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Chris Aiken, MD
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How Long Should We Continue Esketamine?

Steven Hamilton, MD, PhD. The Permanente Medical Group, Department of Psychiatry, Kaiser Permanente San Francisco Medical Center.

Dr. Hamilton has no financial relationships with companies related to this material.

Highlights From This Issue

Feature article. Psychotherapy may help patients stay well after esketamine, but we lack clearly effective strategies here (other than continuing esketamine).

Q&A. Consider ECT for depression that is severe, catatonic, or psychotic.

Research update on page 6. Hospitalization for suicidality comes with risks. Those who made recent attempts (within one week) are most likely to benefit.

In 2019, the FDA approved intranasal esketamine (Spravato) in treatment-resistant depression (TRD), followed soon after by an indication in depression with suicidality. The move ignited a wave of excitement for this glutamatergic dissociative anesthetic, first synthesized as racemic ketamine half a century ago. With its efficacy in TRD and rapid action, esketamine filled several unmet needs. But as its use has grown, so have questions about how long to continue the treatment.

A typical course of treatment

The standard protocol for esketamine involves administering it twice weekly for four weeks, followed by four weekly treatments. Doses must be given in a supervised (office or inpatient) setting, and providers must be enrolled in

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Q&A With the Expert

ECT: An Update
W. Vaughn McCall, MD, MS

Professor Emeritus, Department of Psychiatry and Health Behavior; Medical College of Georgia, Augusta University.

Dr. McCall reports that he is a consultant for Alza TV, Axon Medical Technologies, Carelon, Haleon, and Idorsia. Dr. Aiken has reviewed this educational activity and has determined that there is no commercial bias as a result of this financial relationship.

TCPR: Who is ECT best for?

Dr. McCall: Let's start with the FDA label, which was updated in 2015. ECT is indicated for severe major depressive episodes that are treatment resistant (ie, two failed antidepressant trials) or require a rapid response. The approval covers bipolar and unipolar depression for ages 13 and up, and the 2015 update adds coverage for catatonia. The update also moved ECT from a Class III to a Class II device, which is a big change. Class II devices require some training to use but have more established safety and efficacy. They include devices such as catheters, powered wheelchairs, and transcranial magnetic stimulation (TMS) (Luchini F et al, *World J Psychiatry* 2015;5(2):182–192).

TCPR: What predicts a good ECT response?

Dr. McCall: Psychotic features, catatonic features, and few psychiatric comorbidities. In the past, catatonia was seen as a subtype of

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How Long Should We Continue Esketamine?

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a Risk Evaluation and Mitigation Strategy (REMS) program. These regulations are designed to prevent abuse or diversion of the Schedule III drug, as well as to monitor for blood pressure elevation, sedation, and dissociation after the dose. Other common side effects include dizziness and nausea.

Some patients remain well after that two-month course, but many relapse, and the best approach to prevention remains unclear. Cognitive behavioral therapy has some support, but attempts to sustain the benefits with other medications have failed, including lithium as well as medications that share in esketamine's glutamatergic mechanism like lamotrigine, riluzole, and d-cycloserine (McMullen EP et al, *Adv Ther* 2021;38(6):2795–2820). Only repeated treatments with ketamine/esketamine reliably sustains response.

Recent esketamine trials have tested continuation of this drug at a reduced frequency, much as we do with maintenance ECT. In the acute esketamine trials, this approach did not look promising. Esketamine worked quickly but tended to fizzle out. Several industry-sponsored trials were no longer positive at the 28-day mark in an analysis of eight disparate studies (Hock RS et al, *J Clin Psychiatry.*2022;84(1):21r14086). Importantly, for the subgroup of studies that examined patients with TRD, esketamine remained superior to placebo at 28 days. Longer-term maintenance trials paint a more positive picture, but these trials have problems.

Maintenance trials

Three trials tested long-term maintenance with esketamine: SUSTAIN-1, SUSTAIN-2, and SUSTAIN-3. In SUSTAIN-1, esketamine was either continued or substituted with a placebo in 297 patients who achieved either stable response (n=121) or remission (n=176) in a four-month course of esketamine treatment (Daly EJ, *JAMA Psychiatry* 2019;76:893–903). All patients had tried (and failed) an antidepressant before starting esketamine, and all started a new antidepressant during the trial.

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Intranasal Esketamine (Spravato)	
FDA Indications	Treatment-resistant depression in adults as an adjunct to an oral antidepressant. Major depression with acute suicidal ideation or behavior.
Dosage	Twice weekly for four weeks, then once weekly for four weeks, then every one to two weeks. Start with 56 mg, then increase to 84 mg as tolerated.
Side Effects	• Common: Sedation, dissociation, blood pressure increases, nausea, transient cognitive impairment, bitter taste. • Rare: Respiratory depression.
Interactions	CYP2B6 and CYP3A4 metabolize esketamine and noresketamine with some contribution from CYP2C9 and CYP2C19. Naltrexone and benzodiazepines may interfere with response.
Contraindications	Known hypersensitivity to esketamine or ketamine. Aneurysmal vascular disease or arteriovenous malformation and intracerebral hemorrhage.
Cost	• 56 mg: $784.12 per dose. • 84 mg: $1,171.42 per dose.
Monitoring	Patient must be monitored by a healthcare provider for at least two hours after dosing. Esketamine cannot be dispensed for home use. Provider and patient must be registered with Risk Evaluation and Mitigation Strategy (REMS) program (SpravatoREMS.com).

How Long Should We Continue Esketamine?

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The duration of maintenance therapy was variable (average of four months). Relapse rates were much lower with maintenance esketamine compared to placebo (25.8% vs 58.6%, number needed to treat [NNT]=4 for stable responders; 26.7% vs 45.3%, NNT=6 for remitters).

The SUSTAIN-2 and SUSTAIN-3 trials employed a less rigorous design, testing esketamine continuation open-label and without a control group. Together, they followed 1,950 patients for one to three years on maintenance esketamine, dosed every one to two weeks (most patients were dosed at the two-week interval). These patients tended to stay well, with increasing remission rates over time and minimal loss of response. These trials did not uncover any new safety concerns or tolerance to esketamine's benefits. There were no significant trends in treatment-emergent psychosis, cognitive impairment, substance use disorders, or suicidal ideation. On average, patients tended to stay well on esketamine (Wajs E et al, *J Clin Psychiatry* 2020;81(3):19m12891; Zaki N et al, *Neuropsychopharmacology* 2023;48(8):1225–1233).

Risks

Although no long-term problems showed up in the SUSTAIN trials, potential adverse effects include bladder dysfunction, neurocognitive impairment, and drug misuse. Those problems are well documented in studies of ketamine abuse and the basic science literature. Notably, the therapeutic doses used in the SUSTAIN trials were much lower than recreational levels, and the patient population was also more selective. Patients with personality disorders, recent prominent suicidal intention, psychotic symptoms, substance use disorders, or significant cardiovascular disease were excluded.

In clinical practice, assess for bladder dysfunction by asking about dysuria and hematuria. Detecting cognitive impairment demands more effort, such as periodic monitoring with standardized tools. To monitor misuse, ask about use of online ketamine services during the screening process, and consider random drug screens and use of state prescription drug monitoring programs during maintenance therapy.

What to do

Esketamine is often used for patients who have not responded to other options, and in our experience these patients often need continued treatment to stay well. Psychotherapy offers hope and may be effective for prevention even if it did not work acutely in depression. In the clinic where I practice, we administer the medication in a group format and provide a guided meditation and discussion about the experience.

During maintenance, attempt to increase the intervals between treatments, carefully monitoring longitudinal depression outcomes with standard instruments (eg, Montgomery-Åsberg Depression Rating Scale, Patient Health Questionnaire, Quick Inventory of Depressive Symptomatology) as well as measures of functional improvement (eg, Work and Social Adjustment Scale). Avoid going beyond the FDA-approved maximum dose of 84 mg. Carefully assess whether the patient had a true response to esketamine. Some patients wish to continue esketamine despite experiencing only momentary relief of symptoms without any meaningful improvement. Consider other options for TRD, such as switching to a monoamine oxidase inhibitor, transcranial magnetic stimulation, or augmenting with lithium or a second-generation antipsychotic.

The SUSTAIN-3 trial provides evidence that patients will benefit from reinitiation of esketamine if relapse occurs (Castro M et al, *CNS Drugs* 2023;37:715–723). For a quick visual of esketamine facts, see the table "Intranasal Esketamine (Spravato)" on page 2.

CARLAT VERDICT

Ketamine and esketamine have succeeded as fast-acting therapies for TRD and suicidality. However, we don't have a reliable way to sustain their benefits other than continued dosing. The studies that support continued dosing do not fully rule out the possibility of tolerance and withdrawal.

Ketamine vs Esketamine

Many providers believe that intravenous (IV) racemic ketamine is more effective than esketamine. The bioavailability of IV ketamine is essentially 100%, while intranasal esketamine is about half that. Racemic ketamine also contains both the active enantiomers, while esketamine has only one, and there is scientific debate about which enantiomer is a more effective antidepressant or causes dissociation.

The clinical data, however, are mixed. None of the four studies that compared ketamine and esketamine found a meaningful difference, but these studies were small and only two were randomized (Nikayin S et al, *JAMA Psychiatry* 2022;79(7):736–738). In meta-analytic comparisons, ketamine was the consistent winner, with a large effect size (around 1.0) compared to a small one (around 0.3) for esketamine (Bahji A et al, *Expert Opin Drug Saf* 2022;21(6):853–866). However, these analyses were not based on direct comparisons and involved studies of different designs.

In practice, the decision often comes down to cost. Esketamine is more expensive, but most insurers cover it for treatment-resistant depression or acute suicidality, after prior authorization. Ketamine is generally not covered by insurers so requires more out-of-pocket costs, which vary by clinic.

Expert Interview
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schizophrenia, but it is more recognized as part of severe mood disorders in DSM-5 and ICD-10, where it has its own stand-alone codes (van Diermen L et al, *Br J Psychiat* 2018;212(2):71–80).

TCPR: What does catatonia look like in outpatient psychiatry?

Dr. McCall: Catatonia is very impairing, so you do see it more often in the hospital, including the medical floors where patients may be admitted for altered mental status. In outpatients, you might see severe ambivalence, where they walk into the office and take two steps forward, then stop and take a step back. They don't know if they are going forward or backward, then they sit and they think, "Well, maybe I should stand." There is a tremendous flattening of affect, reduced movements, few gestures, but with a sense of tension about them. It's as if they've been "turned off," but that description belies an internal state of great psychic tension. Catatonia is very responsive to ECT. If you misdiagnose catatonia, the patient may be condemned to a really awful prognosis. It can be fatal, such as from deep venous thrombosis.

TCPR: Are catatonic patients always stuporous, or does it come and go?

Dr. McCall: It can come and go, and relatives might describe that. There is also excited catatonia where patients are pacing, agitated, but in a purposeless way, and this also responds to ECT. Some factors predict poorer response to ECT, like depression with borderline personality disorder. Here the response is not zero, but it is reduced, and they tend to relapse faster (Fink M et, *J ECT* 2016;32(3):149–150).

TCPR: Where does ECT stand in relation to TMS and the ketamines?

Dr. McCall: Two recent studies compared ECT to other interventions, one to intravenous ketamine and another to magnetic seizure therapy (MST), which is different from TMS. MST is an investigational approach that involves producing a seizure with high-powered magnetic fields (Anand A et al, *N Engl J Med* 2023;388(25):2315–2325; Loo C et al, *J ECT* 2024 [Epub ahead of print]). In both trials, the other intervention was essentially equivalent to ECT, but I wouldn't put too much stake in that because the remission rate for ECT in those trials was very low, around 20%. Normally we see 50%–60% remission rates. So either the ECT was suboptimal or the patient selection was so broad that they let a lot of patients in who normally don't respond well to ECT, like people who have psychiatric comorbidities or who barely meet the criteria for major depression *(Editor's note: See the table "Interventional Psychiatry: What to Expect" on page 3).*

"Medical treatments have benefits and risks, so how do we know which wins? The court to which I would appeal is the court of quality-of-life research."

W. Vaughn McCall, MD, MS

TCPR: I believe the ketamine study excluded psychotic patients.

Dr. McCall: Yes. It also took very few hospitalized patients, and it didn't screen out personality disorders. Patients were also limited to nine ECT treatments, while in practice many require 12.

TCPR: What about ECT vs TMS?

Dr. McCall: TMS protocols have become more aggressive over the last two decades, and these changes have been associated with better antidepressant effects. There may be a place of overlap where both ECT and TMS are appropriate for less severe presentations of depression. But ECT is the choice when it comes to patients who have psychotic depression, catatonia, or profound self-neglect such as food refusal with massive weight loss.

TCPR: What should we tell the patient when referring them to an ECT service?

Dr. McCall: I'd start with a discussion about the likelihood of improvement, which is going to depend on the factors above. In the best case, with psychotic features and no significant comorbidities, I tell them, "I have great hopes, like 80% or greater, that this is going to be a life-changing experience." Next, I'd clarify the side effects. There's the nuisance side effects: Patients could wake up from the treatment with a headache, sore muscles, or temporary confusion, and they may feel frightened that they don't know exactly what's going on when they start to wake up. Then we talk about the amnesia, which comes in two forms.

TCPR: What are they?

Dr. McCall: There's anterograde amnesia, where patients' ability to learn and master new information may not be as good for a period of time. Then there's retrograde amnesia, where patients may forget things they knew before starting ECT. For anterograde, I'll caution them not to make important decisions like buying property for a couple of weeks. But with the new ways of doing ECT—right unilateral, ultra-brief titrated ECT, dosed to the individual—about two weeks after it's over, their performance on memory tests looks like it did before they had ECT, or maybe even better.

TCPR: How significant is the retrograde amnesia?

Dr. McCall: How far back the memory loss goes is highly variable, and again it's going to be less with right unilateral ECT. I would say, "What we've got at stake is maybe the last few weeks or even a month of memory—a potential spotty memory loss here and there going back a month before the ECT started." I don't sugarcoat it. Patients find it acceptable if you just tell them straight up what's at stake. They'll say, "The way that I felt the last several months, there is nothing I really need to remember." You can also focus on what will be spared. They're not going to forget the names of their children or events that happened years ago.

TCPR: Are there cases where the amnesia is worse?

Dr. McCall: We still see rare patients who complain of memory loss weeks and months after ECT. It may be that the ECT didn't work all the way and that the cognitive problems are due to residual depression, but we don't know, and I'd be careful not to invalidate their experience.

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TCPR: In the public sphere, some argue that ECT causes brain damage.

Dr. McCall: The Church of Scientology has been spreading that message since its founding in the 1950s, and there is no scientific basis to it. First, "brain damage" is not a medical term. Studies look at *brain injury* and *neuronal injury*, and there is no evidence that ECT causes these things. There is no shrinkage in hippocampal or other volumes on MRI, no increase in biomarkers of neuronal injury, and no increased risk of dementia. Researchers have looked at neuronal cells in primate studies, and there is no injury after ECT. There've been several autopsy examinations of human brains from people who received significant ECT, up to 1,250 treatments, and again no injury. Scientologists have argued that ECT cooks the brain with electricity. However, a recent paper modeled this and found the temperature change during ECT is within the range of normal physiology (Swartz CM, *J ECT* 2024;40(2):72–77; Swartz C et al, *J ECT* 2023;39(3):158–160).

Interventional Psychiatry: What to Expect

Treatment	Frequency	Activity Limitations	Maintenance Schedule (optional)
ECT	1-hour sessions 3 days a week for 3–4 weeks	Cannot drive on day of session, unable to work during treatment	Weekly to monthly
Ketamine (IV) and Esketamine (IN)	30–45 minute sessions Twice weekly for 4 weeks, followed by 4 weekly treatments	Wait 2–3 hours before driving	1–2 per month
SAINT TMS	10-minute treatments, hourly over a 10-hour period for a 5-day course	None beyond time commitment	Unknown
TMS	3–45 minute sessions* 5 days a week for 6 weeks	None	1–8 per month

**3 minutes for intermittent theta burst stimulation (iTBS); 20 minutes for deep TMS (H coil, Brainsway); 45 minutes for traditional TMS (figure-8 coil)*

TCPR: I have seen studies where neuroprotective factors like BDNF increase after ECT.

Dr. McCall: Yes. There is also some increase in brain volume after ECT, which is the opposite of what you'd expect with injury, and it isn't due to swelling either. But those increases fade after about six months, and we don't know if they are linked to ECT's efficacy or not. My own view on this is that medical treatments have benefits and risks, so how do we know which wins? The court to which I would appeal is the court of quality-of-life research. I've had the privilege of working on four clinical trial data sets with ECT, and quality-of-life measures were always better after ECT, not worse (McCall WV et al, *J Psychiatr Res* 2018;97:65–69). Scientologists might argue, "Of course they think their life is better. They are so brain damaged they don't know how bad it is." But we had loved ones rate whether they thought the patient's life had gotten better, and they agreed that the patient's life had improved. The patients were not disabled, but rather enabled.

TCPR: How do you prevent relapse after ECT?

Dr. McCall: The relapse rate is high, and there is a classic study by Harold Sackeim's group that guides us in what to do about it. They found most patients (84%) relapsed within six months with just a placebo. Nortriptyline as monotherapy was better (60%), but the lowest rate was with nortriptyline-lithium combination (40%), and these were all unipolar patients. So that's my go-to strategy, although if a patient has bipolar, I'd use lithium without the antidepressant. The most potent strategy for protection against depressive relapse would be lithium (plus or minus the antidepressant) plus step-down, continuation ECT on a weekly basis for four weeks. Additional ECT after that point would be on a case-by-case basis (Sackeim HA et al, *JAMA* 2001;285(10):1299–1307).

TCPR: I looked at that study and noticed nearly all the relapses in the lithium group were in the first month.

Dr. McCall: Yes, the first month is a precarious time, and step-down ECT may help there. This is when you taper down the ECT, giving it weekly for an extra month after the usual course. I was part of a study led by Charlie Kellner that tested this in a controlled trial of older adults, and the four or five step-down treatments protected against relapse for an additional month without any worsening of cognition (Kellner C et al, *Am J Psychiatry* 2016;173:1110–1118).

TCPR: How do we manage medications when patients are receiving ECT?

Dr. McCall: We tend to continue the antidepressant. Lithium is less clear. There's some literature suggesting an adverse interaction with ECT if the serum levels are 0.7 mEq/L or higher, such as causing confusion. Some hold the lithium the night before ECT, and others stop it altogether during treatment. If the patient is taking an anticonvulsant for bipolar disorder, we worry that it might interfere with the seizure threshold, so we often lower the dose.

TCPR: What about benzodiazepines?

Dr. McCall: Benzodiazepines can also interfere with seizures, but they are hard to completely get rid of, so we may reverse it during the anesthesia or apply anesthesia with flumazenil. Also, patients can't have anything by mouth on the morning of ECT to prevent aspiration, so we try to hold everything but the most essential meds then. But for all of these decisions, you can usually defer to the ECT team.

TCPR: Thank you for your time, Dr. McCall.

Research Updates IN PSYCHIATRY

SUICIDE

Does Psychiatric Hospitalization Prevent Suicide Attempts?

Vishwani Sahai-Siddiqui, MD. Dr. Sahai-Siddiqui has no financial relationships with companies related to this material.

REVIEW OF: Ross EL et al, *JAMA Psychiatry* 2024;81(2):135–143

STUDY TYPE: Analysis of past data using machine learning

When a patient presents with active suicidality, we usually recommend psychiatric hospitalization to keep them safe. But does this actually reduce future suicidality? This study looked at whether hospitalization is effective in preventing future suicidality and aimed to create a personalized approach using advanced data analysis.

Investigators analyzed data from 196,610 visits to EDs and urgent care clinics by veterans who had either suicidal ideation (SI) or suicide attempts (SAs) between 2010 and 2015. Patients were grouped based on their psychiatric diagnosis and on the nature and timing of their suicidality (SI only, SA in the past week, or SA the day before). The primary outcome was whether patients had another SA within the next year.

- About 71.5% of these patients were hospitalized, and the rest were discharged home. The overall risk of another SA within a year was 11.9% for those who were hospitalized and 12.0% for those who weren't, a negligible difference.
- Hospitalization significantly reduced SA risk in patients with an SA within the past day, with reductions ranging from 6.9% to 9.6% across diagnoses.
- Overall, no significant risk reduction was observed for patients with SI only or an SA in the past two to seven days. The exceptions to this trend were patients with depression who had an SA two to seven days prior to the visit—hospitalization did lower future risk of SA for this group.
- The machine learning model identified that hospitalization reduced SA risk in 28.1% of patients but increased it in 24.0%.

CARLAT TAKE

Assessment of suicidality should be done case by case. Hospitalization for suicidality should not be a reflex decision. Those most likely to benefit with respect to future suicidality are patients with SAs the day before, or, in the case of depression, within the past week. However, for those with SI or more remote SAs, hospitalization does not clearly demonstrate benefits and may even pose risks.

ANXIETY

Benzodiazepines, Quetiapine, and Pregabalin for Short-Term Anxiety

Dominic Le, MD. Dr. Le has no financial relationships with companies related to this material.

REVIEW OF: Munkholm K et al, *Eur Arch Psychiatry Clin Neurosci* 2024;274(3):475–486

STUDY TYPE: Meta-analysis of placebo-controlled trials

Patients often ask for rapid-acting medications for the short-term treatment of anxiety, but how safe and effective are the options?

Researchers reviewed randomized controlled trials (RCTs) that examined benzodiazepines, sedating antipsychotics and antidepressants, antihistamines, melatonin, Z-drugs, and pregabalin for treating acute stress disorder, adjustment disorder, mild to moderate depression, and anxiety. Primary outcomes were the Hamilton Rating Scale for Anxiety (HAM-A), daily functioning, and serious adverse events.

Their search yielded 34 RCTs involving 7,044 patients. Benzodiazepines, quetiapine, and pregabalin significantly reduced anxiety compared to placebo. Compared to placebo, the standardized mean differences on the HAM-A after one to four weeks of treatment were -0.58 (95% confidence interval [CI]: -0.77 to -0.40) for benzodiazepines, -0.51 (95% CI: -0.90 to -0.13) for quetiapine, and -0.58 (95% CI: -0.87 to -0.28) for pregabalin. Notably, no significant differences in symptom reduction were found between them. However, the authors rated the certainty of this evidence as low to very low. Only a handful of trials reported symptom chronicity—a significant absence, as the focus of this review was on acute symptoms. Adverse side effects were inconsistently reported, and thus researchers did not draw conclusions regarding tolerability.

CARLAT TAKE

In this study, quetiapine and pregabalin are viable alternatives to benzodiazepines for treating new-onset acute anxiety over short time periods. When choosing among them, consider cardiac history, as quetiapine is associated with the risk of arrhythmia, as well as metabolic side effects and tardive dyskinesia. Generally, aim for quetiapine ≤ 150 mg daily, starting as low as 12.5 mg every eight hours as needed. When dosing pregabalin, consider chronic kidney disease due to its renal excretion. For most patients, start at 75 mg twice daily.

NEUROMODULATION

Magnetic Seizure Therapy: A Safer, Gentler Alternative to ECT?

Dee Rapposelli. Ms. Rapposelli has no financial relationships with companies related to this material.

REVIEW OF: Deng ZD et al, *JAMA Psychiatry* 2024;81(3):240–249

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CME Post-Test

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1. What is the recommended initial dosing protocol for intranasal esketamine in treatment-resistant depression?
   - [ ] a. Twice weekly for eight weeks, followed by weekly treatments
   - [ ] b. Twice weekly for four weeks, followed by weekly treatments for four weeks
   - [ ] c. Weekly treatments for eight weeks
   - [ ] d. Daily treatments for two weeks, followed by biweekly treatments

2. Which clinical feature most strongly predicts a good response to ECT?
   - [ ] a. Psychotic features in depression
   - [ ] b. Multiple psychiatric comorbidities
   - [ ] c. Personality disorder traits
   - [ ] d. Mild depressive symptoms

3. In a 2024 study by Ross et al on psychiatric hospitalization for patients presenting with suicidality, findings indicate that:
   - [ ] a. Hospitalization reduces the risk of future suicide attempts in all patients with suicidal ideation or recent suicide attempts
   - [ ] b. Hospitalization is most effective in reducing suicide risk for patients who attempted suicide within the past day
   - [ ] c. Hospitalization substantially reduces risk for patients with suicidal ideation but no recent suicide attempts
   - [ ] d. Hospitalization increases future suicide risk for all patients with psychiatric diagnoses

4. Which strategy is recommended for long-term esketamine maintenance treatment?
   - [ ] a. Annual cognitive assessments and monitoring only if symptoms arise
   - [ ] b. Weekly drug screening and urine tests for bladder function
   - [ ] c. Continued esketamine therapy without additional monitoring
   - [ ] d. Periodic assessment of depression and cognition

5. According to the FDA, ECT is indicated for severe bipolar or unipolar depression that is treatment resistant or requires a rapid response, as well as for catatonia.
   - [ ] a. True
   - [ ] b. False

Research Updates

Continued from page 6

STUDY TYPE: Randomized clinical trial

ECT is fast-acting and very effective for severe treatment-resistant depression (TRD). However, despite refinements, the risk of adverse neurocognitive effects remains. Magnetic seizure therapy (MST) uses the same principle as transcranial magnetic stimulation (TMS) but at higher, seizure-inducing doses. This can induce more focal, less stimulatory seizures than ECT. Several small studies have shown a benefit. The efficacy and safety of MST, previously demonstrated in these smaller studies, was finally confirmed in a multicenter, double-blind randomized clinical trial of MST vs ECT.

The trial included 73 adults with severe TRD. A total of 38 subjects were randomized to standard ultrabrief pulse, right unilateral ECT, while 35 subjects were randomized to MST (which induces seizures at the brain's vertex). The treatment groups were equivalent in terms of anesthesia protocols, as well as in demographic characteristics such as age, sex, race/ethnicity, education level, and depression severity. The primary endpoint was change from baseline in total score on the 24-item Hamilton Depression Rating Scale (HDRS-24). Response was defined as a reduction in HDRS-24 of at least 50%. Remission was defined as a reduction of at least 60% and a total score of 8 or less. Patients were followed for up to six months.

No significant differences were seen between groups in rates of response (51% MST vs 43% ECT) or remission (45% MST vs 42% ECT). Sustained benefit across six months

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also was similar. The mean number of treatments to remission, however, was greater for MST (9 vs 7). This concerned the study authors because the increased exposure to general anesthesia required during the treatment course could have deleterious effects. They noted that dosing studies are warranted to see if treatment time to remission can be optimized.

MST did display some benefits over standard ECT. Time to orientation was much more rapid, and autobiographical memory was sharper. Two cases of nausea/vomiting were reported following treatment with MST whereas five serious adverse events occurred in the ECT group, including three cases of worsening depression, one case of increased blood pressure, and one case of prolonged ictal agitation.

CARLAT TAKE

This study suggests that MST is as effective as ECT. It required an average of two more sessions than ECT, but it was also associated with fewer serious adverse events—especially fewer cognitive side effects.

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