Electroconvulsive Therapy
Evidence and Challenges

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Electroconvulsive therapy (ECT) is a treatment for severe psychiatric illnesses. In 2001, a JAMA editorial1 accompanying a report2 of continuation medication treatments after ECT reviewed the evidence for efficacy, the risks of relapse, and the controversies in electrode placement and memory effects. Additional studies warrant another look at this treatment.

Present ECT techniques use sedation, muscle paralysis, ventilation with oxygen, and brief-pulse electrical stimuli that virtually eliminate the past risk of fracture and minimize transient cognitive dysfunctions. The mortality rate (about 2 deaths per 100,000 treatments) is less than that reported for normal childbirth and is associated with the anesthesia risks.3

Remission Efficacy for Depressive Illness

Many studies documenting the efficacy of ECT for depressive illness have been published,3 finding ECT superior to “sham” ECT and to medications in the treatment of patients with severe depressive illness. Two multisite collaborations—the Consortium for Research in ECT (CORE)4 and Columbia University Consortium (CUC)2—studies are illustrative. Both were designed to examine relapse prevention after successful ECT involving patients with major unipolar depression. The 2 patient groups were similar in mean age (53 and 59 years), sex ratio (70% female), and pretreatment severity (mean Hamilton Depression Scale scores, about 34). Index episode duration was 24 to 31 weeks (CUC study) and 45 to 49 weeks (CORE study). At remission, the mean Hamilton scores were 5 to 6 (±3).

Remission rates were 55% (159 of 290 patients completing the CUC study) and 86% (341 of 394 patients completing the CORE study). These results compare favorably to the initial 30% remission rate with citalopram and the remission rates of about 23% with bupropion, 21% with sertraline, and 25% with venlafaxine for patients who did not respond to citalopram in the Sequeined Treatment Alternatives to Relieve Depression (STAR*D) trial of outpatients with nonpsychotic major unipolar depression.3

Relapse Prevention

Although many patients’ depressive illness remits with proper treatment, relapse is frequent and preventive continuation treatments, often for months and occasionally longer, are necessary. In the CUC study, patients whose depressive illness had remitted were randomly assigned to continue taking either placebo, the tricyclic antidepressant nortriptyline alone, or the combination of nortriptyline and lithium. Both treatments were monitored for adequacy of blood levels.2 Using the same dosing and serum level monitoring standards, the CORE study compared the combination of lithium and nortriptyline with continuation ECT on a rigid schedule.4

In the CUC study, 84% of those receiving placebo, 60% receiving nortriptyline, and 39% receiving the combination medication had relapsed by 6 months. The 6-month relapse rate for the nortriptyline-lithium combination in the CORE study was 32% and 37% for ECT. There was a slight advantage for continuation ECT in the time to relapse, 9.1 weeks vs the medication’s 6.7 weeks.4

The benefit of continuation ECT confirms clinical practice.3 Although continuation medication is easier to administer and is preferred, continuation ECT is useful for patients who relapse despite the prescription of medications and for those who may not tolerate medication trials.

Efficacy in Psychotic Depression

About 37% of the patients in the CORE study were psychotic.4 Remissions appeared earlier and were more robust than for those without psychosis, 95% vs 83%.6

Commonly recommended treatment algorithms for psychotic depression find that antidepressants alone achieve about a 30% remission rate, antipsychotics about 50%, and the combination about 70% over 4 months.7 The response rate to ECT is higher and occurs within 4 weeks. Thus, ECT is a primary treatment for psychotic depression and is preferred to multiple medication trials.7,8

It is common, however, for patients with psychotic depression to be inadequately treated before referral for ECT. Only 2 of 52 (4%) of patients with psychotic depression in the CUC study and only 5 of 106 patients (5%) in the CORE study had received adequate antidepressant and antipsychotic medication trials.9,10 Failure to identify the psychotic form of the

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Depressive illness and inadequate pharmacotherapy are possible explanations.

**Impact on Suicide Risk**

Suicide is a principal cause of death of patients with mood disorders, with half of the suicides in the United States occurring within weeks of seeing a medical caregiver, often a primary care physician. Antidepressant agents have no demonstrated acute effect on suicide risk but may have a weak effect by reducing the number of depressive episodes. The long-term risk is substantially reduced when patients are treated with lithium.

Electroconvulsive therapy reduces the acute risk. In the CORE study, 29.5% of the patients were rated on the Hamilton scale at baseline as expressing suicidal thoughts or reporting suicidal acts. Those scores were reduced to 0 after a week in 38% of patients, after 2 weeks in 61%, and at the end of the course in 81%. These findings are consistent with CUC reports.

**Effect of Prior Medication Treatment**

Depressed patients are characterized as “treatment resistant” when they do not respond to 2 antidepressant treatment trials estimated as adequate for dosing and duration. Sufficiency of prior medication trials can be estimated using an Antidepressant Treatment History Form (ATHF). Some authors report that nonresponders to adequate pharmacotherapy before ECT are substantially less likely to respond to ECT than patients experiencing inadequate pharmacotherapy. In the CORE study, adequacy of prior treatment, assessed with the ATHF, bore no relation to treatment efficacy.

**Effect of Electrode Placement**

Seizures are induced using two electrodes placed on the head, and many placements have been extensively studied. In bilateral ECT, the electrodes are applied to both temples. In unilateral ECT, 1 electrode is placed on the nondominant temple (right usually) and a second near the vertex on the same side. Unilateral ECT was introduced as a strategy to reduce the immediate subjective confusion and verbal memory problems accompanying treatments.

The different remission rates between the CUC and CORE studies may be ascribed to different electrode placements and energy dosing. The CORE study used bilateral ECT and energy dosages 50% above the calibrated seizure threshold for all patients. The CUC study used unilateral ECT with energy dosing set at 150% above the seizure threshold. Other studies found that energies in unilateral ECT must be 6 to 8 times above the seizure threshold to match the efficacy of bilateral ECT.

In the CUC study, patients first received a mean of 7 unilateral ECT treatments, followed by bilateral treatments for a total mean of 10.5 treatments to remission. In the CORE study, the average mean of bilateral treatments to remission was 7.3, a savings of about 3 anesthesia inductions and seizures. The ease of use of bilateral ECT, in which the energy dosing can be estimated by age-related algorithms, its consistent achievement of remission and the only modest cognitive advantage of high-dose unilateral ECT support the continued clinical use of bilateral ECT.

**Brain Stimulation**

Recent interest in stimulating the brain has focused on the technologies of repeated transcranial magnetic stimulation, vagus nerve stimulation, and deep brain stimulation. The last 2 require surgical intervention to implant devices and electrodes. Because these modalities do not elicit grand mal seizures, they have been suggested as replacements for ECT on the stated assumption that the treatments will achieve equivalent reductions in depression and lesser effects on memory. However, the efficacy of these interventions in relieving depressive illness is not established. The latest randomized study (n=46) comparing repeated transcranial magnetic stimulation and ECT established a significant reduction in the Hamilton scores for ECT (58%) but not for repeated transcranial magnetic stimulation (22%), despite ECT treatment characteristics that were not optimal (unilateral ECT at 2.5 times the calibrated seizure threshold).

Although the US Food and Drug Administration (FDA) approved vagus nerve stimulation for resistant depression based on marginal efficacy data, insurance providers are refusing to reimburse for these procedures, and this approval for resistant depression is undergoing reexamination by the FDA. The deep brain stimulation experience is too limited to be clinically applied except in a proper research setting.

**Conclusions and Needs**

The 2 collaborative ECT studies summarized above are recent hallmarks of ECT research, verifying the treatment’s antidepressant efficacy, the need for continuation treatment, and the relative efficacy of different electrode placements. Ongoing studies examine the effect of concurrent antidepressant use on ECT efficacy and relapse rates.
Electroconvulsive therapy practice is unregulated, and the education of physicians in its prescription and administration is poor. Electroconvulsive therapy is not a required subject in US medical schools and, surprisingly, is not a required skill in psychiatric residency training. The lack of experience with ECT during residency training and the failure to require such experience for specialty certification limits the ability of clinical psychiatrists to recognize patients for whom ECT may offer effective relief.

Privileging for ECT practice at institutions is a local option, no national certification standards are established, and no ECT-specific continuing training experiences are required of ECT practitioners. As a consequence, unsettling observations of variable clinical practices have surfaced. These include lower remission rates in community hospital services (30%-47%) and higher 6-month relapse rates (77%) than in the academic CUC and CORE studies.23 By contrast, the UK Royal College of Psychiatrists has adopted a voluntary certification scheme that warrants study in the United States.24

The ECT devices approved for use in the United States are limited in their energy range, making it impossible to deliver the high energies necessary for effective unilateral ECT in older patients. Seizure threshold increases substantially with age.3 For unilateral ECT to be administered with assured equivalent efficacy as bilateral ECT, a revision of the FDA instrument standards will be required. Electroconvulsive therapy devices in Canada and Europe deliver twice the energy of US instruments.

The therapeutic mechanism of ECT is not well studied. After more than 70 years of clinical experience, with the efficacy and safety ensured, a sustained search for why induced seizures relieve mood disorders is overdue. Many theories have been proposed.1,2,4 Differences among patient groups in concentrations of brain glia, psychodynamic interpretations, and alterations in neurochemical activity have not illuminated the therapeutic process. Although induced seizures elicit neuronal changes similar to those found in myocytes in cardiac defibrillation, this mechanism has not been studied in ECT.

Another hypothesis derives from compelling data that vegetative dysfunction and abnormal hormone regulation characterize mood disorders. These functions are normalized with repeated seizure inductions, perhaps through the release of extraordinary amounts of brain peptides and subsequent systemic hormonal changes.7,25 At present, this neuroendocrine model offers the best opportunity for understanding the ECT process.

Despite its well-documented efficacy and safety, ECT is widely stigmatized as a last-resort treatment. This image is largely the result of professional and public preoccupation with the effects of ECT on memory and the failure to fairly consider the treatment’s benefits compared with alternative treatments. The high incidence of chronicity and recurrence in severe psychiatric illnesses should encourage greater attention to improvements in ECT practice and to studies of its mechanism of action.

Financial Disclosures: Dr Fink reported that he receives book royalties that are paid to the Scion Natural Science Association, a nonprofit research organization. Dr Taylor reported that he receives royalties from books on related topics.

REFERENCES