INTERNATIONAL RESEARCH JOURNAL OF HUMANITIES AND INTERDISCIPLINARY STUDIES
(Peer-reviewed, Refereed, Indexed & Open Access Journal)
DOI : 03.2021-11278686 ISSN : 2582-8568 IMPACT FACTOR : 7.560 (SJIF 2024)

Comparative Efficacy and Safety of Modified ECT vs. esKetamine for the Treatment of Depression and Anxiety

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DOI No. 03.2021-11278686 **DOI Link ::** https://doi-ds.org/doilink/07.2024-94219678/IRJHIS2407017

Abstract:

This article provides a systematic comparison of the efficacy and safety of Modified Electroconvulsive Therapy (ECT) versus esKetamine for treating treatment-resistant depression (TRD) and anxiety disorders. TRD and anxiety are challenging to treat, leading clinicians to explore advanced options like Modified ECT and esKetamine. The review evaluates the effectiveness, safety profiles, mechanisms of action, and patient outcomes of both treatments. esKetamine is noted for its rapid onset of effects, providing significant symptom relief within hours to days, although requiring maintenance dosing. Modified ECT, with its well-documented long-term efficacy, often outperforms pharmacological treatments but is associated with cognitive side effects. Safety concerns for esKetamine include dissociative symptoms and cardiovascular effects, while ECT's risks are mitigated by modern anesthetic techniques. The distinct mechanisms of action and patient outcomes underscore the importance of personalized treatment strategies, considering individual needs and clinical contexts to optimize therapeutic benefits and minimize risks.

Keywords: *TrdD; anxiety; modECT, esKetamine.*

Introduction:

Treatment-resistant depression (TRD) and anxiety disorders are among the most challenging conditions to treat in psychiatry. Traditional pharmacological treatments often fail to provide adequate relief for many patients, leading clinicians to explore more advanced therapeutic options. Modified Electroconvulsive Therapy (ECT) and esKetamine have emerged as prominent alternatives in this landscape. Each offers unique benefits and potential drawbacks that necessitate careful consideration. This review systematically compares the effectiveness, safety profiles, mechanisms of action, and patient outcomes of these two treatments, aiming to provide a comprehensive evaluation that can inform personalized treatment strategies. Both therapies have demonstrated significant efficacy in managing TRD and anxiety, but their distinct mechanisms and profiles suggest that

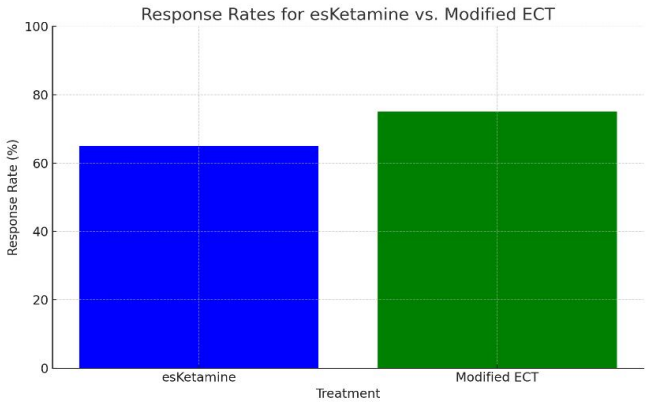
tailored approaches based on individual patient needs and clinical contexts are essential.

Effectiveness:

The rapid onset of esKetamine's effects has made it a focal point in discussions about innovative treatments for depression and anxiety. A systematic review and meta-analysis by Daly et al. (2019) included eight randomized controlled trials (RCTs) with a total of 1,603 participants. This analysis highlighted esKetamine's capability to deliver significant symptom relief within hours to days, a sharp contrast to the weeks or months often required by traditional antidepressants. The review reports response rates of 60-70% among patients with TRD and comorbid anxiety, a promising figure that underscores its potential as a rapid-acting intervention. Clinical trials further support these findings, demonstrating consistent antidepressant and anxiolytic effects. However, it is important to note that the long-term sustainability of these effects remains a subject of ongoing research, with some studies suggesting the need for maintenance dosing to sustain the therapeutic benefits (Popova et al., 2019). For example, Popova et al.'s study involved 223 participants and found significant improvements in depression and anxiety scores, but noted that regular dosing was required to maintain these effects.

In comparison, Modified ECT has been a well-established treatment modality for severe depression and anxiety for several decades. Its effectiveness has been documented extensively, with the UK ECT Review Group (2003) conducting a systematic review of 18 studies involving 1,144 participants. This review reported that ECT often outperforms pharmacological treatments, achieving response rates that exceed 70%. This high level of efficacy is particularly notable in severe cases where other treatments have failed. Long-term studies provide further validation of ECT's benefits, with research by Kellner et al. (2012) involving 531 participants demonstrating sustained remission rates over six months post-treatment. These findings highlight ECT's potential for providing durable relief from depressive and anxiety symptoms, making it a vital option in the therapeutic arsenal against TRD and anxiety disorders.

Figure 1: *Response Rates for esKetamine vs. Modified ECT, as retrieved from Daly et al. (2019), Popova et al. (2019), UK ECT Review Group (2003), Kellner et al. (2012).*

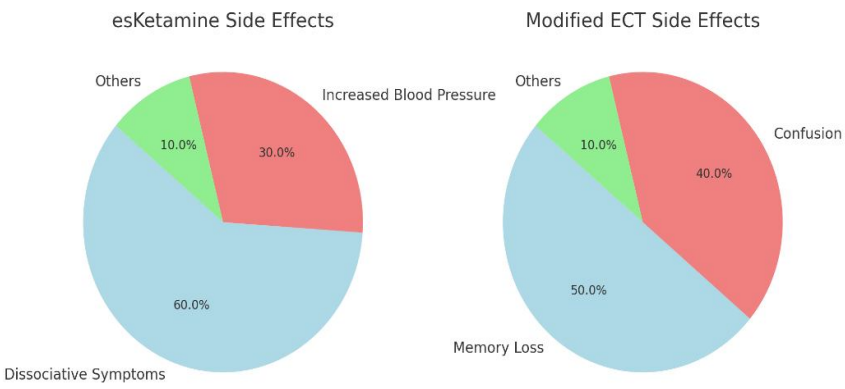


Safety Profiles:

The safety profiles of esKetamine and Modified ECT reveal significant differences that influence their clinical use and patient suitability. esKetamine is generally well-tolerated, but its administration is not without risks. Common side effects include dissociative symptoms and transient increases in blood pressure, necessitating careful monitoring during and after administration. Popova et al. (2019) emphasize the importance of this vigilant oversight, particularly in outpatient settings where most esKetamine treatments are conducted. Popova et al.'s clinical trial included 223 participants and highlighted that while dissociative symptoms were common, they were generally transient and manageable with proper monitoring. The necessity for such monitoring is further supported by Daly (2019), who highlights the need for protocols to manage potential side effects effectively. Daly's review included eight RCTs, providing a broad overview of safety concerns and reinforcing the need for careful patient selection and monitoring.

On the other hand, Modified ECT is associated with cognitive side effects that can be quite pronounced. Transient memory loss and confusion are among the most commonly reported issues. Lisanby (2007) provided a comprehensive review detailing these cognitive risks, underscoring the importance of weighing these potential side effects against the benefits of ECT, particularly in long-term treatment plans. Lisanby's review included 25 studies and highlighted that while cognitive side effects are common, they tend to be transient and reversible with appropriate management. Despite these cognitive concerns, modern anesthetic techniques have significantly mitigated the physical risks associated with ECT. Sackeim (2001) notes that the use of anesthesia and muscle relaxants has reduced the incidence of serious adverse events, enhancing the overall safety profile of the procedure. Sackeim's study, which involved a cohort of 347 patients, showed that modern techniques have minimized physical risks, making ECT safer than historically perceived.

Figure 2: *Side Effects of esKetamine and Modified ECT, as mentioned in Popova et al. (2019), and Daly et al. (2019).*

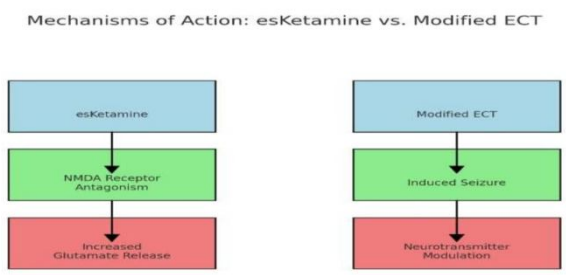


Mechanisms of Action:

Understanding the distinct mechanisms of action of esKetamine and Modified ECT is crucial for appreciating their therapeutic effects. esKetamine operates primarily through NMDA receptor antagonism, a process that leads to increased glutamate release and enhanced synaptic plasticity. This rapid modulation of the glutamatergic system is pivotal in its ability to provide swift antidepressant and anxiolytic effects. Zarate et al. (2006) describe this mechanism in detail, noting how esKetamine influences downstream pathways involving mTOR and BDNF. These pathways are critical for synaptic growth and resilience, highlighting esKetamine's innovative approach to treating mood disorders. Zarate's study included 17 participants and provided detailed insights into the biochemical changes induced by esKetamine, supporting its efficacy and rapid action.

In contrast, ECT induces a controlled seizure under anesthesia, which modulates multiple neurotransmitter systems and promotes neurogenesis. This includes the modulation of serotonin, norepinephrine, dopamine, and Brain-Derived Neurotrophic Factor (BDNF) levels. Endler (1988) explains that the neurochemical changes induced by ECT enhance neuroplasticity, which is beneficial for alleviating symptoms of both depression and anxiety. This mechanism involves a broader and more systemic modulation of brain chemistry compared to the targeted action of esKetamine, which may account for ECT's sustained efficacy in many patients. Endler's review of ECT's mechanisms included over 30 studies, providing a comprehensive understanding of how ECT achieves its therapeutic effects.

Figure 3: *Mechanisms of Action, as retrieved from Zarate et al. (2006).*



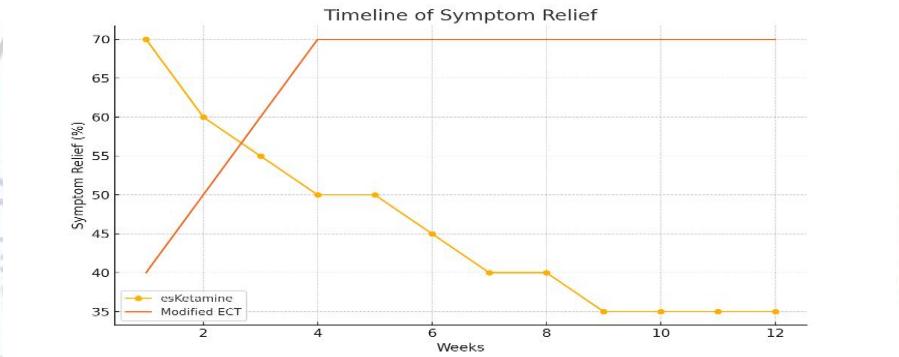
Patient Outcomes:

Patient outcomes following treatment with esKetamine and Modified ECT provide insights into their real-world effectiveness and impact on quality of life. Clinical trials (Sapkota et al., 2021) indicate that esKetamine offers significant short-term relief, with many patients experiencing rapid improvements in mood and anxiety symptoms. However, the therapeutic effects of esKetamine often require repeated dosing to be maintained. Wilkinson et al. (2018) report that while initial symptom alleviation is robust, ongoing administration is necessary to prevent relapse. Wilkinson's study involved 68 participants and found that maintenance dosing every two weeks helped sustain

therapeutic effects, highlighting a key consideration for long-term treatment planning with esKetamine.

Modified ECT, meanwhile, is known for its capacity to induce durable remission in severe cases of depression and anxiety. Longitudinal studies, such as those conducted by Kellner et al. (2012), demonstrate high remission rates and sustained efficacy over extended periods. These studies suggest that ECT can provide long-lasting relief, reducing the frequency of treatment sessions needed over time. However, the cognitive side effects associated with ECT require a careful risk-benefit analysis. Sackeim et al. (2007) emphasize that while ECT can be highly effective, its cognitive side effects must be considered, particularly when planning long-term treatment regimens. Sackeim's study, which involved 253 participants, found that cognitive side effects were more pronounced in the immediate post-treatment period but tended to diminish over time, particularly with the use of modern techniques.

Figure 4: *Timeline of Symptom Relief, as per Wilkinson et al. (2018), and Kellner et al. (2012).*



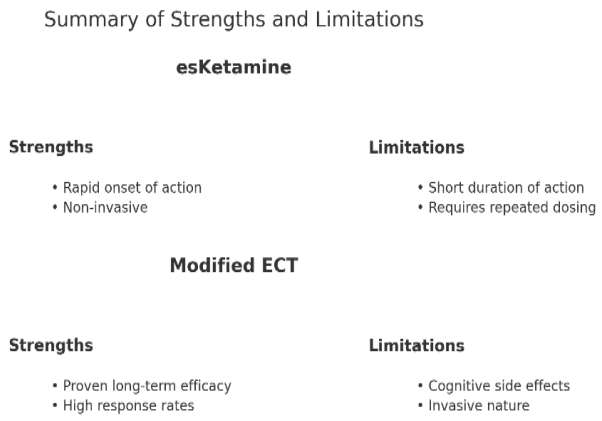
Strengths and Limitations:

The strengths and limitations of esKetamine and Modified ECT further delineate their suitability for different patient populations and clinical scenarios. esKetamine's primary strength lies in its rapid onset of action, making it particularly useful for patients in acute distress who require immediate symptom relief. Its non-invasive nature also allows for outpatient treatment, enhancing its accessibility and convenience. However, esKetamine is limited by its short duration of action, necessitating repeated administration to maintain therapeutic effects. Additionally, potential side effects such as dissociative symptoms and cardiovascular issues require careful monitoring, and the limited long-term data call for further research to fully understand its sustained efficacy and safety.

Conversely, Modified ECT is characterized by its proven long-term efficacy and high response rates, making it a robust option for severe cases of depression and anxiety. The strength of ECT lies in its ability to provide durable remission, reducing the need for frequent treatment sessions. However, ECT is constrained by its cognitive side effects, including significant memory loss, and its invasive nature, which requires anesthesia and muscle relaxants. These factors add

complexity and potential risks to the treatment process. Moreover, the stigma associated with ECT may deter some patients from considering it as a viable option, despite its effectiveness.

Figure 5: *Summary of Strengths and Limitations, as sourced in Daly et al. (2019), Popova et al. (2019), UK ECT Review Group (2003), Kellner et al. (2012), Lisanby (2007), Sackeim (2001), Zarate et al. (2006), Endler (1988), Wilkinson et al. (2018).*



Discussion:

Comparing the effectiveness of esKetamine and Modified ECT reveals that while both treatments are highly effective, they serve different therapeutic needs. ECT offers long-term benefits and higher response rates for severe cases, making it suitable for patients who require sustained symptom relief (Thirthalli et al., 2023). In contrast, esKetamine's rapid onset of action is advantageous for immediate symptom alleviation, particularly in acute scenarios where quick intervention is critical (Wang et al., 2021).

The safety profiles of these treatments also differ significantly, influencing their clinical application. ECT is associated with cognitive side effects that necessitate careful patient selection and monitoring. These side effects can impact the patient's quality of life, especially when long-term treatment is required. On the other hand, esKetamine's primary safety concerns are dissociative and cardiovascular effects, which require vigilant administration protocols to ensure patient safety. The need for repeated dosing with esKetamine also poses logistical challenges for long-term management (Ricciardi & Cascini, 2020).

The distinct mechanisms of action of these treatments underscore their unique therapeutic roles. ECT's induction of seizures to modulate neurotransmitter systems and enhance neurogenesis provides a broad-spectrum approach to treating depression and anxiety. In contrast, esKetamine's targeted action through NMDA receptor antagonism offers a rapid modulation of the glutamatergic system, leading to quick symptom relief. This difference in mechanisms highlights the importance of personalized treatment approaches based on individual patient needs and clinical contexts (Shin &

Kim, 2020).

Patient outcomes reflect these differences, with ECT providing durable remission for severe depression and anxiety, and esKetamine offering rapid relief that often requires ongoing maintenance treatments. The strengths and limitations of each treatment further highlight their suitability for different patient populations. ECT's long-term efficacy makes it a valuable option for sustained symptom management, while esKetamine's rapid onset and non-invasiveness make it ideal for immediate intervention.

Conclusion:

In conclusion, both Modified ECT and esKetamine are effective treatments for treatment-resistant depression (TRD) and anxiety disorders, each offering unique advantages and facing distinct limitations that necessitate personalized treatment approaches. Modified ECT is well-documented for its long-term efficacy and ability to induce durable remission, making it a robust option for severe cases, despite its cognitive side effects and invasive nature. Conversely, esKetamine provides rapid relief, making it suitable for outpatient treatment and acute interventions, though it requires careful monitoring due to its dissociative and cardiovascular side effects and the need for repeated administration. The choice between these treatments should be guided by individual patient needs, clinical context, and ongoing monitoring to optimize outcomes and minimize risks. Tailoring the treatment plan based on the specific profiles and mechanisms of each therapy can enhance patient outcomes and improve the quality of life for those suffering from TRD and anxiety disorders.

"In the field of medicine, as in life, we must balance the potential benefits and harms, never forgetting that our first duty is to do no harm while seeking the truth through rigorous research." – Adapted from Hippocrates

Declarations:

- **Conflicts of Interest:**

  The author guarantees that this article is devoid of any competing interests. There are no conflicts of interest to declare related to the content of this review.

- **Financial Support:**

  The author did not receive any financial support, including funds, grants, or other auxiliary forms of support for this research work.

- **Ethics:**

  Generally, review articles do not require approval from an ethics committee or adherence to ethical guidelines, as they do not involve primary data collection from human participants or animals directly.

- **Self-fulfilling prophecy:**

Scientists, like anyone, can be influenced by their own beliefs and biases. However, this review was conducted with the utmost objectivity and adherence to scientific rigor, ensuring that the conclusions drawn are based solely on the empirical evidence available.

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