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Research Article

Depression Scores before and after Electrocompulsive Therapy with Propofol versus Ketamine Anesthesia: A Prospective Observational Study

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Abstract

Background: Major depressive disorder (MDD) is a severe condition marked by persistent sadness and functional impairment. While electrocompulsive therapy (ECT) is effective for treatment-resistant cases, the comparative effects of propofol and ketamine as anesthetic agents remain unclear. ***Objective***: To compare the effects of propofol and ketamine anesthesia on depression severity in patients undergoing ECT using HDRS scores at multiple time points. ***Methods***: In this prospective observational study, 50 patients with treatment-resistant depression were assigned to receive ECT with either propofol- or ketamine-based anesthesia. Depression severity was measured using HDRS at baseline, 1 week, 1 month, and 3 months post-treatment. Secondary outcomes included relapse rates and additional ECT sessions. ***Results***: Patients receiving ketamine showed significantly greater HDRS reductions at all follow-ups (p<0.05), fewer relapses, and less need for additional ECT sessions compared with those receiving propofol. However, ketamine was associated with higher blood pressure. ***Conclusions***: Ketamine was associated with more robust and sustained improvement in depression scores following ECT than propofol. Further studies are needed to confirm these findings and to investigate other anesthetic options.

Keywords: Electrocompulsive therapy, Ketamine, Propofol, Treatment resistant depression.

درجات الاكتئاب قبل وبعد العلاج الكهربائي القهري مع البروبوفول مقابل تخدير الكيتامين: دراسة رصدية مستقبلية

الخلاصة

الخلفية: اضطراب الاكتئاب الشديد (MDD) هو حالة شديدة تتميز بالحزن المستمر والضعف الوظيفي. في حين أن العلاج الكهربائي القهري (ECT) فعال في الحالات المقاومة للعلاج، فإن التأثيرات المقارنة للبروبوفول والكيتامين كعوامل تخدير لا تزال غير واضحة. **الهدف**: مقارنة آثار تخدير البروبوفول والكيتامين على شدة الاكتئاب لدى المرضى الذين يخضعون للصدمات الكهربائية باستخدام درجات HDRS في نقاط زمنية متعددة. **الطرائق**: في هذه الدراسة القائمة على الملاحظة المستقبلية، تم تعيين 50 مريضا يعانون من الاكتئاب المقاوم للعلاج لتلقي العلاج بالصدمات الكهربائية إما مع التخدير القائم على البروبوفول أو الكيتامين. تم قياس شدة الاكتئاب باستخدام HDRS في خط الأساس، أسبوع واحد، شهر واحد، و 3 أشهر بعد العلاج. تضمنت النتائج الثانوية معدلات الانتكاس وجلسات العلاج بالصدمات الكهربائية الإضافية. **النتائج**: أظهر المرضى الذين يتلقون الكيتامين انخفاضا أكبر بكثير في HDRS في جميع المتابعات (p<0.05)، وانتكاسات أقل، وحاجة أقل لجلسات العلاج بالصدمات الكهربائية مقارنة بأولئك الذين تلقوا البروبوفول. ومع ذلك، ارتبط الكيتامين بارتفاع ضغط الدم. **الاستنتاجات**: ارتبط الكيتامين بتحسن أكثر قوة واستدامة في درجات الاكتئاب بعد العلاج بالصدمات الكهربائية مقارنة بالبروبوفول. هناك حاجة إلى مزيد من الدراسات لتأكيد هذه النتائج والتحقيق في خيارات التخدير الأخرى.

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INTRODUCTION

Depressive disorders are a significant cause of global disability, with approximately 30% of patients failing to respond to standard treatments, such as selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants [1]. Electroconvulsive therapy (ECT) is an established intervention for treatment-resistant depression, often augmented by anesthetics like propofol and ketamine, though their specific impact on efficacy remains unclear [2,3]. The present prospective observational study was undertaken to compare depression severity before and after ECT when using propofol- or ketamine-based anesthesia. We focused on changes in Hamilton Depression Rating Scale (HDRS) scores at baseline, one week, one month, and three months post-treatment. In addition to these main observations, we also examined remission rates and the need for additional ECT sessions. To reduce potential assessment bias, the clinicians evaluating patients' depression severity were unaware of which anesthetic agent each patient received. Major depressive disorder (MDD) is characterized by persistent low mood, loss of interest, and impaired functioning, often accompanied by suicidal ideation [4]. Its pathophysiology involves dysregulated

neurotransmitter activity, such as reduced serotonin, dopamine, and norepinephrine levels, along with structural changes in brain regions like the hippocampus and prefrontal cortex [5,6]. Stress-related hypercortisolism and diminished brain-derived neurotrophic factor (BDNF) exacerbate these changes, contributing to treatment resistance [7]. Current pharmacological therapies, though effective for some, often fail in cases of severe depression, necessitating interventions like ECT. Depression involves complex interactions between genetic predispositions and environmental stressors. Neuroendocrine dysregulation, particularly involving the hypothalamic-pituitary-adrenal (HPA) axis, is a critical factor. Elevated glucocorticoid levels disrupt neurogenesis and synaptic plasticity, further impairing mood regulation [8]. Additionally, reduced BDNF levels in the mesolimbic dopamine pathway are associated with increased susceptibility to stress [7]. These insights emphasize the importance of addressing underlying neurobiological factors in treatment. Propofol, a short-acting anesthetic working as a GABA receptor modulator, is commonly used due to its rapid induction and stable recovery profile but may reduce seizure duration, potentially affecting therapeutic outcomes [9]. Ketamine, an N-methyl-D-aspartate receptor antagonist with sedative-analgesic properties, offers advantages such as respiratory stability, neuroplasticity enhancement, and possible antidepressant effects [10,11]. This observational study investigates the comparative effects of propofol and ketamine anesthesia on depression outcomes in patients undergoing ECT. Changes in HDRS scores over time were recorded to examine differences in response between these two commonly used anesthetic agents.

METHODS

Study design and setting

This prospective observational study was conducted at Al-Fayhaa Teaching Hospital, Basrah, Iraq, focusing on two commonly used anesthesia protocols—ketamine- vs. propofol-based anesthesia—for patients undergoing electroconvulsive therapy (ECT). A total of 50 patients, aged 18–60 years and diagnosed with treatment-resistant major depressive disorder (MDD), were enrolled. The sample size was determined by feasibility and resource availability rather than a formal power calculation.

Inclusion and exclusion criteria

Patients met inclusion criteria if they had chronic depression unresponsive to at least two adequate antidepressant trials and a Hamilton Depression Rating Scale (HDRS) score >23, with referral by a psychiatric committee. Exclusion criteria included pregnancy, breastfeeding, unstable medical conditions, contraindications to ECT (e.g., recent myocardial infarction or increased intracranial pressure), chronic drug abuse, prior ECT failure, or markedly unstable vital signs.

Intervention and outcome measurement

Each patient was assigned to receive ECT under either ketamine or propofol anesthesia, ensuring equal group sizes (25 in each). Participants fasted for eight hours prior to the procedure, with intravenous access established and standard monitoring in place. Full airway management equipment was readily available for all patients. The ketamine group received intravenous ketamine (1–1.5 $mg \cdot kg^{-1}$) and succinylcholine (0.5 $mg \cdot kg^{-1}$), while the propofol group received intravenous propofol (1–1.5 $mg \cdot kg^{-1}$) with the same dose of succinylcholine. ECT parameters were standardized across groups: bilateral electrode placement, current of 800 mA, frequency of 90 Hz, and a total of 6–8 ECT sessions over approximately 3–4 weeks. Outcome assessors—psychiatrists evaluating depression severity—were unaware of each patient's anesthetic assignment to reduce potential observer bias. Depression severity was measured at baseline, one week, one month, and three months post-treatment using the Hamilton Depression Rating Scale (HDRS). The primary outcome was the change in HDRS scores from baseline to the end of the ECT course. Secondary outcomes included remission rates (HDRS score ≤7), need for additional ECT sessions, and relevant vital sign changes. Participants' vital signs were monitored throughout anesthesia induction and ECT sessions, consistent with clinical standards.

Ethical consideration

Ethical approval for this study was obtained from the Scientific and Ethical Research Committee at the Training and Human Development Center, Basrah Health Directorate (Certificate ID: 806 in March 6th, 2025), and written informed consent was secured from each participant (and relatives where applicable). All procedures adhered to institutional guidelines for patient safety. An independent monitoring committee was proposed to ensure the study protocol was followed and to oversee data collection.

Statistical analysis

Statistical analyses were conducted using SPSS (version 26). Qualitative data were expressed as frequencies and percentages, while quantitative data were presented as mean ± standard deviation or median with ranges. Normality of data was assessed using Shapiro-Wilk and Kolmogorov-Smirnov tests. Non-parametric data were analyzed using the Mann-Whitney U test, and statistical significance was set at $p< 0.05$. The authors used AI-assisted tools, including ChatGPT (OpenAI) and other AI-driven research databases, to aid in literature searching, text drafting, and statistical verification. All statistical analyses were performed using SPSS (Version 26), and AI

assistance was used to cross-check interpretations but not to conduct original calculations. The authors reviewed and verified all AI-generated content for accuracy and scientific validity.

RESULTS

The study was conducted from October 2023 to August 2024. A total of 55 patients were assessed for eligibility, and 5 participants were excluded due to not meeting inclusion criteria or declining participation. The remaining 50 patients were assigned to one of two anesthesia protocols during electroconvulsive therapy (ECT): 25 received ketamine-based anesthesia, and 25 received propofol-based anesthesia. No participants were lost to follow-up or discontinued treatment; all 50 individuals completed the study and were included in the final analysis. Table 1 summarizes the demographic characteristics.

Table 1: The demographic data distribution among the studied groups (n=25 in each group)

Variables		Group I Ketamine	Group II Propofol	*p*-value
Age	Mean±SD	28.96±7.21	29.0±9.32	0.987
	Min-Max	18- 42	18-48	
Gender n(%)	Male	12(48)	15 (60)	0.395
	Female	13(52)	10 (40)	

The mean age was similar between groups (28.96±7.21 years in the ketamine group vs. 29.0±9.32 in the propofol group, p= 0.987). The proportion of males (48% in ketamine vs. 60% in propofol, p= 0.395) also did not differ significantly. Thus, the two groups were broadly comparable at baseline. Vital signs measurements are presented in Table 2.

Table 2: The vital signs of participants in both groups (n=25 in each group)

Variables		Group I Ketamine	Group II Propofol
DBP	Before	80.2±7.3	79.4±6.9
	After	100.4±3.8	90.8±4.6
	p-value	0.001	0.875
SBP	Before	119.5±10.8	122.6±11.91
	After	130.4±12.5	125.5±11.8
	p-value	0.03	0.673

Values were expressed as mean±SD.

Patients who received ketamine experienced a significant increase in diastolic blood pressure from 80.2±7.3 mmHg to 100.4±3.8 mmHg and in systolic blood pressure from 119.5±10.8 mmHg to 130.4±12.5 mmHg (both $p< 0.05$). In contrast, the propofol group showed smaller increases (79.4±6.9 to 90.8±4.6 mmHg diastolic, 122.6±11.9 to 125.5±11.8 mmHg systolic), which were not statistically significant ($p> 0.05$). Table 3 shows the HDRS scores at baseline, 1 week, 1 month, and 3 months post-ECT. Baseline scores were comparable (29.36±1.91 in the ketamine group *vs.* 29.6±1.95 in the propofol group, p= 0.663). Both groups exhibited significant reductions by 1 week; however, the decrease was more pronounced in the ketamine group (15.72 ± 2.8) compared to propofol (20.76±3.35, p= 0.001). This pattern persisted at 1 month (16.6±2.06 *vs.* 20.56±2.74, p= 0.001) and at 3 months (19.4±2.75 *vs.* 21.8±3.02, p= 0.004), indicating a sustained improvement among ketamine recipients.

Table 3: the HDRS among both groups before ECT, 1 week after ECT, 1month after ECT, and 3 months after ECT (n=25 in each group)

Variables		Group I Ketamine	Group II Propofol	*p*-value
HDRS	Baseline	29.36±1.91	29.6±1.95	0.663
	Min-Max	27-33	25-33	
	1 Week	15.72±2.8	20.76±3.35	0.001
	Min-Max	11-20	16-26	
	1 Month	16.6±2.06	20.56±2.74	0.001
	Min-Max	12-20	16-25	
	3 Months	19.4±2.75	21.8±3.02	0.004
	Min-Max	16-24	16-26	

Values were expressed as mean±SD.

Among the 25 patients who received ketamine anesthesia, 11 (44%) required more ECT sessions, whereas 18 (72%) of the 25 receiving propofol needed more treatment (p= 0.045). This difference corresponds to an absolute reduction of 28% in the proportion of patients requiring extra sessions (ARR= 28%) and a relative risk (RR) of 0.61 for needing further treatment with ketamine compared to propofol. From these results, the number needed to treat (NNT) is approximately 4, indicating that four patients receiving ketamine instead of propofol would prevent one more patient from requiring further ECT. While such metrics are typically associated with interventional trials, they do illustrate the potential magnitude of difference in other ECT usage between the two anesthesia approaches (Table 4).

Table 4: The patients' need for more ECT (n=25 in each group)

Variables		Group I Ketamine	Group II Propofol	*p*-value
Need more ECT	Yes	11(44)	18(72)	0.045
	No	14(56)	7(28)	

Values were expressed as frequence and percentage.

DISCUSSION

This prospective observational study compared depression outcomes in patients undergoing electroconvulsive therapy (ECT) with either propofol- or ketamine-based anesthesia. The primary observation—greater and more sustained reductions in Hamilton Depression Rating Scale (HDRS) among those receiving ketamine—suggests that the anesthetic choice may influence ECT efficacy. Patients who received ketamine also had a lower proportion requiring additional ECT sessions, indicating potential clinical advantages over propofol in routine practice. Although both agents facilitated effective ECT, ketamine was associated with more pronounced antidepressant benefits. Correlations among individual background factors, including age, sex, prior ECT exposure, family history, and others, were initially considered. However, due to a substantial number of exclusions resulting from missing data, conclusive results could only be obtained for age and sex, with no significant impact

observed for these factors. Because ECT outcomes can be affected by multiple patient-specific factors (e.g., illness severity, comorbidities), we initially explored correlations with age, sex, prior ECT exposure, and family history. Missing data limited formal analysis for certain variables, but no significant associations emerged for age or sex in the available subset. Baseline HDRS scores were comparable across the ketamine and propofol groups, yet post-treatment differences were robust at each follow-up interval. Notably, 72% of patients in the propofol group required additional ECT, versus 44% among ketamine recipients (clinically relevant findings) that may inform anesthetic selection in ECT protocols. Relapse prevention remains a critical issue in treating major depression with ECT. While the current data point to ketamine's possible utility in prolonging remission, the precise number of sessions required to sustain benefits is still unclear. Further studies should investigate whether ketamine maintenance, adjunct pharmacotherapy, or individualized ECT schedules best preserve long-term remission. Our findings are consistent with prior research demonstrating ketamine's antidepressant properties in both ECT and non-ECT settings. Phillips et al. and Schwartz et al. reported reductions in depressive symptoms and suicidal ideation in treatment-resistant cohorts receiving ketamine infusions [12,13]. Similarly, Wang *et al*. found that ketamine–propofol combinations augmented seizure duration during ECT, correlating with improved clinical outcomes compared to propofol alone [14]. Zarate *et al*. also highlighted ketamine's rapid-onset effects in bipolar depression [15], though Goforth *et al*. cautioned that ketamine's impact may wane without ongoing treatment strategies [16]. Limited research has examined long-term outcomes of ketamine-ECT combinations, underscoring the need for further large-scale studies.

Study limitations

This study's prospective design, standardized protocols, and blinded outcome assessments help mitigate many biases commonly encountered in observational research. By measuring depression severity at well-defined intervals and ensuring that the evaluating psychiatrist was unaware of the anesthetic agents, we reduced both selection and measurement bias. However, certain limitations remain. First, the modest sample size (n = 50) and single-center nature may limit the broader applicability of these findings. Second, while the groups were comparable at baseline and no patients were lost to follow-up, no formal randomization was employed, leaving open the possibility of unmeasured confounders. Third, missing data on some background factors (e.g., family history, prior ECT responses) could not be fully explored. Despite these caveats, the prospective enrollment, balanced group sizes, and blinded outcome assessments bolster the reliability of our results, highlighting the need for larger, possibly multi-center, confirmatory studies.

Conclusion

This observational study suggests that the choice of anesthetic can significantly influence ECT outcomes for treatment-resistant depression. While both propofol and ketamine were associated with substantial HDRS score reductions, patients receiving ketamine showed more robust improvement and required fewer additional ECT sessions. These results align with emerging literature on ketamine's antidepressant properties and lend support to its use as a potentially advantageous anesthetic in ECT settings. Nevertheless, larger, multi-center investigations—with randomization or other rigorous designs—are needed to confirm these findings, refine ketamine dosing protocols, and establish its long-term benefits in treatment-resistant depression.

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Conflict of interests

The authors declared no conflict of interest.

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Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

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