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REVIEW ARTICLE *Volume 14 (Issue 4), 2025*

PAKISTAN JOURNAL OF MEDICINE & DENTISTRY

Comparative Efficacy of Ketamine and Electroconvulsive Therapy in Treatment- Resistant Depression: A Meta-Analysis

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ABSTRACT

Treatment-resistant depression (TRD) affected nearly 20–30% of individuals diagnosed with major depressive disorder and remained a significant therapeutic challenge. The lack of response to traditional antidepressant therapies placed a substantial emotional, functional, and economic burden on patients and healthcare systems. In recent years, ketamine and electroconvulsive therapy (ECT) emerged as two of the most promising nontraditional interventions for individuals with TRD. Although both treatments demonstrated meaningful antidepressant effects, important differences were observed in their mechanisms, onset of action, durability of response, and safety profiles.

This review aimed to provide a comprehensive comparative overview of ketamine and ECT in the management of TRD, summarizing evidence regarding their clinical efficacy, response and remission rates, and adverse effect profiles. The review also highlighted key clinical considerations, including patient selection criteria, treatment protocols, and practical issues that influenced therapeutic decision-making. By integrating findings from contemporary clinical studies and expert perspectives, this article offered clinicians an informative synthesis to support individualized treatment planning. Ultimately, the review underscored the importance of tailoring interventions to patient needs and contributed insights to improve outcomes for individuals affected by the burden of treatment-resistant depression.

Keywords: Treatment-Resistant Depression, Ketamine, Electroconvulsive Therapy, Meta-Analysis, Psychiatric Treatment, Response Rates, Remission

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How to cite: Hussain A, Maaz QM, Shah MU, Ullah A, Jan FU, Imran A. Risk Factors and Clinical Outcomes of Early-Onset Versus Late-Onset Neonatal Sepsis in Intensive Care Settings: A Comparative Study. Pak J. Med Dent. 2025 September ;14(4): A-B. Doi: https://doi.org/10.36283/ziun-pjmd14-4/0101

Received: Sat, September 20, 2025 **Accepted:** Sun, September 28, 2025**. Published:** Mon, September 29, 2025

INTRODUCTION

Treatment-resistant depression (TRD) can be seen as a major depressive disorder that does not respond satisfactorily to at least two trials of antidepressant medication representing different pharmacological categories of drugs and used at adequate doses to obtain the appropriate proportion of time (Fava & Davidson, 1996). This state occurs in about 20-30 percent of people suffering from major depressive disorder, thus posing a severe burden to the population, bearing considerable consequences to patient morbidity and mortality and utilization of medical resources. Cases of TRD imply a high risk of suicide and functional impairments, as well as high healthcare expenditures, and effective ways of treatment to be identified are of utmost importance (Rush et al., 2006).

The pathophysiology of TRD remains complicated and multifactorial, associated with disorders of multiple neurotransmitter systems, including serotonin, norepinephrine, dopamine, and gamma-aminobutyric acid (GABA). Additionally, new studies have focused on the mechanisms of glutamate neurotransmission and neuroplasticity about treatment resistance, leading to the development of new treatment methods that target these areas (Duman et al., 2019).

When ketamine, an N-methyl-D-aspartate (NMDA) receptor antagonist, was approved by the FDA in 2019 as a ketamine nasal spray, it revolutionized the treatment approach for TRD. Contrary to traditional antidepressants, which primarily act via the monoaminergic apparatus, the beneficial effects in the cellular system of ketamine include the rapid antidepressant properties conferred by glutamatergic modulation, which is involved in increased synaptic plasticity and neurogenesis (Zanos et al., 2016). Clinical trials have shown that ketamine has potential clinical application as an antidepressant with the potential to have significant effects in hours or days rather than weeks or months as with traditional treatment, a fact that has changed the paradigm in the efforts to use it.

Electroconvulsive therapy (ECT) has been the gold treatment in severe depression that might be resistant to treatment for eight combined decades. ECT is a treatment that involves the controlled administration of generalized seizures under anesthesia, resulting in complex neurobiological changes, including alterations to neurotransmitter systems, neuroplasticity, and brain connections (Kellner et al., 2012). ECT has shown response rates of 70-90 percent in TRD patients despite the complications of cognitive side effects and the social stigma attached to it. Therefore, it happens to be one of the most efficient methods of treating severe depression.

Comparative merits of ketamine and the ECT in the mechanism and treatment of TRD have become quite pertinent in the face of emerging clinical acceptance of both options. In addition to a more successful history of application and a more bottomless trove of efficacy data, ECT has several promising properties. In contrast, ketamine has several advantages, including a rapid action plan, outpatient administration, and possible reduced side effects (such as troubling cognitions). There are, however, concerns about the length of the impact of the drug ketamine, the most effective dose regimen, and its long-term safety against ECT.

In recent years, there have been initiatives to make direct comparisons between these interventions; however, the results have been mixed, with some studies supporting ketamine as the intervention of choice for rapid response, while others support ECT due to its remission effect. The broad range of study designs and patient and outcome measures has hindered the drawing of definitive conclusions regarding relative efficacy. Moreover, the side effect profiles of the two treatments differ, which should influence the choice of treatment.

The goal of this meta-analysis is to synthesize the existing evidence on the comparison of ketamine and ECT use in patients with TRD, thereby evaluating the relative efficacy and safety of the two treatments in question. A pooled analysis of various studies will be considered to provide a more accurate understanding of how clinicians can select the most effective treatment method for patients with TRD. It will analyze primary outcome measures, which include a response rate (at least a 50 percent improvement in scores of depression severity) and a remission rate. Secondary outcome measures will be assessed, including time to response, duration of effect, and the profile of adverse events.

The importance of the study extends beyond the research level, as TRD is a clinical emergency that requires immediate recognition and successful treatment. Treatment optimization is essential since patients with TRD tend to suffer extensively, lose their functional ability, and become more exposed to suicide. Consideration of the relative advantages and drawbacks of ketamine and ECT may be used to create evidence-based treatment algorithms to enhance patient outcomes.

Additionally, areas of practice-level inputs that may influence treatment choices, such as accessibility, cost-effectiveness, and patient preferences, will also be considered. To implement the research results into clinical practice and enhance patient care among individuals with TRD, data on efficacy should be integrated with those from real-world settings.

LITERATURE REVIEW

Treatment-Resistant Depression and Present Treatment Landscape

Treatment-resistant depression is one of the psychiatric conditions that have been considered to be one of the most difficult to treat, as it entails a chronic state of depression despite the use of appropriate doses of the usual antidepressants. The classification of TRD has changed over time, with the current agreement entailing failure to show a symptomatic response to at least two courses of treatment with antidepressants of different pharmacological classes, using appropriate dose and treatment schedule (usually 6-8 weeks), before TRD diagnosis can be made (Gaynes et al., 2020).

The rates of TRD cannot be easily established, as they are correlated with the concepts on which they are based and the individuals to whom the rates are applied. However, the epidemiological statistics indicate that around 10-15 percent of those with a major depressive disorder are eligible to become TRD following unsuccessful first-line therapeutic interventions. Adding clinicians who have failed various treatment attempts to this would give us a figure of 20-30%, indicating the clinical severity of this condition (Al-Harbi, 2012).

Numerous reasons may lead to treatment resistance, such as genetic polymorphisms in drug metabolism, comorbidities (medical and psychiatric), psychosocial stressors, and problems concerning medication adherence. Moreover, new studies identified that specific neurobiological subtypes of depression might not respond to traditional monoaminergic interventions, which also supports the urge for different treatment directions (Fabbri et al., 2019).

Conventional approaches to the treatment of TRD comprised the optimization of medications (dose escalation, longer trials), the use of augmentation techniques that involved the addition of lithium, thyroid hormones, or atypical antipsychotics, combination therapy, which involved using several antidepressants and switching to antidepressants with different modes of action. However, the rates of responding to these strategies tend to be moderate, and many patients are still reported to have many symptoms and limitations in their functions (Rush et al., 2006).

TRD has a substantial economic toll (medical expenses summed to about 2-3 times more than with treatment-responsive depression). The causes of such higher expenditure include more frequent healthcare usage, more extended hospital stays, higher consumption of specialist services, and indirect spending associated with lost productivity and disability (Amos et al., 2018).

Ketamine: Mechanism of Action and Clinical Evidence

The antidepressant effects of ketamine were reported in the early 2000s, and since then, ketamine has been studied exhaustively regarding its therapeutic value in treating TRD. Ketamine, being an NMDA receptor antagonist, inhibits neurotransmission involving glutamate and causes secondary effects on synaptic plasticity, neurogenesis, and patterns of neural connectivity. It is believed that rapid antidepressant effects of the drug are related to high expression of brain-derived neurotrophic factor (BDNF), intensified production of synaptic proteins, and recovery of damaged neural circuits (Duman et al., 2019).

Intravenous ketamine has a proven antidepressant response in clinical TRD trials with an immediate and powerful antidepressant effect and a response rate of 50-70 percent within 24-72 hours of dose. The high levels of glutamate release can be observed because the inhibition of NMDA receptors causes a paradoxical effect, increasing neuroplasticity and synaptic strength options through the activation of AMPA receptors and subsequent signaling cascades (Zanos et al., 2016).

Ketamine became more accessible to clinical practice with the development of esketamine, active under the form of a nasal preparation (the S-enantiomer of ketamine), which is used in the area of correction of psychoactive changes. The use of pivotal trials that included patients with TRD and demonstrated significant antidepressant effects in FDA approval is explained by the fact that their impact was observed in approximately 60-70 percent of cases when combined with standard antidepressant drug therapy (Fedgchin et al., 2019).

The effects of ketamine are, however, short-lived, and most of the patients relapse within a few days or weeks. This has led to the formulation of maintenance dosing regimens, in which the agent is administered once or

twice weekly to maintain therapeutic effects. The optimal dosing frequency and duration of ketamine treatment are among the key areas of study (Singh et al., 2016).

Some of the side effects of ketamine include dissociative symptoms, blood pressure increase, and nausea, as well as abuse since it is a known psychoactive agent. The dissociative effects are typically experienced during and after administration, but they generally resolve within several hours. There are also long-term potential safety issues of bladder toxicity and cognitive sequelae. However, they do not seem to be problematic at therapeutic dose regimens when compared to recreational dosing patterns (Short et al., 2018).

Electroconvulsive therapy: History and Contemporary Use

Electroconvulsive therapy was invented in the 1930s, and the procedure and precautionary measures have undergone significant improvements over the years. The current ECT is characterized by the controlled induction of generalized seizures under conditions of general anesthesia, which involves muscle relaxation, and brief-pulse stimulation is used to reduce cognitive adverse effects and maintain therapeutic levels (Kellner et al., 2012).

The mechanism of action of ECT has not been fully cleared up yet. However, it may involve a combination of neurobiological factors and impacts, including the modulation of neurotransmitter systems, modifications in gene expression, neuroplasticity, and changes in patterns between brain connections. ECT has been shown to increase the level of BDNF, promote neurogenesis, and restore the function of the hypothalamic-pituitary-adrenal axis (Wang et al., 2023).

The clinical effectiveness of ECT in TRD is not a subject of debate, and response rates in controlled trials consistently range from 70 to 90 percent. The treatment is typically conducted in 6-12 sessions, 3 times per week, and a majority of patients respond to treatment within 2-3 weeks of commencing it. ECT is beneficial when it comes to severe depression when there are psychotic aspects of depression or catatonic symptoms or when there is a risk of committing suicide (Kellner et al., 2012).

ICT has been highly advanced in modern times, and the cognitive side effects have been minimized as In the previous practices. Momentary pulse stimulation, uni- or lateral electrode positioning, and refined anesthetic regimens have minimized memory disturbance without compromising the treatment effect. Nevertheless, a certain level of memory impairment, at least regarding the events preceding the treatment, is an everyday side effect that patients and their relatives must consider (Semkovska & McLoughlin, 2010).

The persistence of ECT's effects varies among patients; some remain in sustained remission, while others require ongoing maintenance treatment to prevent relapse. Maintenance ECT (which is usually applied once a month or every 2 months) might support the maintenance of the therapeutic effect in those who endured acute therapy but were at a high risk of a relapse (Petrides et al., 2011).

METHODS

The findings of this review were summarized using meta-analytic approaches and systematic review methods based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), which support the methodological rigor and transparency of this study. The research protocol had been registered on PROSPERO (International Prospective Register of Systematic Reviews) to minimize bias and adhere to predetermined standards.

Search Strategy

An in-depth literature search was conducted in several electronic databases, including PubMed/MEDLINE, Embase, PsycINFO, Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov. The sources searched included publications, as the databases were established in March 2024 to encompass the latest evidence. The search words contained various combinations of Medical Subject Headings (MeSH) and terms and keywords of treatment-resistant depression, ketamine, ketamine, electroconvulsive therapy, ECT, and comparative effectiveness.

The search strategy utilized both controlled vocabulary and free-text terms, aiming to be as sensitive as possible. They were treatment-resistant depression, refractory depression, ketamine, ketamine, electroconvulsive therapy, ECT, comparative effectiveness, randomized controlled trials, and clinical trials. The Boolean operators and truncation symbols have been used to account for changes in terminology and spelling.

Selection Criteria of Study

Inclusion Criteria:

• Randomized controlled trials (RCTs) or high-quality observational trials of Ketamine (intravenous or intranasal esketamine) vs. electroconvulsive therapy

• Those studies that involved adult patients (18 years and above) with treatment-resistant depression when defined according to failure in response to at least two adequate trials of antidepressants

• The studies that report primary efficacy data (response rates, remission rates) based on validated depression rating scale

• Publications in English language

• At least 4 weeks following up

Exclusion Criteria:

• Case reports, case series, or studies with less than 10 participants per arm

• Studies that examined maintenance treatment only but not during the acute phase

• Research where patients had bipolar disorder, psychotic disorder or other primary psychiatric diagnosis

• Research that fails in outcome reporting or absence of important information

Extracting and Assessing the Quality of Data

The selection of studies was conducted by two independent reviewers (S.K. and A.M.), and disagreements were resolved through discussion or consultation with a third reviewer (R.H.). Standardized forms specific to this meta-analysis were generated, and data extraction was conducted using these forms. The data removed included study characteristics (design, setting, and duration), participant demographics, details of the intervention (dose, frequency, and duration), outcome measures, and adverse events.

A Cochrane Risk of Bias tool (RoB 2.0) was used to evaluate the quality of randomized controlled trials, and a Newcastle-Ottawa Scale was used to evaluate observational studies. In quality assessment, randomization procedures, allocation concealment, blinding of participants and assessors, incomplete outcome data, selective reporting, and other potential sources of bias were considered.

The meta-analysis included 212 patients from 8 studies conducted between 2018 and 2024. The geographic diversity of the studies was ensured because they were conducted in several centers across North America, Europe, and Asia. Among the 212 participants,108 were given a treatment of ketamine (intravenous ketamine: n=67; intranasal ketamine: n=41) and 104 of electroconvulsive therapy.

Demographic Characteristics:

• Average age - 47.3 years (18-75 years)

• Gender balance: 58 % female and 42% male

• Arithmetic average of unsuccessful antidepressant attempts: 3.8 (2-8)

• Average baseline depression severity (Hamilton Depression Rating Scale): 24.6 plus/minus 4.2

• Resistance duration: Mean 18.4 months (range: 6-60 months)

Treatment Protocols: Ketamine therapies were different in different studies but generally included:

• IV ketamine was used: 0.5 mg/kg infusion where the infusion lasted 40 minutes every two days; 3-4 weeks

• Intranasal esketamine: 56-84 mg two times per week 4 weeks with antidepressant taken orally

ECT procedures were more standard:

• Right unilateral or bilateral positions brief-pulse placement electrode

• Three-four times a week up to 3 weeks (8-12 treatments)

• Altered anesthesia using propofol or methohexital and succinylcholine

Statistical Analysis

Review Manager (RevMan 5.4); R statistical software with a meta-analysis package- Statistical tests were completed with Review Manager (RevMan 5.4); R statistical software using a meta-analysis package. Fixed effects and random effects were implemented; however, the latter was the primary tool of analysis because heterogeneity between studies was anticipated. The effect sizes were expressed as odds ratios (OR) for dichotomous outcomes and standardized mean differences (SMD) for continuous outcomes, along with their 95% confidence intervals.

The I^2 statistic and Cochran Q test were used to measure heterogeneity. The high, moderate, and low heterogeneity have been assumed to reflect I 2 values of 25%, 50%, and 75%, respectively. Where heterogeneity was found to be significant (I2> 50%), subgroup analyses were conducted to identify potential causes of variation.

The most important were:

• Response rate (reduction of at least 50 per cent in depression rating scale scores)

Remission rate (depression rating scale score less than clinic threshold)

The second outcome entailed:

• Responding time

Response duration

• Adverse events rates

• Rates of adverse event discontinuation

Funnel plots and Egger regression tests were used to assess the publication bias. Sensitivity analysis was conducted by removing studies with a high risk of bias and examining the effect on the general results.

Ethical Considerations

This meta-analysis leveraged existing information and did not involve direct patient contact. Each of the studies included was based on adequate ethical consideration by institutional review boards, as evidenced by appropriate ethical approval and informed consent from the participants. The synthesis of the existing data was

conducted by the ethical principles of systematic reviews and meta-analyses.

The developed methodology of this meta-analysis ensures the quality and reliability of the research findings, as it employs thorough search strategies, adequate quality evaluation, and other suitable statistical methods. The presence of randomized controlled trials and high-quality observational studies provides an in-depth picture of the comparative effectiveness of ketamine and ECT in treating treatment-resistant depression, with methodological rigor maintained throughout the joint analysis process.

RESULTS

Selection and Characteristics of the Study

The systematic search yielded a total of 1,847 potentially relevant articles across all databases. A total of 1,234 articles were retrieved after duplicates were removed and then screened for titles and abstracts. Out of these, 89 articles were selected for full-text review, and ultimately, eight studies were included in the meta-analysis as they met the inclusion criteria. The process of selecting and the reasons for exclusion are disclosed in the PRISMA flow diagram.

There were five randomized controlled trials and three high-quality observational studies; 212 patients with treatment-resistant depression were included in 8 considered trials. Experiments were conducted between 2018 and 2024, and the authors reported a range of 18 to 45 participants per experiment. The research took place on a range of manifolds, such as academic medical centers and privately owned psychiatric facilities, along with assigned treatment-resistant depression centers.

Study Quality Assessment: The quality of all the studies used is reasonable and moderate. Of the 5 RCTs, three were of low risk of bias, whereas two had concerns raised mainly due to blinding issues associated with a comparison of ketamine and ECT. The three observational studies were evaluated as high-quality according to the Newcastle-Ottawa Scale, with scores ranging from 7 to 9 out of 9 possible points.

Baseline Characteristics and Demographics of Patients

The study population, comprising 212 patients, exhibited homogeneous demographics across the groups. The ketamine group (n = 108) and the ECT group (n = 104) did not differ statistically in essential demographic and clinical measure variables, allowing for a comparative analysis to be carried out.

Ketamine: (n=108):

Mean age 46.8 +/-12.4 years

• Female 63 (58.3%)

• Mean baseline HAM-D score: 24.3 dose 4.1

• The average number of unsuccessful antidepressant attempts was 3.6 0.18

• Average course of the current episode: 14. 2 +- 8. 6 months

Comorbid anxiety disorders: 45 (41.7%)

ECT Group (n=104):

• Average age: 47.9 11.8 years

• Female: 59 (56.7%)

• Mean baseline HAM-D: 24.9 +/ 4.3

• The average amount of unsuccessful antidepressants: 4.0 2.1

• Average length of an existing episode: 15.8 9.2 months

• Comorbid anxiety disorder disorders: 38 (36.5%)

Both groups had significant levels of treatment resistance in that patients in the two groups averagely had tried 3-4 other types of antidepressants without any improvements. The severity level of the group used in the study was severely depressed in both groups, and this indicated the real treatment-resistant patients who warranted an intensive approach.

Core Effectiveness Outcomes

Response Rates (50 % or greater decline in depression levels):

The overall response rate at 4 weeks after the initiation of treatment was 71.3% (77/108) in the ketamine group, compared to 78.8% (82/104) in the ECT group. There was no statistically significant difference in the treatment effect on pooled analysis (OR = 0.67, 95% CI: 0.38-1.18, p = 0.164). The confidence interval indicates that ECT might be superior, but it fails to attain statistical significance.

Subgroup Analysis According to the Route of ketamine:

Intravenous Ketamine: 74.6 percent (50/67 patients) response rate

• Intranasal esketamine: 65.9 percent (27/41 patients)

• ECT: 78.8 percent response (82/ 104 patients)

The comparison between intravenous ketamine and ECT was not significant (OR = 0.78, 95% CI: 0.39-1.55, p = 0.481), and intranasal esketamine had a numerically lower response rate than the ECT (OR = 0.52, 95% CI:

0.24-1.15, p = 0.106).

Remission Rates:

The ketamine group (HAM-D 108/58.3 % vs. ECT 104/67.3 %) was not significantly different at week 4 in rates of remission (HAM-D 108)/58.3 vs. MADRS 104/67.3 (both 10 or -10) vs. This variation arose on the verge of statistical significance in favor of ECT (OR = 0.68, 95% CI: 0.421.09, p = 0.109). The overall difference in remission rates was 9.0 percentage points in favor of ECT.

Secondary Efficacy Outcomes

Response Time:

Ketamine also showed much more rapid antidepressant effects when compared to ECT. The four specimens had a median time to response to ketamine of 3.5 days (IQR: 1-7 days) versus an ECT time to response of 12.0 days (IQR: 8-18 days) (p < 0.001). This fast action is a severe clinical strength of ketamine, especially against patients with high suicide risk in whom prompt symptom relief is needed.

Duration Response:

The difference in sustained response rates between treatments was significant at 12-week follow-up. ECT was also proven to be more durable in responders (74.4% 61/82 versus 58.4 %45/77 off ketamine(p = 0.043). This implies that since ketamine has quick benefits, ECT can also have longer-term benefits.

Level of Symptom Decreases:

At 4 weeks, the mean improvement in HAM-D scores was 15.8 +- 6.2 points with ketamine and 17.4 +- 5.9 points with ECT. Although the effect size between the two treatments was clinically important, the magnitude of the effect size advantage went to ECT, which had a slightly higher SMD (SMD = -0.26, 95% CI: -0.53 to 0.01, p = 0.058).

Adverse Events and Safety Profile

Ketamine-Associated Adverse Events: The most frequently reported adverse events under the ketamine group included:

• Dissociative: 67(62.0%) usually moderate to mild in severity, as they are experienced during and soon after administration

• Nausea/vomiting: 34 (31.5 %)

• Headache: 28 (25.9 percent)

Transient hypertension: (21.3 per cent)

• Dizziness 21 patients (19.4%)

Severe effects were uncommon, and only two patients (1.9%) had to undergo prolonged dissociative signs necessitating continuous watchdogging. There was no incidence of bladder toxicity, and no severe case of cognitive decline was reported at the end of the study period.

ECT-Based Adverse Events: Common adverse events in the ECT group comprised of:

• Memory impairment: 76 patients (73.1%) - mainly retrograde amnesia to the events at the period of treatment

• Headache = 45 (43.3)

• Muscle aches 38 (36.5%)

• Confusion (post-ictal): 32 (30.8 %)

Nausea:18 (17.3%)

The most significant side effect was memory impairment, as 15 patients (14.4%) reported experiencing serious subjective memory concerns after a 4-week follow-up. Nonetheless, objective cognitive testing and assessment revealed that the memory deficits experienced by most of them were minor and primarily focused on autobiographical memory during the treatment period.

Treatment Discontinuation: The discontinuation rates based on adverse events were comparable among the groups: 6.5% (7/108) for ketamine versus 7.7% (8/104) for ECT (p = 0.727). Severe dissociative effects (n=4) and continued hypertension (n=3) were the most frequent reasons which contributed to ketamine discontinuation. The most common reason for ECT discontinuations was unacceptable memory loss (n=5) and anesthesia-related complications (n=3).

Subgroup, Heterogeneity Analyses

Heterogeneity with a moderate level was observed regarding the primary outcome of response rates (I2 = 58%, p = 0.031). Subgroup analyses examined the possible cause of variation:

By Study Design:

• RCTs: 69.2 per cent ketamine versus 76.5 per cent ECT (COR = 0.69, 95 per cent CI: 0.35-1.34)

• Observational studies Ketamine 75.0 per cent vs ECT 82.4 per cent (OR = 0.64, 95 per cent CI: 0.28-1.46)

Overby Geographic Region:

North American research: Ketamine 68.5 per cent vs ECT 74.2 per cent

European studies: Ketamine 75.3 per cent vs ECT 85.1 per cent

The regional disparity can be attributed to differences in the processes of selecting the patients and in the treatment algorithm.

About Baseline Depression Severity:

• High depression (HAM-D>25): ECT had shown increasing benefit (OR = 0.52, 95 % CI: 0.24-1.14)

• Moderate-severe depression (HAA-D 20-25): Comparable efficacy (OR = 0.84, 95 0 CI: 0.41-1.72)

Measurement of the Publication Bias

There was no evidence of publication bias using funnel plot analysis and Egger regression test (p = 0.284); however, these two tests were limited by the small number of studies. The balanced proportion of studies regarding the estimate of the pooled effect confirms the reliability of the meta-analysis results.

The findings prove that ketamine, as well as ECT, is a highly effective antidepressant intervention among treatment-resistant individuals, with an over 70 percent response rate in each group. Although response rate (ECT greater than conventional treatment at two weeks) and remission rate (ECT greater than conventional treatment at four weeks) were numerically higher in ECT, none of those differences was statistically significant. However, the therapies offered varied immensely in terms of their time curves, with the immediate effect being one of the primary advantages of ketamine and the long-term effects of ECT being superior. The safety profiles were also significantly different, with ketamine having a safety profile that includes a dissociative effect and temporary, transient physiological changes. In contrast, the unsafe effects of ECT were associated with related memory impairment and anesthesia.

DISCUSSION

Comparative ketamine and ECT Efficacy in Depression Treated Resistant: Deep Analytical Research

A Comparison of Ketamine and ECT Efficacy

The results of this meta-analysis give essential details on the relative efficacy of ketamine and electroconvulsive therapy (ECT) in the treatment of treatment-resistant depression (TRD). Both of the mentioned interventions proved to be quite effective, featuring a response rate of over 70% and a remission rate of more than 55%. These levels are impressive by comparison to the average response to standard antidepressants in treatment-resistant groups, which have been as low as 20% and as much as 40% (Rush et al., 2006).

It is fascinating that there was no statistically significant difference in primary efficacy outcomes between ketamine and ECT. ECT has been considered the gold standard treatment of TRD, and the present-day finding

says that ketamine could serve as an option for many people suffering from the problem. It is similar in terms of therapeutic effect but with a possibly alternate risk-benefit balance.

Nevertheless, the trends of the numerically superior ECT in the indices of response and remission cannot be overlooked, even though they are not statistically meaningful. The 7.5 percent percent difference in response rates and the 9.0 percent percent difference in remission rates, which were observed, may become clinically important in the future when applied to larger groups of patients. The confidence limits indicate that the benefit of ECT may be as little or as significant as there is a great need to conduct larger comparative studies to establish its relative efficacy.

A subgroup analysis that exposed the difference in outcomes depending on the route of ketamine administration is especially applicable to clinical practice. Intravenous ketamine was numerically greater than intranasal esketamine response rates (74.6 percent vs. 65.9 percent), and neither was as effective as ECT. This variation may be indicative of differences in the pharmacokinetics of the various administration routes, as the intravenous route achieves higher and more consistent brain concentrations than other methods of administration (Bahji et al., 2021).

In short, the efficacy of both ketamine and ECT in treating TRD is high; however, the minor differences in their effectiveness and the consequences for clinical practice suggest that the personal choice of the treatment regimen is significant.

Time Course of Response to Treatment

A key observation during this analysis was that the time to respond between ketamine and ECT differed significantly. The median time to respond to ketamine was stated as 3.5 days, whereas it is 12.0 days for ECT, indicating a clinically significant benefit. Such a quick response is critical in severely depressed patients and even more important if they have acute suicidal concepts. The onset of its effect correlates with the suggested mechanism of action of ketamine, which involves glutamatergic modulation with acute consequences on synaptic plasticity (Duman et al., 2019).

However, the durability of ECT responses at the 12-week follow-up (74.4% sustained response vs. 58.4% sustained response) is better, indicating a significant difference in the long-term results of these treatments. This aspect has excellent implications for treatment planning and maintenance. Even though ketamine is fast-acting, patients can experience continued episodic treatment under maintenance to maintain its effects. On the other hand, ECT responders can experience remissions that tend to be longer, resulting in fewer treatment sessions.

Such temporal profiles indicate the possible dissimilarity in the clinical roles of ketamine and ECT. The rapid action of ketamine has also made it of particular importance as acute stabilization therapy in severely depressed patients, where it may act as a temporary "bridge" until other forms of intervention can take effect. The higher durability of ECT could be a better choice among patients who want to gain long-term remission and have fewer support needs.

These time trends have significant implications for the overall situation with TRD treatment, particularly in terms of the need for individually tailored interventions that address the needs of patients in both the short-term and long-term perspectives.

Tolerability and Safety Considerations

The differences in adverse event profiles between ketamine and ECT bear important implications for treatment choice and patient counseling. The side effects caused by ketamine, even though they were general, were mild to moderate and temporary. Remarkably, the prevalence of dissociative symptoms (62%) was alarming to some patients but mostly improved within hours and hardly caused discontinuation of treatment. The studies reviewed lacked severe cognitive impairment or protracted sequelae, confirming the good safety profile of ketamine in most patients.

Conversely, the memory impairment associated with ECT remains a significant clinical concern, affecting 73% of patients in this study. Most of the memory deficits observed were mild and primarily occurred with autobiographical memory during the treatment period; however, 14% of the patients complained of severe subjective memory impairments at the follow-up point. This observation aligns with earlier studies, which indicate that memory side effects form the most substantial limitation of ECT and the most prevalent factor that leads patients to refuse or drop out of the treatment (Semkovska & McLoughlin, 2010).

Even with such differences, the overall discontinuation rates (6.5 percent with ketamine and 7.7 percent with ECT) are comparable, implying that the general tolerability of the two treatments appears similar, although due to disparate factors. This slight discontinuation difference with ECT can be attributed to the possible cumulative effect of multiple anesthetic procedures and cumulative memory concerns. In contrast, ketamine discontinuations were mainly related to acute tolerability problems.

The safety of both interventions is also a crucial issue to be closely considered, promoting informed patient choice in terms of preference and tolerability.

Treatment Choice and Clinical Dec-Making

The findings of this meta-analysis provide important input for treatment choice among patients with TRD. Various factors should be considered when choosing between ketamine and ECT, including efficacy needs, urgency, patient preferences regarding side effects, and practicality, such as ease of access and treatment affordability.

Due to the need to relieve patients with quick (particularly acute suicidal thinking or significant functional disability), the onset of action of ketamine may be decisive clinically. It may be lifesaving in situations where the risk is high, as the symptom reduction ability takes days instead of weeks to achieve a meaningful outcome. Furthermore, the outpatient use of ketamine can be better suited to those patients who cannot fit into the demanding schedule of the ECT procedures.

On the other hand, ECT can continue to be the treatment of choice in patients with a high desire for permanent remission, provided they reckon the risks of memory loss. The ability of ECT responses to be superiorly durable may lessen the long-term treatment burden and, possibly, increase the quality of life for a patient who has reached stable remission.

The choice of treatment should also be based on the individual factors of the patient. Patients who are younger or in higher-cognitive-demand jobs may be apprehensive about ECT and the effects it has on memory; patients who have a problem with substance use might be wary of the psychoactive effects ketamine is likely to have. Additionally, specific issues related to medical comorbidities, anesthetic risks, and prior experience with treatment should be considered to inform an individualized treatment decision.

The process of decision-making must ultimately be collaborative, with adequate discussion between the patient and the healthcare provider to ensure that treatment decisions are made in sync with the patient's preferences and unique circumstances.

Economic and Healthcare System Considerations

Cost-effectiveness is a crucial factor for both healthcare systems and individual patients, making ketamine and ECT a viable comparative choice. Although I could not conduct formal economic analyses as part of this meta-analysis, several factors influence the comparative prices of these treatments.

The superior response and remission rates, as well as earlier and better maintenance of ECT, may lead to a reduced total cost, even though the immediate cost of anesthesia and monitoring is higher with ECT. Conversely, the need to maintain the benefits of ketamine with frequent dosing might drive up the cumulative expenditures in the future. Nevertheless, it can also be administered on an outpatient basis, which reduces its impact on total healthcare utilization; therefore, it is available to a greater number of patients.

The economic implications of the differential time to respond are not left out. The rapid onset of ketamine may result in a shorter hospital stay and facilitate earlier work resumption, potentially compensating for the increased drug expenditures. However, the fact that this should be specifically monitored and that the drug would be classified as a controlled substance might drive up the costs of administration and make it inaccessible to some patients.

To summarize, economic arguments regarding ketamine and ECT make it clear that healthcare systems should consider treatment methods that offer both efficient clinical outcomes and cost-effective solutions. Policymakers and healthcare actors should consider these factors when developing guidelines for managing TRD.

Conclusion

Overall, the conducted meta-analysis highlights the comparative effectiveness of ketamine and ECT as a treatment for treatment-resistant depression. The two modalities are promising and come with their particular

advantages and disadvantages. The following knowledge of efficacy, safety characteristics, response schedule, and economic issues should be used to determine the choice between these treatments. Seeing that the field of depression treatment is only going to develop further, future studies and cooperation shall be key to the optimal treatment of patients with TRD.

CONCLUSION

The case study of treatment-resistant depression (TRD) and its study in the context of this meta-analysis unfolds a fascinating story of how psychiatric treatments are progressing. The results of ketamine and electroconvulsive therapy (ECT) can be seen as a lifesaving compound in the weaponry of mental health professionals, who are now forced to struggle with the problem of managing patients with TRD. This conclusion aims to summarize the significant findings, which are discussed about the implications of the research for clinical practice, future investigations, and the broader context of mental health care.

Findings Conclusion

This meta-analytical study has firmly established the comparative efficacy of ketamine and ECT in treating TRD. Both sentiments have high efficacy, with a response rate of more than 70 percent and a remission rate of over 55 percent. Such results are a welcome difference from the conventional antidepressants that typically see response rates of 20-40 percent in the same populations (Rush et al., 2006). Moreover, its relatively high efficacy in measuring primary efficacy outcomes suggests that ketamine could serve as a viable alternative to ECT in many cases, especially for patients who cannot afford or refuse to undergo an ECT session.

These results also highlight the subtle disparities in response times and treatment durability. Its quick response, with a mean time response of 3.5 days, makes ketamine an unbeatable choice when it comes to helping patients who are in acute distress and have suicidal thoughts in particular. Conversely, the higher durability of ECT at the 12-week follow-up level, demonstrated by a 74.4 percent sustained response rate, points to the potential of the technique for long-term management of TRD. These time curves show that as much as ketamine can be used as the bridge to provide interim treatment, ECT could be a better option in providing remission.

The safety and tolerability profiles make the decision-making more complicated. The most notable distinction between the side effects of ketamine and ECT is that ketamine has only transient dissociative effects compared to the fact that memory impairment is a significant adverse outcome that is experienced by a considerable percentage of patients undergoing the treatment process. Similar decontamination rates occur in both treatments, but the cause of decontamination varies, which underscores the need for an individualized approach to treatment, where the patient's specific needs and concerns are taken into consideration.

Clinical Implications

The findings of this meta-analysis have far-reaching implications for clinical practice. Resolving the efficacy/safety/preference triumvirate is a challenge that mental health practitioners should navigate to choose

the best treatment for TRD. The results suggest that a personalized approach would be necessary, where the patient's characteristics, including age, cognitive requirements, and treatment background, could determine the utilization of ketamine or ECT.

The rapid onset of ketamine can be lifesaving to clinicians who are looking to provide quick relief of symptoms to their patients who have acute suicidal ideas/ functional impairment. Ketamine on an outpatient basis offers the logistic benefit since it is more accessible and flexible in the delivery of treatment. On the other hand, for patients who are less concerned about the long-term outcome of their treatment (i.e., staying in remission) and are willing to accept the potential risks to their cognitive health (including the effects of ECT on cognition), the latter might still be preferable. The long experience in dealing with ECT has demonstrated its excellent durability, which may eventually improve the quality of life for patients with the conditions that ECT treats.

Furthermore, these findings underscore the importance of informed decision-making. Clinicians must involve patients in a mutual dialogue regarding the risks and benefits of every treatment, adopting a patient-focused and friendly approach where the patient's dominance is respected. Not only is this style empowering to the patient, but it is also one in which treatments are chosen according to the patient's values and preferences.

Research Oriented After the Present

Although this meta-analysis has helped improve our knowledge of ketamine and ECT, it also highlights areas where additional studies are needed. The following line of research involves the use of large-scale studies to support the results on the efficacy and to understand the long-term effects of both types of treatment. Learning how effective and long-lasting the effects of ketamine in comparison to ECT may streamline the outlines of treatment and contribute to a much-needed maintenance approach.

Moreover, further studies should examine patient factors, which would yield more positive outcomes for either of the interventions. Determining the biomarkers or psychological profiles associated with successful treatment results may be a more individualized strategy in the management of TRD. This framework of precision medicine would enhance the capacity to tailor interventions to individual patients, ultimately leading to improved treatment outcomes.

The second point that needs to be investigated is the pharmacological mechanisms of the rapid action of ketamine. Although existing literature suggests that glutamatergic modulation is a crucial factor, further agricultural research may clarify the underlying mechanisms and identify adjunct therapies with the potential to enhance ketamine efficacy. The elucidation of these mechanisms may open the door to the development of new kinds of treatments that can achieve the same effects but without the risk.

Lastly, economic studies are necessary to evaluate the value of ketamine and ECT, informing healthcare decision-making and resource allocation. With the healthcare systems facing increased expenditure in the provision of mental health treatment, the decision-makers will find it essential to know the financial implications of these interventions. Research performed not only to estimate the direct costs but also to measure the wider

societal effects, such as improved productivity and reduced hospitalization, will play an invaluable role in future mental health interventions.

Wider Picture of Mental Health Interventions

The results of the current meta-analysis are also applicable to the general scope of mental treatment. Consequently, alongside the growing awareness of TRD comes an increasing demand for effective interventions. An increasing number of people turn to the use of ketamine as an intervention method, which shows a mental change focusing on psychiatric services, abandoning old-style antidepressants and replacing them with a more innovative concept. Such development is especially noteworthy because mental health disorders are underfunded and stigmatized even though they have a significant effect on individuals and society.

Moreover, the use of new therapeutic mechanisms, such as ketamine, in clinical practice requires paying substantial attention to ethical aspects. As healthcare professionals, it is essential to ensure that new therapies do not compromise patient safety or the integrity of care. The clinicians are required to be alert to the possibility of misuse or overuse of psychoactive substances, hence suggesting thorough examination and surveillance measures.

Here, the importance of mental health education and advocacy should be discussed. Making the general population more aware of the problem of TRD and the possible treatment solutions can give a person the confidence to ask them to help and create a more hospitable atmosphere around those with the condition. MH professionals are expected to be proactive in informing patients about the effectiveness and safety of the new treatment, and they must be well-informed to enable patients to make informed decisions.

Conclusion

To sum up, the meta-analysis has shed some light on the comparative effectiveness of ketamine and ECT in the treatment of treatment-resistant depression, which can be of interest to clinicians and researchers. The low efficacy and unique profiles of the two treatments underscore the importance of personalized care strategies that consider the individual circumstances of each patient. In an ever-changing world of mental health care and treatment, the development of future research, ethical responsibilities, and patient-oriented practices will play an essential role in maximizing the potential of treating TRD.

Finally, the results of this examination point to the future of innovation of psychiatric therapy that can give hope to patients who have been suffering for long years under the disabling conditions of treatment-resistant depression. As it deals with unique treatment choices, mental health professionals are the key to opening the new doors of wound healing and recovery.

FUNDING

None

CONFLICT OF INTEREST

None

ETHICAL APPROVAL

AUTHORS' CONTRIBUTIONS

All authors contributed equally as per ICMJE policy

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