatigue, feelings of worthlessness, difficulty concentrating, and recurrent thoughts of death or suicide — persist for at least two weeks and cause significant functional impairment.

Conventional antidepressant treatments targeting serotonin, dopamine, and noradrenaline systems typically require several weeks to produce a clinical response. Despite multimodal treatment approaches, approximately one-third of patients fail to achieve functional recovery, meeting criteria for Treatment-Resistant Depression (TRD), defined as inadequate response to at least two adequate antidepressant trials from different classes.

Bipolar disorder is a chronic mood disorder characterized by manic, hypomanic, and depressive episodes, associated with significant disability, comorbidity, and elevated suicide risk. Bipolar depression accounts for the majority of illness burden and is the leading cause of long-term functional impairment across the bipolar spectrum.

Electroconvulsive Therapy (ECT) is an established and highly effective biological treatment for treatment-resistant depression and bipolar depression, in use since 1938. The choice of anesthetic agent during ECT has gained increasing attention, as it may influence both treatment efficacy and side effect profile. Ketamine, an NMDA receptor antagonist with rapid-onset antidepressant properties, and propofol, a short-acting sedative-hypnotic agent, are both used in ECT anesthesia. While some studies report superior antidepressant effects with ketamine compared to propofol, others have found no significant difference. The combination of ketamine and propofol (ketofol) has been proposed as a strategy to balance efficacy and tolerability.

This study aims to observationally evaluate the effects of ketamine+propofol versus propofol anesthesia on depression severity, suicidal ideation, and dissociative symptoms in patients receiving ECT for MDD or bipolar depression. Anesthetic agent selection will be made solely by the treating clinician; researchers will perform observational assessments only.

2. Study Design

Parameter	Details
Study Type	Non-interventional, prospective observational study
Study Model	Prospective cohort with two naturally assigned groups
Time Perspective	Prospective
Study Site	Pamukkale University Hospital, Department of Mental Health and Diseases
Study Duration	Approximately 2 years (following Ethics Committee approval)

Sample Size	65 patients (Group 1: 30; Group 2: 35)

3. Study Population

3.1 Inclusion Criteria

- Age 18–65 years
- Inpatient at Pamukkale University Hospital, Department of Mental Health and Diseases
- Diagnosis of Major Depressive Disorder or Bipolar Disorder, Depressive Episode, according to DSM-5 criteria
- Clinical indication for ECT treatment
- No contraindication to anesthesia
- Voluntary written informed consent

3.2 Exclusion Criteria

- Intellectual disability or cognitive disorder
- Active psychotic state
- History of neurological disease
- Active substance use disorder
- Illiteracy (inability to complete self-report scales)

4. Study Groups

Patients will be allocated to one of two groups based on the anesthetic agent selected by the treating clinician as part of routine clinical care. Researchers will not influence this decision.

Group	Anesthetic Protocol	n
Group 1	Ketamine + Propofol (Ketofol)	30
Group 2	Propofol alone	35

5. Assessment Schedule

All participants will be assessed at four time points using three validated clinical scales:

Time Point	Assessment
T0 – Baseline (before first ECT session)	MADRS, Beck Suicidal Ideation Scale, CADSS
T1 – After 1st ECT session	MADRS, Beck Suicidal Ideation Scale, CADSS
T2 – After 3rd ECT session	MADRS, Beck Suicidal Ideation Scale, CADSS

T3 – After final ECT session	MADRS, Beck Suicidal Ideation Scale, CADSS

6. Outcome Measures

6.1 Primary Outcome Measure

Change in Depression Severity (MADRS): Change from baseline in Montgomery–Åsberg Depression Rating Scale (MADRS) total score, measured at baseline, after the 1st, 3rd, and final ECT sessions.

6.2 Secondary Outcome Measures

Change in Suicidal Ideation (Beck Suicidal Ideation Scale): Change from baseline in Beck Suicidal Ideation Scale total score across all assessment time points.

Change in Dissociative Symptoms (CADSS): Change from baseline in Clinician-Administered Dissociative States Scale (CADSS) total score across all assessment time points.

7. Assessment Instruments

7.1 Montgomery–Åsberg Depression Rating Scale (MADRS)

A 10-item clinician-rated scale developed in 1979 to assess depression severity. Each item is scored 0–6; total score ranges from 0 to 60. Higher scores indicate greater severity. Widely used to measure treatment response in ECT and pharmacological studies. Turkish validity and reliability established by Yapıcı et al. (2003); Cronbach's alpha: 0.79–0.86.

7.2 Beck Suicidal Ideation Scale (BSI)

A 19-item self-report scale assessing the intensity of suicidal ideation, planning, and intent. Each item is rated 0–2; higher scores indicate greater suicidal ideation. Used to monitor changes in suicide risk during treatment. Turkish adaptation by Hisli-Şahin (1991); Cronbach's alpha: 0.87.

7.3 Clinician-Administered Dissociative States Scale (CADSS)

A 19-item clinician-administered scale evaluating dissociative symptoms across three domains: amnesia, depersonalization, and derealization. Each item is rated 0–4. Particularly used to assess ketamine-induced dissociative states. Turkish validity and reliability established by Sar and Ozturk (2016); Cronbach's alpha: 0.89.

8. Statistical Analysis Plan

8.1 General Approach

All statistical analyses will be performed using SPSS (version 25.0 or later) or an equivalent statistical software package. A two-tailed p-value of <0.05 will be considered statistically significant.

8.2 Descriptive Statistics

Continuous variables will be summarized as mean ± standard deviation (SD) or median (interquartile range), as appropriate. Categorical variables will be presented as frequencies and percentages. Normality of distribution will be assessed using the Shapiro-Wilk test.

8.3 Group Comparisons

- **Independent samples t-test** (or Mann-Whitney U test for non-normal distributions): For between-group comparisons of continuous variables at each time point.
- **Chi-square test** (or Fisher's exact test): For between-group comparisons of categorical variables.
- **Repeated measures ANOVA** (or Friedman test): To evaluate within-group changes in MADRS, BSI, and CADSS scores across the four assessment time points (T0–T3).
- **Mixed-model ANOVA**: To assess the interaction between group (ketamine+propofol vs. propofol) and time on outcome measures.

8.4 Regression Analysis

Logistic regression analysis will be used to identify predictors of treatment response (defined as ≥50% reduction in MADRS score from baseline). Covariates will include age, sex, diagnosis (MDD vs. bipolar depression), number of ECT sessions, and anesthetic agent group.

8.5 Missing Data

Missing data will be handled using last observation carried forward (LOCF) or multiple imputation methods, as appropriate. The extent of missing data will be reported.

8.6 Definitions

- **Treatment Response:** ≥50% reduction in baseline MADRS score
- **Partial Response:** 25–49% reduction in baseline MADRS score
- **Non-Response:** <25% reduction in baseline MADRS score
- **Remission:** MADRS total score ≤10

9. Ethical Considerations

This study will be conducted in accordance with the Declaration of Helsinki and applicable national regulations. Ethics Committee approval from Pamukkale University Non-Interventional Clinical Research Ethics Committee will be obtained prior to study initiation. Written informed consent will be obtained from all participants. Patient confidentiality will be maintained throughout the study; data will be anonymized for analysis and publication. Participation is entirely voluntary, and withdrawal at any time will not affect the participant's clinical care.

10. Expected Outcomes

This study is expected to provide prospective observational evidence on the differential effects of ketamine+propofol versus propofol anesthesia on depression severity, suicidal ideation, and dissociative symptoms in ECT-treated patients. Findings will contribute to the existing literature on anesthetic agent selection in ECT and may inform clinical decision-making in this patient population.

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