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Differences in Outcomes in Patients with Treatment-resistant Depression (TRD) Receiving Electroconvulsive Therapy (ECT) vs. Ketamine Infusion Therapy

Kimberly Crowley, RN

Background

Depression is a common psychiatric disorder that impacts an estimated **300 million people** globally. Up to ⅓ of those suffering from depression have “**treatment-resistant depression**” or TRD.

Depression is considered “treatment resistant” when a patient has tried two or more antidepressant medications without improvement in their depressive symptoms.

Patients with TRD experience compromised quality of life and may struggle with suicidal ideation or self-injury — **30% of patients with TRD attempt suicide at least once in their life.**

Electroconvulsive therapy (ECT) is considered the gold standard treatment for TRD. However, **ketamine infusion therapy** is emerging as another potential option for patients with TRD.

This study is important to the ACU as we have a patient population who receives ECT treatments for depression & associated mental health issues. It is important to consider other potential ways we may serve patients who struggle with TRD, in order to improve their lives & prevent suicide.

Problem

In patients with treatment-resistant depression, how does ketamine infusion therapy compare to electroconvulsive therapy (ECT) in its impact on depressive symptoms and remission rates?

Review of Literature

Anand, Amit et. al (2023) | Level I, Quality A

- **Purpose:** to determine if ketamine infusion therapy is noninferior to ECT for treatment of nonpsychotic TRD
- **Population:** patients between ages 21-75 referred to ECT clinics for treatment-resistant major depression without psychotic features. 195 patients received ketamine tx and 170 received ECT.
- **Methods:** Open-label, randomized noninferiority trial. Initial tx was three weeks long: ECT 3x/week or ketamine (0.5mg/kg) 2x/week. Primary outcome measured was response to tx (decrease of $\geq 50\%$ from baseline score).
- **Results:** A response occurred in 55.4% of patients in ketamine group vs. 41.2% in the ECT group. Relapse occurred in 19% of ketamine group and 35.4% of ECT group at one month; 25% and 50.9% at three months; and 34.5% and 56.3% at six months.
- **Conclusion:** The trial showed noninferiority of ketamine to ECT with respect to the primary outcome of treatment response according to the QIDS-SR-16.

- **Limitations:** ECT was started with right unilateral placement and switched to bilateral placement in the event of inadequate response. If started with bilateral placement, higher % of patient response may have been observed. Other limitations include lack of placebo group and maintenance treatment not being studied.

Basso, Laura et. al (2020) | Level 1, Quality B

- **Purpose:** to compare clinical efficacy & neuro-cognitive functioning in patients with TRD treated with either ketamine or ECT.
- **Population:** hospitalized patients with TRD. 50 total patients were studied: 25 patients received ketamine treatment and 25 were treated with ECT.
- **Methods:** Mixed factorial design with symptom severity and neurocognitive performance as variables. Patients were treated with a 4-week, 3x/week course of ECT or a 2-week, 3x week series of ketamine infusions (0.5mg/kg). Infusions were administered over 40 minutes. Clinical assessments were performed before 1st treatment, after 50% of treatments were complete, and after last treatment.
- **Results:** Mean percentage reduction in symptom severity (determined via MADRS ratings) differed between the two groups. From beginning to mid-treatment cycle, symptoms reduced in severity by 35% in ECT group vs. 47% in ketamine group. However, from beginning to end, symptoms reduced in severity by 55.7% in the ECT group vs. 50% in the ketamine group.
- **Conclusion:** Ketamine showed a faster onset of action than ECT. However, by end of treatment ECT patients showed greater reduction in symptom severity. Ketamine therefore may be a useful option when there is an urgent need for symptom improvement.
- **Limitations:** Small sample size (50 total subjects). Patients treated with ketamine were less severely depressed at the start of the intervention than those treated with ECT but with their current depressive episodes lasting twice as long on average. This may have affected outcomes.

Ekstrand, Joakim et. al (2022) | Level I, Quality A

- **Purpose:** to compare efficacy of multiple racemic ketamine infusions with standard ECT in hospitalized patients with TRD
- **Population:** hospitalized patients diagnosed with TRD. Total study numbers were 91 patients in the ECT group and 95 in ketamine group.
- **Methods:** Randomized, parallel, open-label study. Pts received IV ketamine at a fixed dose of 0.5mg/kg over 40 minutes. Standard ECT protocol was followed. Patients received between 1 and 12 treatments in either group. Pts were evaluated with MADRS scale at baseline, 4-5 hours after the first treatment, the day after each subsequent treatment, and at follow-ups. Non-responders (patients who did not achieve a 25%+ reduction of MADRS baseline score by 6 sessions received no further treatments as study participants. Some patients were followed up with at 1 week following the completion of the treatment series, as well as 3-, 6-, and 12-month intervals.
- **Results:** In the ECT group, 63% of patients achieved remission vs. 46% in the ketamine group. At the 12-month follow-up period, 64% of initial remitters in the ECT group relapsed compared with 70% in the ketamine group.
- **Conclusion:** Remission rates were significantly higher and decreases

in MADRS scores were significantly larger in pts after ECT treatment than after ketamine infusion treatment. Ketamine was shown to be inferior to ECT for hospitalized patients with unipolar depression.

- **Limitations:** Patients received different amounts of treatment sessions from one another and were cut if they were considered “non-responders” at the halfway point (6 treatments). This may have affected patient outcomes.

Next Steps

- Given mixed findings, further research is needed to compare the efficacy of ketamine infusion therapy to ECT for patients with TRD and evaluate its potential to become a mainstream treatment.
- Once further research is completed, Mid Coast Hospital ACU-OPD could consider integrating ketamine infusion therapy as an additional treatment option for patients with depression.

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