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Electroconvulsive therapy versus intravenous ketamine as a novel treatment in depressive disorders: Review of the literature

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ABSTRACT

Aim: In this review, we assessed the state of available knowledge regarding the antidepressant action of intravenous ketamine versus electroconvulsive therapy (ECT) in randomized clinical trials and clinical trials. *Methods:* To search for the eligible articles, the PubMed database was used. Five studies were selected using the inclusion criteria, and their findings are presented in our review. *Results:* Five articles were selected. Three of them showed that ketamine is non-inferior to ECT, and in some patients, it had a faster onset and reduced depressive symptoms more significantly than ECT. Two of the selected articles concluded that ketamine is inferior to ECT. However, it is still a potent treatment that can induce response or remission faster than antidepressant drugs, even in patients suffering from treatment-resistant depression. *Discussion and conclusions:* As antidepressant properties of ketamine remain a relatively new discovery, further research needs to be conducted regarding its efficacy in the treatment of depressive disorders in relation to ECT, especially trials enrolling more participants. It is vital to note that even if two trials showed the inferiority of ketamine to ECT, all of them concluded that ketamine exhibits strong antidepressant properties and may prove to be an effective treatment, especially when ECT may be contraindicated, or patients are reluctant to it.

Keywords: Depression; major depressive disorder; ketamine; intravenous ketamine; electroconvulsive therapy.

1. INTRODUCTION

Depression

The two most common mental disorders are depressive disorders and anxiety disorders (Ferrari et al., 2022). Depressive disorders comprise major depressive disorder (MDD) and dysthymia; the data from the Global Burden of Disease (GBD) Study in 2019 shows that 280 million people suffer from depressive disorders - 100 million from dysthymia and 185 million from MDD. Moreover, in just one year, due to the COVID-19 pandemic, the number of people suffering from MDD increased to 246 million (Santomauro et al., 2021). The number of disability-adjusted life years (DALYs) lost due to depressive disorders is 46.8 million, placing them 13th among the most significant contributors to DALYs in 2019 (Ferrari et al., 2022; Global Burden of Disease Collaborative Network, 2021). According to the American Psychological Association (AMA), (2019), in the adult population, clinicians, as the initial treatment of depression, should consider the second generation of antidepressants (serotonin-norepinephrine reuptake inhibitors - SNRIs or selective serotonin reuptake inhibitors - SSRIs) and psychotherapy.

The efficacy of antidepressants varies among patients; some studies indicate that remission is not achieved in even 54% of them, and the percentage of patients withdrawing from this therapy in the first three months can reach 68% (Anderson et al., 2012). Furthermore, even 15-30% of patients cannot sustain the improvement or do not respond to the multiple lines of treatment (Conway et al., 2024; McIntyre et al., 2023). The treatment-resistant depression (TRD) is defined differently across sources. In their systematic review, Gaynes et al., (2020) found that the most common definition is a failure of two treatment trials with adequate dosages and duration. Due to discrepancies in the definition of TRD, the prevalence is difficult to estimate. Zhdanava et al., (2021) estimated that 30.9% of people treated for MDD had TRD.

Electroconvulsive therapy

ECT is one of the oldest therapies for depression that is widely used to this day; it was developed more than 80 years ago, in the 1930s, and to this day, it remains the most effective treatment for depressive disorders, especially for patients that do not respond to antidepressant drugs (Carney et al., 2003; Kirov et al., 2021). To receive ECT, patients must be under brief general anesthesia, electrodes are placed on the head, and an electrical stimulus is passed to induce a generalized seizure, which lasts about 30 seconds; commonly, one course consists of 8-12 treatment sessions, each session is administered two or three times in a week (Kirov et al., 2021). The remission rates are high; some studies indicate 52%, and some even up to 75% Kolshus et al., (2017), Husain et al., (2004); it is exceptionally high considering that many patients receiving ECT are suffering from TRD, and multiple lines of antidepressant drugs have failed.

The typical physical adverse events (AEs) after ECT are headaches, nausea, and muscle aches (Semkovska et al., 2016). Furthermore, ECT can impact cognition and short-term and long-term memory. However, the occurrence and duration of these side effects remain inconsistent. The meta-analysis by Semkovska et al., (2010) showed that these deficits rarely persist two weeks after the ECT session. Tørring et al., (2017) showed that the mortality rate of ECT is estimated to be 2.1 per 100 000 treatments, in contrast, the reported mortality of general anesthesia during surgical operations was 3.4 per 100 000, indicating that death caused by ECT is infrequent. Considering the data we presented, ECT remains one of the most feared and stigmatized psychiatric treatments; many patients are afraid of it, picturing it as a violent electrical shock destroying their brains (Gergel, 2022).

Ketamine

Ketamine is a drug widely used in anesthesia; its mechanisms of action include antagonism towards N-methyl-D-aspartate (NMDA) receptor, weak antagonism towards dopamine receptor and affinity for μ opiate receptors (Feeney and Papakostas, 2023; Berman et al., 2000). In clinical trials, the first reports of antidepressant action of ketamine can be traced back to studies by (Berman et al., 2000; Zarate et al., 2006). Berman et al., (2000), in their trial, enrolled seven patients; ketamine was administered at a dosage of 0.5 mg per kg, and saline solution was chosen as a placebo. The researchers used Hamilton Depression Rating Scale (HDRS) to assess depressive symptoms. Intravenous ketamine treatment significantly decreased HDRS scores; in saline placebo, HDRS scores remained relatively unchanged.

Researchers also indicated that a decrease in the depression severity was not likely due to the feeling of "high" induced by ketamine as depressive symptoms continued to decrease throughout the three-day follow-up, and the "high" returned to the baseline after a couple of hours. A study by Zarate et al., (2006) enrolled 18 patients, and their findings were similar, indicating that ketamine may prove to be a new rapid antidepressant treatment. Patients with MDD and TRD are often prescribed many drugs to help alleviate symptoms of their disorder. SSRIs and SNRIs are unlikely to interact with ketamine as their main target is the monoaminergic system; however, ketamine may have opposing effects on the GABAergic interneurons to benzodiazepines (BZD), with some studies suggesting that BZD do not affect ketamine effects and some suggesting otherwise (Feeney and Papakostas, 2023).

The AEs associated with ketamine can be divided into psychiatric (i.e., dissociation, abnormal sensations, perceptual disturbances, depersonalization, derealization, and may be able to induce psychosis), hemodynamic (e.g., increased blood pressure and heart rate, arrhythmias, palpitations, chest pain), neurologic/cognitive (e.g., drowsiness, dizziness, and light-headedness), abuse liability (schedule III drug in the United States) and genitourinary (symptoms from the lower urinary tract, e.g., painful hematuria, nocturia, urinary urgency, dysuria, incontinence) (McIntyre et al., 2021).

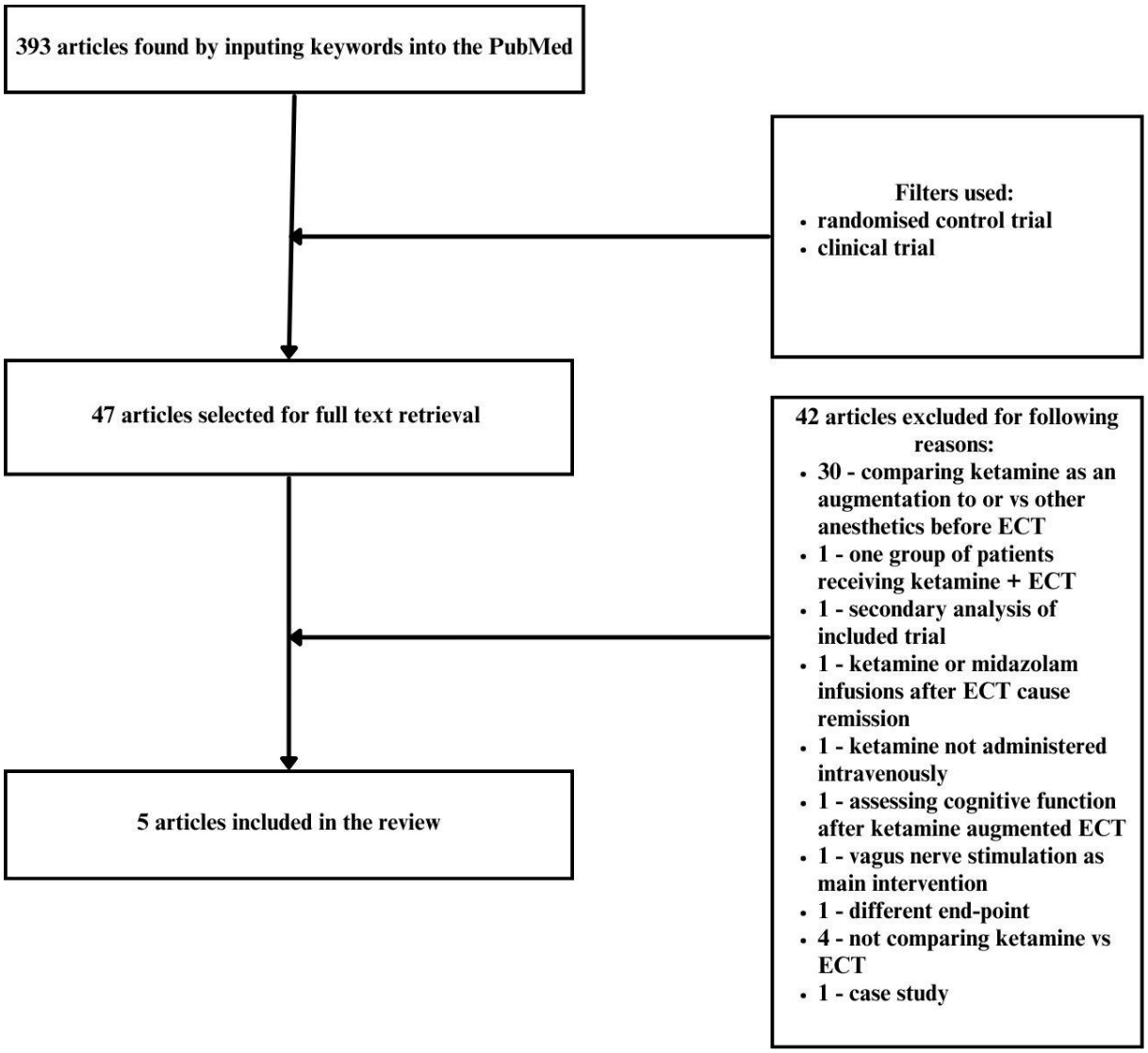

Figure 1 Flow chart presenting the selection process of eligible articles.

2. METHODS

The inclusion criteria that we established are listed below:
Randomized controlled trial (RCT) or clinical trial (CT),
Age of the participants: 18 years or older,
Participants receiving either intravenous ketamine or ECT, not as an anesthetic before ECT or in conjunction with other anesthetics,
Ketamine administered using the intravenous route,
Participants diagnosed with depressive disorders.

We searched PubMed for eligible articles until May 2024. The keywords we inputted into the database were "ketamine" and "electroconvulsive therapy"; this search yielded 393 articles. This combination yielded the greatest number of articles; when additionally inputting "depression" into the search engine, the number of articles was significantly lower - 316 vs. 393 articles. Furthermore, we found the eligible articles in both searches. Applying filters "RCT" and "CT", PubMed yielded 47 articles, from which, after applying the inclusion criteria, we selected five. In Figure 1, we presented the selection process, which was conducted by Marcin Głód and Dominika Kabała. We adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for 2020 (PRISMA) guidelines when writing this review.

3. RESULTS

Study selection

Using the inclusion criteria we developed, we selected five articles. 42 studies were excluded from this analysis; examples are listed below:
Articles that did not compare ketamine as a stand-alone therapy but either as an augmentation to the ECT or in conjunction with other anesthetics before ECT (Dong et al., 2023; Yoosefi et al., 2014),
Ketamine not administered intravenously (Kheirabadi et al., 2020),
Ketamine administered after a completed course of ECT as a relapse prevention (Finnegan et al., 2019),
Articles that investigated only ketamine antidepressant action (Diamond et al., 2014),
Case study (Correll and Futter, 2006).

Study characteristics

We presented the data retrieved from five selected articles in Table 1 and Table 2, as a preliminary data comparison in this form would prove the most effective. After that, we provided a more detailed description of each study. In Table 1, we described the number of sessions of respective treatments and the dosage of ketamine or type of ECT administered.

Table 1 Number of sessions and characteristics of each intervention.

	Outpatient vs. hospitalized	**Number of ketamine infusions administered**	**Dosage of ketamine and duration**	**Number of ECT sessions administered**	**Type of ECT administered**
Anand et al., (2023)	Outpatient (89.1%)	6	0.5 mg/kg over 40 min	9	Right unilateral (in 39% of patients changed to bilateral)
Basso et al., (2020)	Hospitalized	6	0.5 mg/kg over 40 min	12	Right unilateral
Ghasemi et al., (2014)	Hospitalized	3	0.5 mg/kg over 45 min	3	Bilateral
Ekstrand et al., (2022)	Hospitalized	Maximum of 12 (mean 6.8 ± 3.3)	0.5 mg/kg over 40 min	Maximum of 12 (mean 7.8 ± 2.4)	Right unilateral (9% of patients bilateral)

Sharma et al., (2020)	Not stated	6	0.5 mg/kg over 45 min	6	Bifrontal (31% right unilateral)

In Table 2, the articles will be described by:
Column 1: Article and standardized depression scale used,
Column 2: n - number of analyzed patients,
Column 3: Ket score – mean Montgomery-Asberg Depression Rating Scale (MADRS) or Beck's Depression Inventory (BDI) or HDRS scores at the baseline vs. at the end of the trial for the ketamine group (if the score at the end of the trial is not presented number with "- "will indicate the change in the score; if "~" is used the score is not stated but can be approximated from the graph provided in the article),
Column 4: ECT score – mean MADRS or BDI or HDRS scores at the baseline vs. at the end of the trial for the ECT group (if the score at the end of the trial is not presented number with "- "will indicate the change in the score; if "~" is used the score is not stated but can be approximated from the graph provided in the article),
Column 5: Ket vs. ECT – the percentage of participants that responded to the ketamine treatment or ECT, respectively; response was defined as ≥ 50% decrease in depressive symptoms quantified using a depression rating scale,
Column 6: Ket vs. ECT – the percentage of participants that remitted after the ketamine treatment or ECT, respectively; remission was defined as MADRS ≤ 10 or BDI < 9 or HDRS < 8,
Column 7: Conclusion of researchers on ketamine vs. ECT.

Table 2 Number of participants, depression scores, and number of responders and remitters.

	n	**Ket score**	**ECT score**	**Ket vs. ECT - res**	**Ket vs. ECT - rem**	**Conclusions**
Anand et al., (2023) - MADRS	365	32.3 ± 6.2 vs. −15.3 ± 0.7	32.6 ± 6.0 vs. −13.1 ± 0.7	50.8% vs. 41.4%	37.9% vs. 21.8%	ketamine non-inferior to ECT
Basso et al., (2020) - MADRS	50	26.40 ± 4.94 vs. 13.40 ± 6.89	31.17 ± 7.28 vs. 13.75 ± 7.69	not stated	not stated	ketamine non-inferior to ECT
Ghasemi et al., (2014) - BDI	18	34.66 ± 10.7 vs. 10.88 ± 7.49	42.44 ± 9.53 vs. 15.66 ± 7.51	77.78% vs. 77.78%	not stated	ketamine non-inferior to ECT
Ekstrand et al., (2022) - MADRS	186	33.1 ± 6.3 vs. 16.9 ± 13.1	34.5 ± 5.7 vs. 12.2 ± 11.1	not stated	46% vs. 63%	ketamine inferior to ECT
Sharma et al., (2020) – HDRS	25	23.33 ± 4.05 vs. ~ 9	25.15 ± 6.58 vs. ~ 4	66.70% vs. 100%	50% vs. 92.30%	ketamine inferior to ECT

From the five selected articles, three showed that ketamine administered intravenously is non-inferior to ECT, and two showed that ketamine is inferior to ECT. However, in all trials, ketamine proved to be an effective and fast-acting antidepressant treatment.

Articles indicating the non-inferiority of intravenously administered ketamine to ECT

Anand et al., (2023) studied the non-inferiority of ketamine to ECT; the intention-to-treat population comprised 365 patients, making it the biggest sample in our review. Participants were suffering from TRD with MADRS ≥ 20; the mean age was 46 years, and most of them were outpatients (89.1%). The trial involved an initial treatment phase, lasting three weeks, during which either ketamine (twice a

week) or ECT (thrice a week) were administered; then, patients that had a response to treatments were followed for six months; during this time, they received treatment with either ketamine or ECT and follow-up visits were conducted. The dosage of ketamine was 0.5 mg/kg, administered over 40 minutes; ECT administered was unilateral right (in 39% of the participants, ECT was changed to bilateral).

Response to treatments was defined as ≥ 50% decrease in depressive symptoms quantified using Quick Inventory of Depressive Symptomatology–Self-Report (QIDS-SR-16) and MADRS; MADRS scale was also used, but as a part of secondary outcomes; the remission was defined as MADRS score ≤ 10. Participants were allowed to use prescribed psychotropic medications. We decided to present the results of this trial using the MADRS scale, as it was also used in two other trials we selected. Response, according to MADRS, occurred in 50.8% of patients receiving ketamine and 41.4% of patients receiving ECT, with a difference of 9.3% points. Remission, according to MADRS, occurred in 37.9% in the ketamine group and 21.8% in the ECT group. The baseline mean MADRS score for the ketamine group was 32.3 ± 6.2 and 32.6 ± 6.0 for the ECT.

At the end of the three-week treatment, the mean MADRS score decreased by −15.3 ± 0.7 and by −13.1 ± 0.7 in the ketamine and ECT groups, respectively. 25.1% of patients in the ketamine group reported ≥ 1 moderate or severe AE, whereas in the ECT group, it was 32.4% of the participants. For the ketamine group, more frequently appearing AEs were dissociative symptoms, and for the ECT group, musculoskeletal AEs. The relapse in the sixth month of the follow-up was 35.3% for the ketamine and 43.8% for the ECT. The authors stated that the ketamine treatment was non-inferior to the ECT. Basso et al., (2020) enrolled 50 hospitalized participants suffering from TRD MDD; the mean age was 49.08 ± 10.45 years and 49.96 ± 11.82 years for the ketamine and ECT groups, respectively.

Right unilateral ECT was administered over four weeks (12 sessions), whereas the ketamine group received treatment over two weeks (six sessions) at a dosage of 0.5 mg/kg over 40 minutes; additionally, to the intervention, patients also were using prescribed psychiatric medications. The MADRS score was measured thrice: Before (T0), in the middle (T1), and after completed treatment (T2). The response and remission criteria were the same as in the trial by (Anand et al., 2023). The mean MADRS scores for the ketamine group were: T0 = 26.40 ± 4.94; T1 = 13.38 ± 5.27; T2 = 13.40 ± 6.89. The mean MADRS scores for the ECT group were T0 = 31.17 ± 7.28; T1 = 19.52 ± 7.07; T2 = 13.75 ± 7.69. At the baseline, the mean MADRS scores were 26.40 ± 4.94 and 31.17 ± 7.28 for the ketamine and ECT groups, respectively, with $p = 0.010$; researchers indicated that the ECT group was more depressed at the baseline, but the ketamine group had twice the duration of their current episode.

The authors concluded that ketamine demonstrated faster onset and stronger reduction in depressive symptoms than ECT in the middle of the treatment; however, at the end of the intervention, both were equally as effective. It is vital to note that the same effectiveness of ketamine was achieved faster than ECT. Researchers indicated that there may be no need to administer six ketamine infusions as mean MADRS scores did not differ significantly in the middle and after the completed treatment. Furthermore, overall cognitive performance was significantly better in participants treated with ketamine than in the ECT group. The authors did not provide data on how many of the participants were responders and remitters. The data regarding AEs is not presented in the article's main body.

Ghasemi et al., (2014), in their study, enrolled 18 hospitalized participants suffering from MDD; the mean age of patients was 37.6 ± 15.05 years. The bilateral ECT was administered for three sessions every 48h, and the ketamine group received three infusions of 0.5 mg/kg over 45 min every 48h. The mean baseline BDI score was 42.44 ± 9.53 and 34.66 ± 10.7 for the ECT and ketamine groups, respectively; $p = 0.123$. The mean BDI score one week after completion of treatment was 15.66 ± 7.51 and 10.88 ± 7.49 for the ECT and ketamine groups, respectively, with $p = 0.196$. Response criterium was the same as in the previously described studies; one week after the treatment, the percentage of responders was the same in the ECT and ketamine groups - 77.78%, suggesting that both treatments were equally effective.

However, the researchers measured the depressive symptoms using BDI and HDRS; using the HDRS score, the percentage of responders was 88.89% and 100% one week after treatment for the ECT and ketamine groups, respectively. Furthermore, after the first infusion of ketamine, the mean BDI decreased by 42.69%. However, in the ECT group, after the first treatment, the mean BDI score decreased by 11.06%, suggesting that ketamine has a faster onset of action than ECT. The authors did not provide data on adverse events after each intervention. The researchers concluded that ketamine could be a powerful antidepressant agent with effectiveness rivaling ECT and quicker reduction of depressive symptoms.

Articles indicating the inferiority of intravenously administered ketamine to ECT

Ekstrand et al., (2022) investigated the non-inferiority of ketamine to ECT. The trial analyzed 186 hospitalized patients diagnosed with MDD and MADRS score ≥ 20; the mean age of the ketamine group was 55 ± 18 years, and the mean age of the ECT group was 50 ± 18 years. Patients could use previously prescribed psychiatric medications. The dosage of ketamine was 0.5 mg/kg, administered over 40 minutes; ECT was right unilateral (9% of patients received bilateral sessions). The maximum number of sessions for both interventions was set at 12, at maximal antidepressant effect or until remission. The definition of response was the same as in previous articles; remission was defined as the MADRS score of ≤ 10 lasting ≥ 2 sessions. In the group receiving ketamine, 46% (44/95) remitted, whereas in the ECT group, 63% (57/91) participants remitted, with p = 0.026, deeming ECT more effective in treating depression.

The mean MADRS scores at the baseline were 34.5 ± 5.7 and 33.1 ± 6.3 for the ECT and ketamine groups, respectively, with p = 0.11. The final mean MADRS scores were 12.2 ± 11.1 and 16.9 ± 13.1 for the ECT and ketamine groups, respectively, with p = 0.009, significantly lower for ECT. Moreover, authors reported that remission for the ECT group occurred significantly more often in participants aged ≥ 50 years; 77% of them remitted, whereas in younger patients, 50% remitted, p = 0.004. The opposite occurred in the group receiving ketamine; 61% of younger participants remitted and 37% of older patients; p = 0.034. Researchers stated that ECT and ketamine were equally effective in younger patients. The number of sessions required to reach remission was the same in each group, 6.0 ± 2.3 and 6.0 ± 2.7 for ECT and ketamine, respectively; p = 0.84.

AEs were reported by 85 patients in the ECT group and by 85 patients in the ketamine group. However, the number of patients that reported AEs lasting > 24h was twice as large in the ECT group (ECT - 48 and ketamine - 20). The most common AEs associated with ECT were muscle pain, headaches, and amnesia; for the ketamine group, dissociative AEs were blurred vision, anxiety, vertigo, euphoria, and diplopia. For some patients in the ECT group, AEs persisted at the end of the follow-up but mostly were transient in the ketamine group. Severe AEs were also more common in the ECT group (ECT – 23/90; Ket: - 14/91). Twenty-one patients dropped out from the ketamine group, and four patients dropped out from the ECT group due to AEs; however, authors stated that it was most likely due to patients' mindset that ECT, which was previously administered to some patients was available and its AEs are more known.

The percentage of remitters that relapsed during the follow-up was 64% and 70% for the ECT and ketamine groups, respectively; p = 0.44. The researchers stated that ECT was superior to ketamine with higher remission rates and the ability to decrease MADRS scores more significantly; however, ketamine, with its remission rate of 46%, proved to be a potent antidepressant treatment. In contrast to previous articles Ghasemi et al., (2014), Basso et al., (2020), researchers stated that faster onset of ketamine antidepressant action was not observed. The trial by Sharma et al., (2020) comprised 25 participants; the mean age of the patients was 34.42 ± 9.65 years and 41.38 ± 14.26 years for the ketamine and ECT groups, respectively. Patients could use previously prescribed psychiatric medications.

Ketamine was administered intravenously at 0.5 mg per kg over 45 minutes. ECT was bifrontal for nine patients and right unilateral for four patients. Both the ketamine and ECT groups received six treatment sessions of their respective interventions. The definition of response was the same as in previously described articles. The mean baseline HDRS and BDI scores for the ketamine group were 23.33 ± 4.05 and 33.33 ± 9.29, respectively. The ECT group's baseline scores were HDRS 25.15 ± 6.58 and BDI 37.07 ± 6.58. The differences in the baseline scores for both groups were not statistically significant. The mean BDI and HDRS scores after completed treatment are not stated as numbers in the article, only shown on the graph (estimates from the graph – HDRS – 9 for the ketamine and 4 for the ECT groups; BDI – 13 for the ketamine and 7 for the ECT groups).

The ECT after the first session showed a more significant and faster onset of reduction in depression scores. Furthermore, the number of responders and remitters was greater in the ECT group - 100% and 92.30%, respectively, compared to the ketamine group - 66.70% and 50%, respectively. Authors reported that five patients had transient dissociative symptoms during ketamine infusions; because of it, one patient resigned. One patient in the ECT group had prolonged apnea, and one had delayed motor recovery. The authors concluded that ECT is superior to ketamine in its antidepressant action, considering its faster response time and greater percentage of responders and remitters.

4. DISCUSSION

In this review, 393 articles were screened; five met the inclusion criteria and were described in this analysis. Three showed that ketamine is non-inferior to ECT, with Basso et al., (2020) showing that it may have a stronger and quicker onset in reducing depressive

symptoms than ECT. Two of them reported that ketamine is inferior to ECT. The small number of trials comparing the effectiveness of ketamine vs. ECT implicates a need for further research, especially involving a greater number of participants, as only two trials enrolled more than 100 patients, and they presented conflicting results, one showing non-inferiority and one showing inferiority of ketamine to ECT. Moreover, it is vital to consider different approaches to this matter, for example, administering ketamine as an anesthetic before ECT, which could further improve its effectiveness.

Trials that investigated this matter show inconsistent results. Gamble et al., (2018) in their trial, analyzed 24 patients; participants were divided into two groups, one receiving ketamine (0.75 mg/kg) and one receiving propofol (1 mg/kg). All patients receiving ketamine achieved a response to the treatment (50% reduction in MADRS score) and remission (MADRS ≤ 10), whereas in the propofol group, 83% responded to the treatment, and 58% achieved remission. Furthermore, in the ketamine group, a median of three treatments was needed to achieve remission, compared to seven treatments in the propofol group. In contrast to his study, Abdallah et al., (2012) (ketamine 0.5 mg/kg + 3.5 mg/kg thiopental vs. 3.5 mg/kg thiopental alone) and Carspecken et al., (2018) (ketamine 1-2 mg/kg or methohexital 1-2 mg/kg) concluded that ketamine administered before ECT did not reduce depressive symptoms more than the other intervention.

Furthermore, in our review to achieve comparability of results, we included trials that administered ketamine intravenously; in the trial by Kheirabadi et al., (2020), researchers compared antidepressant effects of intramuscular (0.5 mg/kg) and oral (1 mg/kg) ketamine to ECT. The authors concluded that oral and intramuscular ketamine exhibit similar antisuicidal and antidepressant effects as ECT while also having fewer cognitive AEs. The articles presented in this review show ketamine as a promising treatment for TRD. However, it is vital to note that long-term AEs are not fully understood, limiting its usage in a clinical setting (Ekstrand et al., 2022).

Limitations

As previously mentioned, the trials we described mainly enrolled a few patients; only two had more than 100 participants and showed contrasting results. Thus, further studies should include a greater number of participants. Moreover, different scales assessing depression severity were used in the trials, which could hinder an effective comparison of outcomes; however, it was partially remedied using terms such as response and remission. The dosage of ketamine was the same throughout the trials, with some minor variations in the duration of infusion, but the number of sessions varied from three to 12.

Variation in the number of sessions was also the case for ECT. Moreover, the type of ECT used was right unilateral, bilateral, or a combination of both. In the subsequent trials, it is advised to standardize the number of treatments and the type of ECT. Furthermore, it is essential to note that outcomes can be different in outpatient and inpatient participants; most of the trials enrolled hospitalized patients, and the trial that had the greatest number of participants Anan et al., (2023) was mostly (89.1%) outpatient.

5. CONCLUSIONS

Our findings present intravenous ketamine as a novel antidepressant treatment that may be as effective as ECT in a clinical setting. This review shows that further research is vital, as a limited number of RCTs or CTs investigating the efficacy of ketamine in relation to ECT are available. Three of the articles we presented stated that ketamine was not inferior to ECT, while two indicated that ketamine is inferior to ECT. However, all trials showed that ketamine can significantly reduce depressive symptoms.

Abbreviations

MDD: Major depressive disorder
GBD: Global Burden of Disease Study
DALYs: Disability-adjusted life years
AMA: American Psychological Association
SSRI: Selective serotonin reuptake inhibitors
SNRI: Serotonin-norepinephrine reuptake inhibitors
TRD: Treatment-resistant depression
ECT: Electroconvulsive therapy
AE: Adverse event

NMDA: N-methyl-D-aspartate
HDRS: Hamilton Depression Rating Scale
BZD: Benzodiazepines
RCT: Randomized clinical trial
CT: Clinical trial
MADRS: Montgomery-Asberg Depression Rating Scale
BDI: Beck's Depression Inventory
QIDS-SR-16: Quick Inventory of Depressive Symptomatology-Self-Report.

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Author's Contributions
Marcin Głód: Conceptualization, investigation, data curation, writing - rough preparation; supervision; project administration.
Dominika Kabała: Investigation, data curation, visualization.
Adam Jaskulski: Software; resources; writing - rough preparation.
Agata Zapałowska: Formal analysis; resources; writing - review and editing.
Michał Bielecki: Formal analysis; data curation; writing - rough preparation
Milena Szczepańska: Methodology, software, data curation.
Tymon Zatorski: Investigation, writing - review and editing, project administration.

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Informed Consent
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Conflict of interest
The authors declare that there is no conflict of interests.

Data and materials availability
All data sets collected during this study are available upon reasonable request from the corresponding author.

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