Electroconvulsive therapy and its use in modern-day psychiatry

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Electroconvulsive therapy (ECT) has been regarded as a somewhat controversial treatment modality. Despite initial stigmatisation, ECT has remained with us for the past 60 years and is now emerging as a safe and effective treatment option.

ECT is indicated in a wide range of disorders and is often found to be of equal or even superior efficacy compared with currently available pharmacological agents. However, it is not without adverse effects and therefore a sound knowledge of this treatment modality is crucial before its administration. The clinician should have a thorough knowledge of indications, method of administration, patient preparation, required seizure duration, treatment course and side-effect profile.

When Ugo Cerletti and Lucio Bini first introduced electroconvulsive therapy (ECT) in 1938 it was the only effective treatment available for mania and depression.[1] Although ECT was found to be very effective, the introduction of imipramine by Roland Kuhn in 1957 led to a considerable decline in the use of ECT. In the late 1970s the introduction of the phenothiazines and lithium reduced the use of ECT even further.[1]

The first ECTs were administered without anaesthesia or muscle relaxants, which often resulted in patients sustaining fractures of the spine and long bones as well as dislocations. In the early days of ECT, patients were often lined up in dormitories and treated *en masse*[2] at certain hospitals. ECT was also commonly administered in the psychiatrist's office without any emergency equipment being available. Some psychiatrists made house calls and administered the ECT in the patient's own bed.[2]

Inhumane methods of ECT administration had already contributed to its stigmatisation by the time muscle relaxants were introduced by Bennet in 1946. Despite refinement of the technique and increased safety of the procedure, use of ECT was discontinued completely in some states in the USA in the early 1980s because of pressure from politically motivated groups.[1,2]

Use of ECT has, however, reached new heights of recognition as a safe and effective treatment for various psychiatric disorders. This is mainly due to good clinical results and various research publications confirming the efficacy and safety of the procedure. A Medline search of appropriate articles with 'ECT' or 'electroconvulsive therapy' in the title published since 1975 were included in this study.

The aim of this article is to give a general overview of the use of ECT and an updated overview of newer research in this field. It also gives practical guidelines for administering ECT.

Indications for ECT

ECT was initially used for the treatment of dementia praecox (schizophrenia), followed subsequently by trials in the management of other mental illnesses such as bipolar mood disorder (in both the manic and depressive phases) and major depressive disorder (with or without psychosis).

Early studies[1] found major depressive disorder with psychotic features to be the principal indication for ECT, followed by catatonic schizophrenia, manic episodes, major depressive disorder secondary to schizophrenia, undifferentiated schizophrenia, paranoid schizophrenia, disorganised (hebephrenic) schizophrenia and 'depressive neurosis'. Current data suggest that major depressive disorder with psychotic features remains the principal indication for ECT,[3-5] but major depressive disorder without psychotic features, especially when resistant to pharmacotherapy, is also an indication for ECT.[5-7]

Major depressive disorder with psychotic features

ECT is highly effective in the management of major depressive disorder with psychotic features. It has been found to be more effective than either antidepressants or antipsychotics used on their own and at least as effective as a combination of the two.[5] Numerous clinical trials have reported recovery rates greater than 80%. These results

were associated with shorter hospitalisation periods and fewer relapses when compared with control subjects.[3]

Major depressive disorder with melancholic features

ECT has been compared with many antidepressant drugs in the treatment of major depressive disorder with melancholic features. Studies indicate that ECT is at least as effective as tricyclic antidepressants, but with the added advantage of quicker onset of action as well as fewer side-effects.[1,3,8] ECT seems to be more effective than the monoamine oxidase inhibitors (MAOIs).[5] Concerning the newer drugs such as the selective serotonin re-uptake inhibitors (SSRIs), one study comparing ECT with paroxetine in treatment-resistant patients found ECT to be superior to paroxetine with regard to total response and speed of onset as measured by a score reduction in the Hamilton Scale for Depression.[6]

Treatment-resistant major depressive disorder

The definition most frequently used to describe therapy resistance is non-response to two different antidepressants despite adequate drug therapy (adequate dose of a reliable drug for an adequate treatment period).[6] The proportion of patients who do not respond to two different antidepressant trials is estimated at 15 - 20%. Of these patients, 80 - 90% show a marked response to ECT which is rapid and often dramatic.[3,4] Currently, treatment-resistant depression is a common indication for ECT. In a study by Paul *et al.*[4] patients were found to remain free of depression on reassessment 1 year after the initial ECT was done. Most of these patients were maintained on lithium and a tricyclic antidepressant drug during this period.[4]

Suicide

Since ECT has a faster onset of action than antidepressant drug therapy, it should therefore be considered first-line therapy when rapid remission is needed in severely suicidal patients.[4] Various studies have found that depressed patients treated with ECT have a lower rate of suicide compared with depressed patients treated with antidepressants.[3]

Other forms of depression

ECT has not been proved useful in the treatment of dysthymic disorder and adjustment disorder with a depressed mood.

Mania

The traditional management of mania has relied mainly on the use of lithium, which has proved to be successful in approximately 70% of patients with acute mania. Augmentation with neuroleptics has become common practice, carrying with it the risk of various side-effects such as tardive dyskinesia. In the literature, very little emphasis has been placed on the use of ECT for mania despite the fact that various studies have indicated efficacy at least equal to that of lithium.[9] In a recent extensive review, by Muckerjee *et al.*[10] in which all published English-language papers on the use of ECT in acute mania were reviewed, ECT was shown to have an approximate efficacy of 80%, making it possibly superior to lithium.

Schizophrenia

Evidence is lacking to support the efficacy of ECT in patients suffering from schizophrenia. Limited evidence indicates the efficacy of ECT for the short-term relief of symptoms in patients with an acute onset of illness and a shorter duration of symptoms as well as schizophrenia associated with affective symptoms during the acute phase.[5,11] ECT does not seem useful in the treatment of chronic schizophrenia.[5] Trials investigating the role of ECT in the management of depression associated with schizophrenia are lacking at this stage.

Catatonia

Since it was first introduced in the late 1930s, ECT has been recognised as a highly effective treatment for catatonia. Catatonia features not only in catatonic schizophrenia and mood disorders but also as a nonspecific symptom of heterogeneous causes (metabolic, infectious). ECT has proved effective in alleviating catatonia resulting from non-psychiatric illnesses regardless of the cause.[3]

Usually few treatments are necessary to alleviate catatonic symptoms, but some patients may need up to 12 treatments. ECT is the most rapidly effective treatment for lethal catatonia.

Benzodiazepines (especially lorazepam) have also proved successful in the treatment of acute and possibly chronic catatonia. Controversy currently exists as to which of the treatment modalities is superior, with research supporting both possibilities. However, an interesting approach that has recently been explored, namely combining benzodiazepine therapy with ECT, appears to be very promising.

Despite the fact that the concurrent use of benzodiazepines and ECT is generally not recommended (proposed shortened seizure duration and raised seizure threshold), the combination seems to have a synergistic effect in the management of catatonia. The combined therapy was found to be superior to monotherapy in all cases studied.[12,13]

ECT in pregnancy

A number of studies have reported on the safety of ECT in pregnancy. Indications include severe depression and psychosis

and patients in whom high doses of psychotropic drugs may pose unacceptable risks to the fetus, especially during the first trimester of pregnancy.[3,14]

Neuroleptic malignant syndrome

ECT has also been successfully employed for managing prolonged rigidity associated with neuroleptic malignant syndrome. It has been found to be rapidly beneficial and safe provided that neuroleptics are discontinued before ECT.[15]

Parkinson's disease

Lebensohn and Jenkins[16] obtained astonishing results in two patients suffering from Parkinson's disease associated with depressive symptoms. Both patients presented with severe rigidity and bradykinesia, which improved considerably after ECT together with their depressive symptoms. The improvement of parkinsonian and depressive symptoms in these two patients suggests a common biogenic action of ECT on both aspects of their illness.

Other indications

In one study, ECT was proved effective in treating 12 out of 14 patients with post-stroke depression.[17]

ECT has also been found to be safe and effective in treating depressed, mentally retarded patients, including those with previous poor response to antidepressants.[18]

The literature includes a case report[19] on a patient presenting with a severe tic and major depressive episode. The patient experienced complete resolution of his motor and affective symptoms after ECT.

Simultaneous major depressive disorder and panic disorder was studied in 8 patients receiving ECT. All 8 patients experienced improvement in their affective and panic symptoms. Five of the 8 patients were taking psychotropic medication (an antidepressant and/or benzodiazepine); however, the researchers' opinion was that the medication failed to contribute to the response obtained.[20]

One case study reported on a patient suffering from agitated depression secondary to hyperthyroidism. The patient's thyroid hyperfunction and mood symptoms responded to ECT.[21]

Chacko and Root[22] reviewed two patients with dramatic remission of tardive dyskinesia after ECT and considered the cases to be a possible added indication for ECT.

Method of administration

Until recently, uncertainty existed regarding electrode placement and electrical dosage. The fact that numerous electrode placements have been used or recommended by different authors complicates the determination of the ideal placement of electrodes. Opinion is more divided with regard to placement of unilateral than bilateral electrodes. When administering unilateral ECT it is easy to place the electrodes so close together that most of the current passes from one electrode to the other without penetration of the skull.[1] The importance of seizure duration will also be addressed.

Bilateral versus unilateral ECT

The use of right hemispheric unilateral ECT was initially adopted as a means to reduce cognitive side-effects. The efficacy of unilateral compared with bilateral ECT administration has, however, remained controversial.

Sackeim *et al.*[23] did an extensive study investigating the efficacy of unilateral versus bilateral ECT at different stimulus intensities. The highest response rate was obtained with high-dose bilateral ECT, namely 63% compared with the lowest response rate of 17% for low-dose unilateral ECT. The response rate for high- dose unilateral ECT was 43% and for low-dose bilateral ECT 65%. The authors concluded that an increase in electrical dosage increased the efficacy of right unilateral ECT, although not to the level of bilateral ECT. An increase in stimulus intensity was also associated with a more rapid response to treatment independent of the electrode placement.[24]

Stimulus intensity and seizure threshold

Prediction of the initial seizure threshold still remains inaccurate, causing many clinicians to administer electrical dosages greatly in excess of what patients require. According to studies, the seizure threshold for individuals may vary up to 4 000%.[7] It is suggested that the degree to which dosage exceeds the seizure threshold may be more strongly tied to adverse effects than the absolute dosage administered to the patient.[25]

Stimulus titration allows the individual's threshold to be determined and the dosage of subsequent treatments to be defined.

Method of stimulus titration

This entails estimation of seizure threshold at the time of first treatment. Stimuli that are likely to be subthreshold are administered and increased in a stepwise fashion until an ictal response of adequate duration is obtained. This stimulus intensity is then defined as the seizure threshold.[4,23] For low-dose treatments, the stimulus intensity

that produces an adequate ictal response in the first session is also used during the next treatment. For high-dose treatments, however, a stimulus intensity of 2.5 times greater than the seizure threshold is administered during the second and subsequent treatments.[23]

Seizure length, frequency and course of administration

For ECT to be effective, bilateral grand mal seizures should be induced, since both sub-convulsive treatments and unilateral seizures are clinically less effective.[3,26] A seizure of at least 25 seconds' duration is needed to be effective.[26] ECT therapy usually involves 6 - 12 treatments, but individual variation necessitates thorough evaluation of the patient after each treatment.

Monitoring of seizure length

Motor signs such as jerking of the toes or flickering of the eyelids are sometimes interpreted as signs of a full grand mal seizure. These signs, however, are unreliable since they can also be the result of direct stimulation by the electric currents via peripheral pathways. Furthermore, they give no indication as to the true duration and completeness of seizures. The most reliable method of monitoring remains the electro-encephalogram (EEG), which provides the clinician with the exact pattern of the seizure.

A more simple, reliable method of ECT monitoring is provided by the cuff method. This entails inflating a blood pressure (BP) cuff above the systolic pressure in one arm before the administration of Scoline. This prevents the Scoline from paralysing the specific limb, enabling full tonic-clonic phases of the seizure to be observed. When unilateral ECT stimulation is used the cuff should be applied to the unilateral arm to enable monitoring of the bilateral spread of seizure activity throughout the brain.

In a comparative study by Fink and Johnson[26] the cuff method of monitoring was found to correlate closely with EEG monitoring. Seizure durations calculated using the cuff method were on average 10% shorter than those measured by EEG monitoring. It was suggested that because of its simplicity the cuff method should be utilised routinely during ECT.

Facilitation of seizures using caffeine pretreatment

Increased seizure duration has been proved to improve therapeutic outcome. The raised seizure threshold and concomitant reduction in seizure duration that is often experienced during a course of ECT could necessitate facilitation of the seizures. Caffeine has been shown to lower the seizure threshold and increase the seizure duration, resulting in successful ECT, in cases where adequate seizures could no longer be elicited at maximum stimulus levels.[27]

During facilitation, caffeine sodium benzoate (500 - 2 000 mg) is administered intravenously approximately 10 minutes before the ECT. No significant cardiovascular or other side-effects have been associated with caffeine pretreatment. However, it is advisable to avoid dosages that could result in excessive increases in seizure duration, the reason being that increased seizure duration is associated with an increase in memory impairment. Other limiting factors are the fact that the optimum dosage of caffeine pretreatment has not yet been defined and safety has not been proved in patients with cardiovascular impairment.[27]

Two versus three times weekly treatment

During a 1985 consensus conference in the USA,[5] experts suggested that two to three treatments per week should remain the standard. In a study done in 1995, however, Lerer *et al.*[28] suggested that a frequency of two ECTs per week was associated with fewer cognitive side-effects than three treatments per week. They also found no difference in efficacy between the two groups. However, this study also concluded that three treatments per week initially shared a more rapid rate of response, which would make it the method of choice in patients requiring more rapid intervention.

Patient preparation

Informed consent

The responsibility of informing the patient about ECT before obtaining consent rests with the treating physician. The patient should understand the nature of the procedure, the indication, the reason for choosing ECT as treatment, availability of alternative treatments, the benefits, and potential side-effects.[5,9]

Pretreatment evaluation

The pretreatment evaluation should include a complete medical and psychiatric history and examination, with the focus on risk factors (as discussed elsewhere in this article) for ECT. A neurological evaluation of risk regarding admission anaesthesia should be included in the routine check-up. Routine laboratory evaluations include serum electrolytes, haemoglobin or haematocrit, and an electrocardiogram. Other special investigations should be done when specifically indicated.

Evaluation includes the demonstration of an appropriate clinical indication for the administration of ECT.[5,9]

Drugs that interact with ECT should be adjusted or discontinued if necessary. The following drugs are of special interest:

1. Benzodiazepines are traditionally discontinued as they result in raised seizure threshold and subsequent decreased seizure duration.
2. Lithium should be withdrawn and patients should be essentially lithium-free as indicated by blood levels before ECT. The combination of lithium and ECT has been associated with delirium, neurotoxicity, prolongation of seizures and increased duration of the succinylcholine effect.
3. Theophylline is associated with an increase in seizure duration and lignocaine raises seizure threshold. Both drugs should therefore be avoided during ECT.
4. Clozapine should be withdrawn before ECT because of its association with tardive seizures.
5. Reserpine should not be administered during ECT since it can cause respiratory depression and cardiovascular collapse.
6. Antidepressants, including the tricyclic antidepressants and the MAOIs, have no consistent interactions with ECT.
7. Antipsychotics should be continued in psychotic patients since increased antipsychotic activity could occur when combined with ECT.[14]

Treatment preparation

The patient is fasted for at least 6 hours before the ECT. Premedication is administered and usually includes a muscarinic anticholinergic such as atropine to dry secretions and block vagally mediated bradycardia and asystole. An intravenous line is inserted and a bite block is placed in the patient's mouth. The patient is then pre-oxygenated using 100% oxygen at 5 l/min.

The induction agent of choice is methohexital, which is preferable to thiopental since it is possibly associated with a lower incidence of postictal arrhythmias. Etomidate and ketamine are alternatives that can be used as induction agents, since these drugs do not raise the seizure threshold, unlike barbiturate anaesthetics.

The most commonly used muscle relaxant is succinylcholine, which is administered as soon as the patient is unconscious and has an airway inserted. Alternatives to succinylcholine include atracurium or curare.[5,10,14] ECG monitoring should continue throughout the procedure.

Relapse and maintenance therapy

Although ECT is highly effective in the short term, the relapse rates after initial response to therapy are high. Up to 70% of cases treated for depression and up to 95% of cases treated for depression with psychosis, relapse within 2 - 4 months of completion of an ECT course.[14,23]

Since relapse after ECT is common, some form of maintenance therapy should be administered. The most favourable approach is to maintain patients suffering from depression on an antidepressant or mood stabiliser; however, ongoing pharmacotherapy may be problematic in patients who cannot tolerate the drug side-effects. Also, some new research indicates that patients resistant to adequate drug therapy before ECT will continue to be resistant after ECT.[4]

In such cases continuation of ECT on an outpatient basis may be appropriate. It has been proposed that ECT be continued weekly for the first month after remission. The frequency can then be tapered gradually to monthly treatment. More frequent treatments can be considered in patients at high risk of relapsing. A high risk of relapse may be indicated by an incomplete initial response or a recurrent course of illness.[14]

Following ECT most depressed patients should continue using antidepressant medication or lithium, since the chances of a relapse can be reduced to 20%. Patients suffering from major depressive disorder with psychotic features require the continuation of antipsychotics combined with antidepressants or mood stabilisers.[4,5,14]

Cognitive impairment and other side-effects

Cognitive effects of ECT

Short-term cognitive effects. Disorientation and confusion commonly occurs immediately after awakening from an ECT treatment, lasting minutes to hours. Prolonged disorientation is, however, rare and usually associated with bilateral electrode placement and higher stimulus intensity as well as repeated stimuli during a single ECT session.[5,14,23]

Patients suffering from depression often present with cognitive impairment, making it very difficult to differentiate from the cognitive side-effects of ECT. Anterograde memory, however, seems to be affected differently in depression than with ECT. Depression is associated with a deficient ability to acquire information, whereas ECT temporarily reduces the ability to retain information.[29] On retesting memory activ-

ity 4 days after a successful ECT course, Steif *et al.*[29] found that antrograde memory deficit due to depression (acquisition of information) returned to baseline levels, while retention of information remained impaired.[5]

Long-term cognitive effects. Some patients report difficulties with retrograde memory. It seems that retrograde memory disturbances tend to resolve more slowly and in some cases spotty memory loss may persist for months (usually no more than 6 months) or rarely even years. This deficit is usually modest and it is uncommon for patients to experience these effects as distressing.[5,9]

A study by Sackeim *et al.*[23] focused on the long-term cognitive side-effects of ECT (anterograde memory). At 2-month follow-up after an ECT treatment course all 66 patients participating in the study had significantly improved scores from pretreatment values on the Mini Mental State Examination (MMSE) as well as anterograde memory testing and learning ability. Subjective evaluations of memory were also markedly improved in relation to pretreatment scores.[23]

The study also compared bilateral versus unilateral electrode placement and stimulus intensity in terms of cognitive side-effects. Although it is clear that bilateral electrode placement and higher stimulus intensity are associated with more severe initial cognitive impairment, the study indicates that after 2 months cognitive function was usually enhanced in all patient groups.[5,17,23] However the study did not address retrograde memory issues.

ECT and brain damage

Both the medical community and the public have been sceptical of ECT.

One of the major factors contributing to this is concern that ECT could lead to structural brain damage.

Until recently studies done on humans after ECT treatment, using computed tomography (CT) scans, were of limited value. These studies were retrospective in design. While most of these results were negative, a few studies have reported an association between ECT and structural brain damage.[30,31] These studies remain controversial and have been criticised for potential selection biases.

Several brain imaging studies, using a variety of modalities, have concluded that permanent brain damage is not an adverse effect of ECT. In a recent study by Coffey *et al.*[32] 35 patients were evaluated using magnetic resonance imaging (MRI) before and twice after (at 2 - 3 days and at 6 months) undergoing ECT. Although structural brain abnormalities were present in many patients before ECT, no relation could be found between ECT and brain damage. Neurologists and epileptologists generally agree that seizures lasting less than 30 minutes do not cause permanent neuronal damage.

Taylor *et al.*[33] followed another approach to determine whether any significant brain damage occurs during ECT. Patients with organic brain pathology have elevated serum creatine phosphokinase (CPK) levels. CPK can be divided into three isoenzymes, with the BB isoenzyme occurring mainly in the brain and smooth muscle. Disease or damage to these tissues causes the release of the enzyme followed by an increase in serum levels. In a group of 10 patients receiving ECT, the levels of CPK (BB isoenzyme), remained within normal limits, indicating the absence of brain damage after ECT. Although the number of patients in this study was small, the consistency of the results indicates that this study should be regarded as significant.

Cardiovascular effects of ECT

Cardiovascular complications are the main cause of ECT-associated mortality and morbidity. Initial changes after ECT include sinus bradycardia due to vagal output and a valsalva effect. Sinus bradycardia can lead to a cardiac arrest lasting up to 7 seconds. This is followed by stimulation of the sympathetic nervous system during generalisation of the seizure with subsequent tachycardia, increase in blood pressure and increased myocardial oxygen consumption. Cardiac arrhythmias may occur during this time, but do not persist for more than 4 - 6 hours post ECT. Attempts to treat ventricular arrhythmias with lignocaine or phenytoin should be avoided since these drugs raise the seizure threshold. Bradyarrhythmias can be treated with atropine and tachyarrhythmias with beta-blockers if necessary. Care should be taken to optimise the patient's cardiac status before ECT, focusing specifically on hypertensive patients who may have a pronounced increase in blood pressure during ECT.[5,10,14]

Mortality

The mortality rate associated with ECT ranges from 0.002 to 0.004% per treatment, which is favourably low compared with anaesthesia associated mortality rates of 0.003 - 0.04%.[5,10,14]

Contraindications

In light of the fact that ECT is often administered because of poor response or contra-indications to other treatment modalities available, one should always keep in mind that the potential benefits must be weighed against the risks involved.

Although there are said to be no absolute contraindications to ECT,[5,10,14] certain conditions may carry a substantial risk and ECT should probably be avoided in these instances.

Intracranial pathology

Increased intracranial pressure may be aggravated during ECT, but lack of reported cases limits the ability to conclude on the extent of the risk involved in these cases.

Space-occupying lesions may present a problem since increased cerebral blood flow and increased permeability of the blood-brain barrier could precipitate or aggravate oedema around the lesion, which in turn could lead to herniation. Smaller, asymptomatic lesions, however, seem to be less risky, especially if patient preparation includes aggressive management of hypertension and the administration of steroids before the procedure to reduce oedema.

Intracerebral bleeding. Patients with arteriovenous malformations, unstable aneurisms or evolving haemorrhagic cerebrovascular accidents face a high risk of re-bleeding if ECT is administered soon after the initial haemorrhage. This risk is, however, greatly reduced if ECT is administered after a month has elapsed.

Cardiac pathology

Patients who have suffered a recent myocardial infarction are at great risk of reinfarction should ECT be administered within the first 10 days after initial infarction. This risk, however, resolves significantly after 3 months and therefore a delay in administration of ECT is advisable. If, however, the ECT cannot be delayed, it is of paramount importance to prepare the patient optimally, including maximal oxygenation, antihypertensives (where indicated) and antiarrhythmics.

Previous history

A history of poor or no response to ECT or debilitating side-effects from ECT should also be considered relative contraindications to ECT.

Conclusion

ECT has proved to be an effective and safe treatment modality with a wide range of indications and a favourable safety profile. Despite earlier stigmatisation, ECT has once again become a popular treatment option and a last resort in treatment-resistant patients.

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