Clinical Review

A Review of the Utility of Electroconvulsive Therapy in the Treatment of Psychiatric Illness

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Introduction

Depression, bipolar disorder, and other mental illnesses are becoming increasingly recognized, with millions of individuals suffering worldwide. There is now a good evidence base that people with mental illness utilize healthcare services far more frequently than those without such disorders.[1] Increases in the costs of healthcare delivery to these individuals add millions of dollars per year to healthcare costs for the whole population.[2] As a result, non-psychiatrists and primary care providers are called upon to treat patients with psychiatric problems; primary care has been called the "de facto mental health system."[3] Although safe and effective somatic treatments are available, medicine still has a long way to go in satisfactorily alleviating the suffering of mental illness. It is therefore imperative that physicians who see patients with mental illness have at least basic awareness of safe and effective treatments.

Pharmacologic treatment of depression

The Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial was designed to define which subsequent treatment strategies, in what order or sequence, and in what combination(s) were both acceptable to patients and provide the best clinical results with the least side effects.[4] One of its many outcomes was that treatments were effective, but approximately 33% of patients responded at the first treatment stage, with declining response rates thereafter.[5-10] Furthermore, after a year of concerted treatment, 33% of patients remained ill. The experience of this trial is illustrative of the fact that better treatment options are needed for patients with persistent depression.

History of electroconvulsive therapy

In 1934, Ladislas Joseph von Meduna, a Hungarian neuropsychiatrist, conducted the first experiments in which patients with schizophrenia were treated by inducing repeated seizures. Observational reports had circulated noting that symptoms of dementia praecox (e.g., schizophrenia) were diminished when patients developed epilepsy (e.g., after head trauma or neurologic illness), and that patients with epilepsy had a low incidence of psychosis. Further, Meduna's own neuropathology studies found that the glial cell concentrations in the brains of patients with epilepsy were much higher than normal, whereas glial cell concentrations in the brains of patients with schizophrenia were much lower. Meduna hypothesized that seizures may be "protective" against psychosis and that inducing convulsions in patients with schizophrenia could reduce their symptoms.[11]

Meduna began by giving patients intramuscular injections of camphor, which was a known stimulant medication at lower doses. However, since camphor was painful and variable in its effect, he switched to pentylenetetrazol (Metrazol), a more refined synthetic substance. Although this method promoted seizures, clinical efficacy varied, and numerous adverse effects (especially a sense of panic) were troubling.[12] In 1937, the Italian neuropsychiatrists Ugo Cerletti and Lucio Bini began to induce seizures experimentally with electricity.[13-15] They found that seizures could be more easily induced and regulated with electricity than with pharmacological agents, thereby decreasing the number of missed or recurrent seizures. Electricity quickly replaced pentylenetetrazol as the method of inducing convulsions. Within a few years, electroconvulsive therapy (ECT) became the dominant somatic treatment, not only for schizophrenia but also for major mood disorders.[12]

In 1952, Drs. Holemberg and Thesleff introduced "modified ECT" by using a combination of succinylcholine (muscle relaxant) and barbiturates. A short-acting anesthetic was usually given in addition to the muscle relaxant to spare patients the terrifying feeling of suffocation that can be experienced with muscle relaxants.

The image that many people may have of ECT is from the movies — Jack Nicholson's character in "One Flew Over the Cuckoo's Nest" or Russell Crowe's character in "A Beautiful Mind." As a result, ECT may seem outdated and barbaric, and some even equate ECT providers to criminals. That image is neither accurate nor truthful with current ECT practice.

However, the promise of novel psychopharmacologic agents (with the possible exception of clozapine for schizophrenia) has still left the mental health field with more questions than answers. In the meantime, ECT is still a viable antidepressant treatment option.

Indications for ECT

Depression

Meta-analyses have found that electroconvulsive therapy (ECT) is more efficacious than any other treatment used for severe major depression.[16-19] It is estimated that remission occurs in 70-90% of patients who receive ECT, based on randomized trials.[16,20] This compares with a remission rate of approximately 30% for citalopram in outpatients with nonpsychotic unipolar major depression.[5]

Another meta-analysis of 15 randomized trials (585 patients) compared the effectiveness of ECT with other forms of treatment for depression that included antidepressant medication, transcranial magnetic stimulation, cognitive-behavioral therapy and "sham" ECT. (i.e., ECT without electricity being delivered)[18] The analysis found a significant and large clinical effect favoring ECT. In addition, the specific comparison of ECT with medication also found a significant and large clinical effect favoring ECT. Patients with depression and psychosis had a better response to ECT than those with nonpsychotic depression.

Bipolar disorder

Reviews have reported improvement in approximately 80% of manic patients treated with ECT.[21] This finding is even more impressive considering that many of these patients did not respond to pharmacologic therapy. ECT can also be effective in patients with bipolar depression. One recent randomized, multi-center trial found that ECT was more effective than pharmacological treatment in the acute phase of treatment-resistant bipolar depression.[22]

Schizophrenia

ECT is also an effective treatment option in patients with schizophrenia. In one study in patients with clozapine-resistant schizophrenia, the addition of ECT to pharmacotherapy led to improvement in 50% of participants.[23] A Cochrane Review noted: "The evidence … suggests that ECT, combined with treatment with antipsychotic drugs, may be considered an option for people with schizophrenia, particularly when rapid global improvement and reduction of symptoms is desired. This is also the case for those with schizophrenia who show limited response to medication alone."[24] There is also some evidence that ECT can be used for relapse prevention in patients with schizophrenia.[25] Other indications for ECT include catatonia and neuroleptic malignant syndrome. At Wake Forest Baptist Medical Center, we currently have an active "RUL ECT versus bilateral ECT treatment catatonia study," in which 30 catatonic participants with psychiatric disorders will be recruited in a randomized trial.

Mechanisms of Action

Studies of the mechanisms behind ECT's effects in both clinical and animal studies indicate that ECT increases release of monoamine neurotransmitters, particularly dopamine, serotonin, and norepinephrine.[26-29] ECT also enhances monoamine transmission by desensitizing presynaptic adrenergic autoreceptors. Thus, there are two main hypotheses to explain ECT's effects — neuroendocrine and neurotrophic. Each will be reviewed briefly here.

The neuroendocrine hypothesis suggests that ECT relieves depression by causing the hypothalamus or pituitary gland to release hormones, including prolactin, thyroid-stimulating hormone, adrenocorticotropic hormone, and endorphins.[26] ECT has anticonvulsant properties (perhaps related to neurohormones and enhanced gamma-aminobutyric acid transmission), which has led to the suggestion that these properties are responsible for its therapeutic effects of the treatment.[26]

On the other hand, the neurotrophic hypothesis suggests that ECT works by increasing neurotrophic signaling and inducing neurogenesis (i.e., brain structural plasticity).[26,30-36] Multiple studies have found that ECT increases brain-derived neurotrophic factor and gray matter volume in the

hippocampus, amygdala, and temporal lobes.[30-36] Positron emission tomography studies demonstrate decreased metabolic activity in frontal and cingulate cortex after ECT.[37]

In addition, ECT may change brain connectivity. One functional magnetic resonance imaging (fMRI) study before and after successful treatment with ECT revealed a reduction in global connectivity within the left dorsal lateral prefrontal cortex,[38] whereas another fMRI study found increased right hippocampal connectivity,[39] and a structural study found increased connectivity in dorsal fronto-limbic circuits.[40] Quantitative electroencephalogram studies have demonstrated increased slow (delta) wave activity in the prefrontal cortex after ECT, which is associated with clinical response.[41]

Patient Referral

There are five goals in the evaluation of patients receiving ECT.

1. Obtain a complete psychiatric history and delineate the indication for ECT.
2. Review the patient's preexisting medical conditions and ongoing treatments; determine what further evaluation, testing, or consultation is needed to evaluate potential risk levels.
3. Recommend appropriate modifications of the ECT procedure to minimize risks and maximize benefits.
4. Make a risk-benefit comparison of all viable treatment options.
5. Initiate the informed consent process.[42]

ECT is a medically safe procedure. However, there are some conditions that may increase risks associated with ECT, such as recent (i.e., within 3 months) intracranial hemorrhage, recent (i.e., within 3 months) thromboembolic stroke, intracranial lesion (tumor or infection) causing mass effect, recent (i.e., within 3 months) myocardial infarction, particularly if sequelae are present, unstable angina or decompensating heart failure, or unstable vertebral fracture.[12] These risks highlight the importance of obtaining a complete history, as described in the evaluation above.

ECT has been safely and successfully used in patients with stable atrial fibrillation, stable angina, hypertension, and pacemakers.[43] In addition, ECT has been safely and successfully used in patients with diabetes, asthma, chronic obstructive pulmonary disease, epilepsy, pregnancy, hepatitis, history of head trauma, and many other concomitant medical conditions. Thus, the presence of one or more of these conditions should not automatically rule out the use of ECT.

Part of the medical workup includes:

1. Obtaining laboratory data dependent on clinical condition. At a minimum, a complete blood count and basic metabolic panel should be obtained.
2. Obtaining an evaluation by an anesthesiologist to assess if the patient is healthy enough to safely undergo general anesthesia as part of the ECT session.
3. Checking for loose teeth. Dental damage is a reason that physicians are sued after a course of ECT.
4. Eliminating or minimizing anticonvulsants over 1-2 weeks.
5. Ensuring that gastrointestinal and cardiac medications are taken on the morning of the ECT session, since convulsion will increase intragastric and intracardiac pressure.

Treatment Course

As with other elective medical procedure, written informed consent must be obtained before ECT. ECT is typically begun with three sessions a week for a total dose of 6-12 treatments. The frequency depends on assessment of the treatment's efficacy with potential rate-limiting side effects, such as short term memory problems or headache.[44] Typically, physicians will administer objective rating scales to patients, such as the Hamilton Rating Scale for Depression,[45] to assess response. Treatments continue until patients respond, there are rate-limiting side effects, or until there is a plateau in response.

Before each ECT session, patients should be fasting, except for any cardiac or GI medications. Medical staff recheck the patient's history, ensure fasting status, and place an intravenous line. An anticholinergic agent, such as glycopyrrolate, is administered. During ECT, vagal reflexes are induced on two separate occasions. The first occurs immediately following the electrical stimulus and may be associated with a transient bradycardia or asystole, usually not lasting more than 5–7 seconds.[46] The second may occur as the seizure ends, when a resulting transient bradycardia

may be associated with atrial or ventricular ectopy. It is considered standard of care to premedicate with a muscarinic anticholinergic agent, which may decrease the likelihood and severity of bradycardia or asystole due to vagal effects.[47]

Typical anesthetic agents include barbiturates such as methohexital. Methohexital has the advantages of rapid action, low cardiac toxicity, and a low incidence of postanesthesia confusion.[48] The anesthetic agent is rapidly followed by a paralytic agent, such as succinylcholine. Often, ulnar nerve stimulation is used to assess adequacy of muscle relaxation.

The motor seizure itself lasts 30-60 seconds. The electroencephalographic part of the seizure will typically last 30-120 seconds. Any increases in heart rate that could be considered to be risky in patients in coronary artery disease can be managed during treatment with beta blockers such as esmolol or labetalol.

Continuation/Maintenance Treatments

Algorithms have been developed[49] to help guide clinicians in determining how many more treatments a patient may need after the initial course. Some patients may need treatments biweekly or monthly for an indefinite period, in addition to medication and psychotherapy. The frequency of maintenance treatments should be determined based on the history of the patient's response to maintenance ECT, severity of the patient's current symptoms, degree of cognitive impairment, and practical considerations (e.g., availability of transportation).

Case presentation

A 52-year-old woman with a history of diabetes presented for a routine office visit to the Department of Family Medicine. She has a long history of major depressive disorder, with multiple prolonged psychiatric hospitalizations. She has tried numerous antidepressant medications, with limited success. She has stopped working because of her depression. She has also been in weekly psychotherapy with limited effectiveness. Her hemoglobin A1c is 11.5% and her fasting glucose is 250 mg/dl.

The patient was referred to an ECT provider. She received 10 right unilateral treatments of ECT, at a frequency of three times a week. She responded to the treatment and she received 4 weekly continuation treatments. At her primary care follow-up appointment 6 months later, she was no longer depressed, which allowed her to be more compliant with her diabetic regimen. Her hemoglobin A1c was 6.5%, and her fasting glucose decreased to 95 mg/dl.

Conclusion

As one of the oldest treatments still utilized in modern psychiatric practice, ECT remains valuable and should be considered as part of the therapeutic arsenal for treating patients with continuing depression.

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