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WPA Position Statement on the Use and Safety of Electroconvulsive Therapy

FOREWARD

This Position Statement on the use and safety of electroconvulsive therapy (ECT) has been prepared on behalf of the WPA by the above Working Group of ECT clinicians and researchers at the request of Dr. Afzal Javed, President of the World Psychiatric Association.

WHAT THE POSITION STATEMENT AIMS TO ACHIEVE

In this Position Statement, we aim to summarise the scientific evidence-base on the indications for ECT as well as for the effectiveness, safety and tolerability of modern ECT practice.

INTRODUCTION

ECT is an essential, medical brain stimulation procedure for serious, often treatment-resistant and sometimes life-threatening, mood and psychotic disorders, particularly when a rapid response is required.(1-3) In addition to a robust scientific evidence base, a wealth of global clinical experience with ECT has accumulated since its first development 85 years ago, during which time the procedure has been substantially refined. For example, the use of anaesthesia and muscle relaxation has been routine since the 1950s and practice shifted from a sine-wave stimulus to a more efficient square-wave brief pulse stimulus in the 1980s.

Contemporary ECT involves passing a small electrical charge through the brain to induce a generalised seizure lasting about 30 seconds. This is achieved under controlled conditions, using short-acting generalised anaesthesia plus a muscle relaxant along with oxygenation. ECT is a multidisciplinary procedure and clinics are run and supervised by appropriately trained and experienced psychiatrists and nurses who are also responsible for professional development, supervising trainees and quality assurance within their service. Anaesthesia and airway management are provided by an anaesthetic medical specialist, assisted by trained nurses who also help manage patient recovery immediately after the procedure. Usually, 8–12 treatments are given in a course, two or three treatments per week. Treatment sessions can take place in either in-patient or out-patient settings.

About 1.4 million people worldwide are treated annually with ECT. However, rates of use and indications for ECT vary between, and even within, countries. This is primarily influenced by limited availability of ECT and lack of clinical knowledge about it, as well as stigma and legal restrictions (often ideologically based) on ECT practice. Despite these latter issues, a large body of preclinical (including sham-controlled rodent and primate studies) and translational research over the past few decades indicates that ECT mediates some of its therapeutic effects through molecular and cellular neuroplasticity mechanisms in the brain. Systematic reviews and meta-analyses of historical and

modern randomised trials confirm that real ECT is superior to sham ECT (i.e., where patients were anaesthetised but did not receive an electrical stimulation), that ECT is superior to antidepressant drugs, that different forms of ECT can have different outcomes, and that ECT is superior to other brain stimulation techniques for depression.(4-7)

In Western industrialised nations, the most common indication for ECT is depression, whereas worldwide schizophrenia is the most common indication. This reflects the greater number of published clinical trials of ECT for depression than other disorders, and the priority given to randomised controlled trials and systematic reviews in informing national and international guidelines in Western nations. For a comparison of contemporary international guidelines see (3). ECT is also an exceptionally effective treatment for catatonia, usually related to mood disorders or schizophrenia, and can be used for resistant mania.

ECT can be deemed a second-line intervention when patients have not responded to adequate trials of pharmacotherapy and/or psychotherapy. A recent economic analysis from the USA found that ECT for depression is cost-effective and recommended that it should begin to be considered after two failed therapeutic trials.(8) However, ECT is not a treatment of "last resort" and should never be delayed if the clinical situation is urgent, e.g., catatonia, depression with psychosis, distressing agitation, high suicide risk or deteriorating health due to food/fluid refusal or extreme self-neglect. Other first-line indications for ECT include patient preference and previous good response to ECT.

ECT-RESPONSIVE DISORDERS

Depression

ECT is a highly effective treatment for depression. Real ECT has been shown to be superior to sham ECT (standardised effect size of -0.91 (95% CI -1.27 to -0.54)) and more effective than antidepressant drugs (effect size –0.80, 95% CI –1.29 to –0.29).(4) The remission rate across modern ECT trials is 52%, a remarkably high figure when the main indication is treatment-resistance to pharmacotherapy and psychotherapies.(6) Some clinical features that modestly contribute to predicting remission with ECT for depression are psychosis, older age, and greater overall depression severity.(9) The latter factor may mediate its effect via psychomotor disturbances that are core features of both melancholia and catatonia.

Modern ECT trials in depression have focused on optimising effectiveness and minimising the cognitive side-effects of ECT (see below). This has mainly entailed assessing different electrode placements (e.g., bitemporal, bifrontal and unilateral), electrical stimulus dose (e.g., moderate- and high-dose in relation to the seizure threshold, the minimum electrical stimulus charge required to induce a generalised seizure), and stimulus pulse width (e.g., ultrabrief pulse (0.25 - 0.3 msec) and brief pulse (0.5 – 1.5 msec)).(2) Varying these parameters can influence the effectiveness and cognitive side-effects of ECT and expert advice should be sought when deciding what form of ECT is best for individual patients.

In general, the evidence from meta-analyses of clinical trials is that ultrabrief pulse high-dose (i.e., 6 times seizure threshold) unilateral ECT is less efficacious than brief pulse high-dose

unilateral ECT, which is similar to brief pulse moderate-dose (1.5 times seizure threshold) bitemporal ECT.(5, 6) Ultrabrief pulse high-dose unilateral ECT has fewer cognitive side-effects than brief pulse high-dose unilateral ECT, which in turn affects cognition less than brief pulse bitemporal ECT. Bifrontal ECT is broadly similar to bitemporal ECT but may less frequently induce bradycardia/asystole during treatment sessions. It should be borne in mind that this level and quantity of research on stimulus application is not yet available for other indications for ECT.

If rapid response is required for critical illness, bilateral ECT can be considered as a first-line form of ECT. If minimising cognitive side-effects is a priority, then forms of high-dose unilateral ECT can be considered.

Schizophrenia

There is reasonable meta-analytical evidence to support using ECT as an option for treatment-resistant schizophrenia and related disorders.(10) It may also have a role in clozapine non-responders. There is a need for larger high-quality randomized controlled trials. For this reason, ECT was not recommended for schizophrenia by the Food and Drug Administration (FDA) in the USA in their comprehensive 2018 review of ECT devices (https://www.federalregister.gov/documents/2018/12/26/2018-27809/neurological-devices-reclassification-ofelectroconvulsive-therapy-devices-effective-date-of). However, in many Asian countries ECT has an important role as an effective and acceptable treatment for schizophrenia and many international guidelines have incorporated ECT as a third- or fourth-line option in treatment-resistant schizophrenia and when rapid improvement is required, e.g. suicidality, inanition, risk of harm to self or others.(1, 3)

Mania

ECT can be used to treat mania in the rare instances where pharmacotherapy is not sufficiently effective and where manic symptoms are severe, prolonged, and life-threatening (e.g., excitement, delirium). In such life-threatening circumstances, ECT should not be delayed. In their 2003 review of ECT, the UK National Institute of Health and Care Excellence (NICE; https://www.nice.org.uk/guidance/ta59) supported a role for ECT in the rapid control of mania and ECT has been incorporated as a third- or fourth-line option for mania in several international guidelines.(1, 3) However, the FDA did not include mania in the recommended indications for ECT in their 2018 review and noted that additional studies are required.

Catatonia

Due to severe abnormalities in motor activity, ranging from stupor to excitement, as well as autonomic instability, catatonia is a medical emergency and rapid relief is required before disability or death ensues. There are no major modern trials of ECT for catatonia, the most common causes of which are mood disorders and schizophrenia. However, observational studies and clinical

experience show that catatonia typically responds very well to ECT, which should be considered early if first line treatment with high-dose benzodiazepines does not work.(1-3) Delirious mania and neuroleptic malignant syndrome are catatonia-like syndromes that are medical emergencies where ECT can be effective and life-saving. All relevant international guidelines, including from NICE and the FDA, support ECT for treating catatonia.

Other indications for ECT

Emerging indications for ECT, based mostly on off-label use described in case reports and case series rather than randomised trials, include: neuroleptic malignant syndrome, self-injurious behaviour in autism, agitation and aggression in dementia, Parkinson's disease not responding to standard therapies, and intractable epileptic seizures. The existing evidence base is currently insufficient to firmly endorse ECT for these conditions. In such instances, expert advice should be sought from a senior psychiatrist who is experienced in using ECT for these less common indications.(1, 3)

ECT IN SPECIAL POPULATIONS

ECT can be used for the above indications in adolescents, for whom safety and effectiveness appear to be similar to that in adults. In their 2018 review, the FDA advised that ECT could be used for persons 13 years or older for severe resistant depression and catatonia. In practice, a second opinion from a child and adolescent psychiatrist is advisable along with seeking expert advice from a psychiatrist experienced in ECT practice.

ECT can also be used for the above indications in pregnancy and may be preferable to medications. Risks need to be weighed against those of other treatments or no treatment at all. Close liaison between the ECT psychiatrist, anaesthesiologist and obstetrician is essential. After 20 weeks gestation, ECT should be given where obstetric support is immediately available. Additional anaesthetic management includes placing the pregnant woman in the left lateral position, using pelvic wedge tilt, and avoiding hyperventilation. Both mother and the foetus need to be closely monitored before, during and after ECT sessions.(1)

There is no upper age limit for ECT, which is generally effective, safe and well-tolerated in older adults. However, older adults are likely to have more medical comorbidities than younger ones, e.g., cardiac and respiratory disease, cerebrovascular disease and diabetes. Together, these can increase the risk for medical adverse events and cognitive side-effects. Where possible, physical health screening and optimal management of all known or identified medical conditions is required before starting a course of ECT. Close liaison between the ECT psychiatrist, anaesthesiologist and specialist physicians is essential.

CONTINUATION AND MAINTENANCE ECT

The relapse rate after successful ECT for depression is 37% after three months and 50% after six months.(11) This is similar to relapse rates with pharmacotherapy and reflects the underlying nature of depression itself.

After successful acute treatment of an index illness episode, some patients benefit from continuing with ECT to prevent relapse, but at a lower treatment frequency.(1-3) This is usually for patients at high risk for relapse and/or who are good ECT responders but have experienced little benefit from other treatments. Such "continuation ECT" usually involves an initial schedule of once-weekly ECT sessions for four weeks (sometimes referred to as "tapering"), followed by gradually increasing the treatment intervals over time, e.g., once every two weeks, once every four weeks, etc. The schedule should be flexible and can be adapted to meet the needs of the individual patient, subject to regular clinical review; pharmacotherapy should also be continued.

The term "maintenance ECT" applies to ongoing ECT when the schedule continues beyond six months, when the aim is to prevent recurrence.

Continuation/maintenance ECT is useful for preventing relapse or recurrence of illness episodes in selected patients with depression (unipolar and bipolar) and also schizophrenia (though RCT data are lacking). Because of the wider treatment intervals, continuation/maintenance ECT is not usually associated with cognitive side-effects.

SAFETY AND TOLERABILITY OF ECT

Like all effective medical procedures, ECT has adverse effects that need to be weighed against benefits of treatment. These need to be fully discussed with patients and balanced against medication side-effects, the efficacy and risks of alternative treatments, as well as the potentially devastating effects of unresolved and severe psychiatric illness.

ECT is a remarkably safe medical procedure. The main medical risks of ECT are related to general anaesthesia and the cardiovascular changes that can occur during ECT, including vagally mediated bradycardia and asystole, tachycardia and hypertension. These changes are typically self-limiting and uneventful. Mortality with ECT is extremely low, at about 2.1 deaths per 100,000 treatments. In fact, ECT is associated with reduced all-cause mortality, possibly due to increased medical attention prior to ECT, treatment of the psychiatric disorder itself and reduction in suicide.(12) Reassuringly, there is no credible evidence that ECT causes any brain damage at either the cellular or structural level. In support of its longer-term safety, recent large national registry studies have found no increased risk for dementia or stroke in patients previously treated with ECT.(2, 3)

The effects of ECT on cognition are the side-effects of greatest concern to patients and practitioners but are mostly transient. Meta-analyses of standardised tests assessing short-term memory (e.g., delayed verbal recall) and executive function (e.g., Trail Making Test B; letter fluency effect) reveal that these are the functions most affected by ECT.(13) While interindividual differences occur, at the group level, such objectively measured deficits usually resolve within a few weeks of completing a course of ECT. By that stage, most cognitive measures improve when compared with performance

before starting ECT. ECT often improves many of the cognitive deficits associated with severe depression and schizophrenia.(13, 14)

Less clear is the effect of ECT on retrospective autobiographical memory. This is mainly due to the challenges of quantifying how we can recall previous personal events and information and that depression itself causes deficits in autobiographical memory. Additionally, there is a normal rate of loss of consistency in recall of autobiographical memories of 25–40% over a few months, which overlaps with the range reported in modern ECT trials. What is clear, though, is that bitemporal ECT has more pronounced effects on autobiographical memory than unilateral ECT and that ultrabrief pulse ECT has fewer negative effects than brief pulse ECT.(5, 6)

Objective measures of cognitive performance may not correlate with patients' subjective experience and about one quarter of depressed patients report subjective worsening of their memory after a course of ECT. It is not currently possible to predict who will experience cognitive impairment but risk factors for subjective complaints have been reported to include female gender, younger age, fewer prior subjective memory complaints, being a non-remitter, and treatment with brief pulse rather than ultrabrief pulse ECT.

A key element of ECT practice therefore is to monitor both objective and subjective cognitive function before and throughout the course of ECT. If any deficits emerge, the treatment can then be adjusted to minimise any cognitive side-effects. This can be achieved, for example, by switching from bilateral to unilateral electrode placement, switching from brief to ultrabrief pulse ECT, or reducing the frequency of ECT sessions.

CAPACITY AND CONSENT ISSUES

ECT should be performed in line with local legislation and used where there is evidence for effectiveness as outlined above. As with any other medical treatment, where possible, patients should be assessed for capacity to make decisions to have ECT and valid informed consent is required. Information should be provided about ECT methods, side-effects and potential adverse events as described above as well as other available alternative treatments. Families, carers and advocates can assist with the consent process. For patients who lack capacity to consent to ECT, relevant national mental health legislation needs to be followed if ECT is deemed clinically necessary.

Unmodified ECT (i.e., without anaesthesia and/or muscle relaxant) is an outmoded practice; in some countries, it is illegal, e.g., India. As such, unmodified ECT is not recommended except under extreme conditions where it is considered to be life-saving and anaesthesia facilities are not available.(15)

CONCLUSION

ECT is an essential medical treatment that has been used worldwide for more than 80 years for treating severe mood disorders, catatonia and certain psychotic disorders. This is a testament to its

clinical utility and general safety, tolerability and acceptability. Though usually a second-line treatment, ECT should be considered early in the course of serious debilitating illness where treatment delay poses an unnecessary risk. Refinements in ECT procedures have helped to reduce side-effects. Appropriate national and/or international guidelines on ECT administration should be followed where possible.

RECOMMENDATIONS FOR ACTION

- Access to ECT needs to be improved to be both fair and equitable
- Public and medical education about ECT is essential for improving understanding of ECT in the community, reducing stigma and ensuring appropriate use of ECT
- Further research on optimising ECT technique should focus on maintaining effectiveness and minimising both objective and subjective cognitive side-effects
- Large high-quality randomised controlled trials of ECT are required for treating mania as well as schizophrenia and related disorders
- The WPA should support and promote the work of international research consortia towards understanding the mechanisms of action of ECT

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