

Efficacy of electroconvulsive therapy as a potential first-choice treatment in treatment-resistant depression (Review)

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Abstract. Electroconvulsive therapy (ECT) is a technique that has been used since 1938 to treat several psychiatric disorders as a replacement for chemically induced seizures. Despite its history of stigma, controversy and low accessibility, ECT is found to be beneficial and efficient in severe cases of depression where medication fails to bring results. Titration tables developed over time, based on evidenced-based medicine, have made this treatment technique safe and, in some cases, the first choice of treatment. The aim of the review was to summarize the research conducted on the efficacy of ECT on major depressive disorder and variables studied such as technique, comorbidities and medication as well as the effects and outcomes of this procedure. At the same time, the application and correlations with other psychiatric and neurological disorders, including catatonia, agitation and aggression in individuals with dementia, schizophrenia, and epilepsy were assessed. There are no statistically demonstrated effects due to the fact that a small number of moderate-quality studies have been published; however, the combination of ECT technique with standard medication and care, can improve patient outcome. Furthermore, with regard to ECT, widespread and robust volume changes in both cortical and subcortical regions have been shown. Antidepressant response and volumetric increases appear to be limited by the specific neuroplasticity threshold of each patient.

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1. Introduction

Depression is considered to be one of the most common mood disorders globally with a high risk of mortality (1) and it is predicted to become the first cause of disability and social burden by 2030 (2), with 12.3% global burden of disease reported in 2016 (3).

Electroshock or electroconvulsive therapy (ECT) is one of the alternative treatments to medication-resistant depression. ECT as compared to other treatments is found to be the most efficacious for symptom remission of major depressive disorder (MDD) (3). Historically, this method was introduced in 1938 (4), and has been submitted to changes and improvement ever since (5). There is a large body of studies that compare ECT to other treatments in terms of efficacy of response defined by at least 50% reduction in scores from baseline, assessed by the Hamilton Depression Rating Scale (HDRS) (3), Montgomery-Asberg Depression Scale (MADRS) (3) or Clinical Global Impression (CGI) (3) and total dropout rates at the end of the studies included (3).

ECT is a procedure performed under general anesthesia, in which small electric currents are passed through the brain (up to 800 mA), intentionally triggering a short seizure. ECT seems to cause changes in brain chemistry, which can quickly reverse the symptoms of certain mental health conditions, especially medication-resistant depression and bipolar disorder (6).

Although the summary of research up to 2020 shows that ECT is highly safe, tolerable, with low-mild transient side effects and is highly efficient for medication-resistant

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depression, this method is still associated with reluctance and stigma. Thus, the use rate is low and it is considered the last resort as a treatment choice (1).

The present study included and summarized a total of 38 studies, meta-analyses and reviews covering more than 30 years of research on the efficacy of ECT on MDD. A search for scientific studies published in the last 10 years (2010-2020), highlighting even older researches if the original article was mentioned in this period. The search was carried out on the Web of Science (www.webofscience.com) using several key words and attempting to highlight what were considered the most important findings, at that time. The key words used were: 'electroconvulsive therapy' AND 'ECT' AND 'depression' AND 'medication' leading to 427 results. The search was narrowed by adding 'technique', yielding 37 results, 'safety' with 78 results, and 'relapse' which yielded 61 results. The simple combination of 'ECT' and 'relapse' helped refine the above search by narrowing it to depression. The meta-analysis and reviews helped us to eliminate the duplicates, allowing identification of original articles even if they were older than 10 years.

The aim of the study was to describe the variables included in the study of efficacy, outcomes considered, safety, tolerability and relapse in order to provide an overall view on the efficacy and which are the factors that make the difference.

2. ECT techniques

Just as any other medical intervention, ECT incurs various controllable risks and/or is associated with adverse effects. Adverse effects relate to medical matters include such complications associated with general anesthesia or to cardiac functioning, for instance. Regarding anesthesia, some evidence provided by the meta-analysis conducted by Zheng *et al* (7) suggests that ketamine in combination with other anesthetics are efficient for improving depressive symptoms in early ECT stages, but not post-ECT. This finding must be taken with some caution because the studies included in the meta-analysis reported administration of ketamine at various doses. On the other hand, non-medical adverse effects include disorientation and confusion that may occur immediately post-procedure and remit within a short period of time or difficulties that may extend over a longer time period such as a form of memory impairment (8).

Electrode placement, stimulus dose and pulse width are parameters by which the efficacy, safety and tolerability of ECT treatment are evaluated. Currently, in common practice, three placements have been standardly used: bitemporal (BT), bifrontal (BF) and right unilateral (RUL). In principle, it has been argued that all of these are associated with symptom improvement at the end of the intervention (8). Notwithstanding, there are some differentiating details that will be covered herein.

Modern ECT technique relies on a square wave brief or ultra-brief pulse stimulus to trigger a seizure starting from the seizure threshold that is induced at treatment commencement. Standard (brief) pulse width ranges between 0.5 and 2 msec whereas the ultra-brief pulse is reduced to an interval <0.5 msec. For BT ECT, the stimulus is delivered in a standard manner at a range between 1.5- and 2.5-fold the seizure

threshold while for RUL the stimulus should be ≥ 5 -fold the threshold (8).

For the seizure induced by the ECT to have an antidepressant effect, the energy dose must be delivered in such a manner that it exceeds the seizure threshold. Dose administration methodology indicates that the dose can be set at the first ECT treatment session either by empirical titration or by employing formulas that estimates the dose based on patient's full age (for RUL placement) or half age (for BT). Bjølseth *et al* (9) compared BF and RUL interventions shortly after ECT cessation and also 3 months later in a sample of elderly patients ($n=73$ intention to treat sample), with an age range between 60 and 85 years. The authors of that study found that a formula-based (age-based) dosage may not provide optimal stimulation for the elderly patients because it has been shown that the seizure threshold increases with age.

Dominiak *et al* (10) conducted an open label study in which patients ($n=91$ intention to treat sample) were randomly allocated into RUL and front-BT ECT groups and the formula-based method was used to set the stimulus dose. Those authors concluded that RUL is a safer procedure because it is associated with a lower incidence of high blood pressure and fewer consciousness difficulties. Both RUL and BT ECT triggered various adverse effects in autobiographical memory retrieval, but patients generally tolerated these procedures well. The RUL placement proved to be efficient provided a high energy dose was used (approximately 22% higher than that in BT). Socci *et al* (11) examined a cohort of 402 patients with treatment-resistant depression that underwent the bilateral ECT procedure two or three times a week (the latter was reserved for patients with more severe symptoms). Stimulus dosage was administered initially by the half-age method and was subsequently adjusted to maintain optimal seizure duration at 25 sec. The middle-aged (46-64 years) and the aged (>65 years) patients showed improvement in global cognitive functioning, but anterograde and retrograde amnesia occurred post-intervention. Notwithstanding, Socci *et al* (11) concluded on good tolerability of the bilateral ECT treatment. Even so, there were many situations when the patient exhibited an aggressive reaction to the ECT treatment and a high level of empathy from the doctor's point of view in order to convince the patient about the benefits of the therapy is absolutely necessary (12).

3. ECT effects, safety and tolerability

ECT is associated with a number of medical and cognitive side effects following the procedure. The medical effects are rarely reported, but a review of studies performed on patients with pre-existing severe cardiovascular disease who completed an ECT course, found that minor to severe complications that may have appeared were transitory and did not prevent the completion of the course. Moreover, ECT is effective and relatively safe with a required special monitoring (13).

On the other hand, cognitive impairments have been reported, especially regarding memory functions. Autobiographical memory is found to be mostly impaired with effects lasting up to three weeks post-procedure (10).

Previous findings have shown agreement that a high severity of symptoms were correlated with high cognitive

impairment. Cognitive side effects reported included impairment in attention, executive function, learning and memory capacity; although when depression symptomatology remitted, these cognitive side effects returned at least to a baseline and no improvement was reported, even if they were sometimes linked to alcohol consumption (4,14,15). These findings are supported by another study that reported significantly improved memory functions compared to baseline despite transient side effects on memory and verbal fluency reported immediately after ECT (16).

Other common side effects reported include: headache and nausea/vomiting (1), as well as dizziness and muscle pain, thirst or dry mouth, constipation, drowsiness, insomnia and dysuria with geriatric patients (17), temporary blood pressure elevation and cardiac arrhythmias (10).

There are categories of patients who may require careful consideration before referral to an ECT course of treatment: elderly depressed individuals and depressed patients with comorbid borderline personality.

Riva-Posse *et al* (18), in a literature review, found that elderly patients (age, >65 years) may have a lower rate of response to ECT, are more likely to develop cognitive side effects that last longer (including delirium) and might also suffer from acute cardiovascular as well as other medical complications including medical comorbidities and higher rate of intolerance to antidepressants. With respect to cognitive functioning, Geduldig and Kellner (19) raised a further important issue, namely that there could be a discrepancy between the self-report measures on symptom improvement completed by the elderly depressed patients and their objectively observed cognitive state (by the psychiatric medical providers).

On the other hand, both Geduldig and Kellner (19) and Riva-Posse *et al* (18) concur on the idea that being elderly is a positive predictor for higher remission rates, quicker responses and improvement in clinical features such as suicidal ideation, risk of suicide and psychotic symptoms. In order to attain optimal results in this population, some ECT interventions rely on electrode placement in the non-dominant RUL or in the BF positions and ultra-brief ECT is administered with caution as it necessitates more treatment sessions.

Little research has been conducted on the administration of ECT to depressed patients that have been diagnosed with comorbid borderline personality disorder (BPD). Lee *et al* (20) reported improvement on depressive symptoms for the BPD and the non-BPD patients in their retrospective review study. However, they mentioned that this finding should be taken with caution. The limitations of their research involved the clinical assessment instruments that were used for the review studies that they analyzed. BPD was diagnosed with a screening test, i.e., the McLean Screening Instrument for Borderline Personality Disorder (MSI-BPD) and depression was measured with the Patient Health Questionnaire PHQ-9. Most of the studies reported in the current review assessed depressive status with HRDS or MADRS.

4. ECT outcomes

The studies included in this review followed the outcomes as compared to a baseline immediately after the treatment and after six months. Semkowska and McLoughlin (21) concluded

in a systematic review and meta-analysis from commencement up to 2009 (84 studies with 2,981 participants) that even when subacute impairment appears in pre-treatment scores, during short- and long-term period, improvement in outcomes can be observed in the global cognitive status. The conclusions revealed small improvement in the long-term relative to the baseline with regard to processing speed, attention and working memory; small-medium improvement on verbal episodic memory, recovery of pre-treatment levels for visual episodic memory and spatial problem solving; and small-medium or baseline levels improvements for executive functioning. The studies provided an evidence base to support the conclusion that impairments measured post-ECT treatment are limited within the first 3 days and improvement beyond baseline with small-medium effect remain stable on long-term measures (21).

Another study on 44 patients with impairment in processing speed, executive functioning and memory at baseline confirms the findings of Semkowska and McLoughlin (21). In a naturalistic ECT study, results showed transient impairment in memory and executive function with improvement or stabilizing in the subsequent six months. This study concluded that cognition remains unaffected during and after ECT treatment and showed mild transient negative effects (22).

The effectiveness of ECT in treating depression is already well known. Comparative studies have shown that ECT has a greater antidepressant effect than other pharmacological substances, such as monoamine oxidase inhibitors, tricyclic antidepressants, or selective serotonin reuptake inhibitors (SSRIs) (23). A study by the Consortium for Research on Electroconvulsive Therapy (CORE), which involved 311 patients with depression, showed that the remission rate for patients with melancholy depression was 62.1%, and that for patients with depression without melancholy was 78.7%. In addition, in an analysis performed over the subsequent six months, it was found that in patients who received ECT, the recurrence rate was lower than that in patients who received drug treatment (24).

In the case of bipolar affective disorder, pharmacotherapy (more precisely the use of lithium as a medicine) is often used, but elderly patients have a much lower level of tolerance of lithium than young patients. Pharmacokinetic changes, such as absorption, distribution, elimination from the body, predispose patients to a higher risk of lithium intoxication. In addition, serum lithium levels may increase as a result of the interaction between lithium and other medicines prescribed to the elderly, such as thiazide diuretics, ACE inhibitors or non-steroidal anti-inflammatory drugs. Therefore, ECT is an optimal method in the treatment of bipolar affective disorder (25).

Patients with Parkinson's disease may also have symptoms such as depression and/or anxiety. Pharmacotherapy can induce side effects of levodopa and dopamine agonists, such as hallucinations, paranoid spectrum disorders, and mania. ECT may be a viable treatment option for patients who develop antiparkinsonian drug-induced psychosis (26).

About 30-40% of patients with dementia have psychotic symptoms, 40-60% suffer from depression, and 17-30% from major depression (27). Although effective in treating these symptoms, ECT can cause cognitive impairment in some

patients. However, some patients who received ECT manifested improvements in memory.

ECT can provide rapid and significant improvements in the severe symptoms of many mental health conditions. ECT is used to treat severe depression, especially when accompanied by detachment from reality (overlapping psychotic phenomena), suicidal urges or refusal to eat; treatment-resistant depression, a severe depression that does not improve with medication or other approaches; severe mania, a state of intense euphoria, agitation or hyperactivity, which occurs as part of bipolar affective disorder. Other signs of mania include: impaired decision-making, impulsive or risky behavior, substance abuse and/or overlapping psychotic phenomena; catatonia, characterized by lack of movement, fast or strange movements, lack of speech and other symptoms. It is associated with schizophrenia and other psychiatric disorders. In some cases, catatonia is caused by an organic disease; agitation and aggression in individuals with dementia, symptoms that can be difficult to treat and can negatively affect the quality of life (6).

Patients begin to observe improvement in their symptoms after about six sessions of ECT. No one knows for sure how ECT helps treat severe depression and other mental illnesses. What is known, however, is that many chemical aspects of brain function are altered during and after seizure activity. These chemical changes can build on each other, somehow reducing the symptoms of severe depression or other mental illnesses. Therefore, ECT is most effective in individuals who receive a full cycle of multiple treatments (6).

A variety of studies have shown that ECT alters cerebral blood flow and glucose metabolism, using neuroimaging techniques such as positron emission tomography (PET), single photon emission computed tomography (SPECT) and functional magnetic resonance imaging (fMRI) (28). ECT also modulates the neurotransmission process and influences the expression as well as the release of a wide variety of neurotransmitters in the brain, including transcription factors, neurotransmitters, neurotrophic factors and hormones (29). It has an effect on the transmission of almost all major neurotransmitters in the brain, such as: serotonin, dopamine, acetylcholine, endogenous opioids, epinephrine and norepinephrine (30). ECT has been shown to alter the levels of various biochemical mediators, including neurotrophic factors, to affect neuroplastic changes in the brain. This trophic activity involves both neuroprotection and increased neuronal proliferation. Even a single electroconvulsive stimulus causes the proliferation of neurons in the dentate gyrus of the hippocampus, and newly formed neurons can survive for months (31).

Changes in the volume of brain structures have been consistently reported in psychiatric disorders. Findings have also shown that ECT triggers changes in the volume of the whole brain, as well as its components, such as gray matter, white matter and other brain structures (32).

5. ECT relapse and prognosis

The proportion of the original ECT-treated patients that may experience a significant return of severe depressive symptoms are included into the relapse rate studies (33). Relapse rates are considered at 3, 12 and 24 months and investigate differences in non-C-ECT patients and C-ECT patients. Significant relapse

rate is found within the first six months and decreases significantly with the continuation of pharmacotherapy or C-ECT as compared to the placebo. There are no significant differences between unilateral ECT and bilateral ECT long-term relapse rate, and optimal success rate was confirmed for patients with post-ECT pharmacotherapy continuation treatment (2).

In common practice, various routes have been taken such as continuation and/or maintenance of ECT alone (c-ECT and m-ECT, respectively) or of ECT augmented with pharmacological treatment. Hausmann *et al* (34) distinguished between continuation and maintenance, the main difference being that continuation proceeds up to six months after the termination of the ECT initial treatment and maintenance comprises treatment administration for a period that exceeds six months. Hausmann *et al* (34) reported that there is a significant effect of combined pharmacotherapy and c-/m-ECT on the number and duration of hospitalization of patients. More specifically, those authors claimed that hospitalization rates decreased by 50% following this course of treatment, that the number of inpatient days per year was significantly reduced and that the average number of days spent by patients in the psychiatric ward were reduced from 41.6 days prior to ECT to 22.1 days after c-/m-ECT. The strongest point of their study was that they compared data that was obtained 5 years prior to and 5 years subsequent to ECT. However, caution is required regarding their main finding for multiple reasons. The study sample was heterogeneous because it comprised both patients diagnosed with unipolar and bipolar depression. A relatively small number of participants (n=27) participated in the study, the data were retrospectively collected and no controlled design was implemented. Hausmann *et al* (34) focused exclusively on the combined effect of c-/m-ECT and medication. However, other studies compared the separate effects of c-ECT to those of continued medication (c-Pharm) on the prevention of relapse (35,36). Kellner *et al* (35) conducted a multisite, randomized, parallel design, six-month investigation on patients diagnosed with unipolar depression who attained remission after bilateral ECT. Those authors suggested that both c-ECT and c-Pharm had comparable effect on relapse prevention, with no statistically significant difference identified. In addition, the relapse rates associated with c-ECT and c-Pharm were improved compared to those identified in Sackeim *et al* (37) with placebo and monotherapy with nortriptyline. One of the merits of the study by Kellner *et al* (35) is that it measures the neurocognitive side effects of both non-pharmacological and pharmacological treatment courses. Tolerability to intervention has been found in both cases (with specific side effects for each treatment). Quite importantly, though, Kellner *et al* (35) reported that relapse and discontinuation rates after successful ECT achieved a disconcertingly high level, with c-ECT relapse 37.1% of the time and c-Pharm relapse, 31.6%. Moreover, relapses occurred at a quite early stage in the continuation treatment. A relatively recent meta-analysis (20) performed on 32 studies on c-ECT and c-Pharm for a follow-up period up to 2 years also identified quite elevated relapse rates that occurred relatively early on. More specifically, 51.9% in the c-Pharm condition relapsed within 12 months of treatment cessation (in fact, the majority of 37.7% relapsed within six months) and 37.2% of the

patients in the c-ECT condition relapsed within six months. Jelovac *et al* (33) also reported that it is common practice for ECT patients to receive pharmacological continuation with the same antidepressants that proved to be ineffective before ECT. Tricyclic antidepressants (TCA) represent the treatment of choice for ECT patients even though they do not come free of side effects and adequate doses may be not so well tolerated. Sackeim *et al* (37) observed this very same fact: patients that resisted treatment with tricyclic antidepressants were prescribed TCA as part of the continuation therapy following ECT. The two aforementioned studies, albeit published years apart, converge on the conclusion that patients may benefit if, in the post-ECT period, the medication that did not yield adequate results prior to ECT was discontinued and other pharmacological options were sought. Sackeim *et al* (37) also remarked on the fact that, in their study sample, most relapses occurred within the first months that followed the initial ECT treatment. Their main finding was that patients who were medication-resistant prior to ECT had higher relapse rates than medication-nonresistant patients. At present, there is also a small-scale study (2) in which only data from ECT non-remitters (n=18) were analyzed. The study claims that c-ECT is an effective option for attaining remission within six months and that combining ECT with psychotropic medication may improve the effect of ECT. Nevertheless, the participant sample was very limited and the results were purely descriptive, and therefore could not be submitted to statistical analysis.

Despite the variety in design and clinical instruments that evaluated depression first at baseline and, subsequently, at various points in time pre- and post-ECT, the reviewed studies converge on a consensus regarding the benefits of continuation of ECT and further augmentation with pharmacological treatment as a feasible relapse prevention strategy. Regarding clinical assessment instrument variability, there is, however, a study of symptom severity in a patient cohort (n=4,617), that compared ECT (from its beginning-1960) with pharmacotherapy trials, using as evaluation scale one of the five existing versions of HRDS. The study concluded that patients who were starting ECT suffered from more severe depressive symptoms than patients enrolled in pharmacotherapy. Symptom severity detected upon enrollment in ECT and pharmacotherapy came only from HRSD-17 (38).

Regarding relapse prevention after acute ECT, the most significant bulk of research has focused on ECT and pharmacotherapy, recommendations being either that ECT augmented by pharmacotherapy should be administered during the acute stage or that treatment be continued with either ECT or medication. A significantly less explored option is the combination between ECT and psychotherapy is that of McClintock *et al* (5) who conducted a systematic review on six articles (published in English) that tackled this particular topic. The authors of that study tentatively suggest that ECT augmentation by Cognitive Behavioral Therapy (CBT) or Interpersonal Psychotherapy (IPT) may contribute to symptom alleviation and reduction. More precisely, CBT could target cognitive restructuring in patients, it could increase memory and cognitive flexibility while IPT could address adequate processing of feelings caused by the illness. The proposal is tentative and it invites further consistent research.

6. ECT efficacy

Addictive controlled trials in 20 studies that compared the efficacy of sine wave and brief pulse machines argued that there was no evidence found for differences in their efficacy and ECT proved superior to medication and simulated ECT (39).

A naturalistic study that analyzed 38 patients who showed severe resistant to treatment, concluded that ECT is highly effective and showed a higher than 50% remission rate (40). Those findings are supported by another naturalistic study with 44 patients with MDD that were treated with different ECT methods, (61% RUL, 39% mixed RUL-BT, left unilateral, and/or BT lead placement). Thus, it was shown that the results remained stable for a period of six months post-treatment. Remission of side effects also occurred before the end of ECT treatment sessions (22).

In 2009, Sienaert *et al* (4) published a study on a randomized comparison of ultra-brief BF and unilateral ECT for major depression. They concluded that even if both proved efficacious, unilateral ECT showed more rapid responses (4). These conclusions were further supported by another randomized open label-controlled trial that compared formula-based unilateral with bilateral ECT in the treatment of major depression. The results showed that there were no differences in terms of efficacy, and formula-based unilateral ECT proved safer with blood pressure and effects on consciousness (10).

Efficacy was also supported by a systematic review of randomized controlled trials on geriatric patients showing ECT safety and tolerability with transient side effects (16). In terms of clinical and preclinical studies that compared ECT to antidepressants, ECT appears superior to medication when symptom alleviation is assessed (1).

Magnetic seizure therapy, just as ECT, induces a general seizure under anesthesia, but the seizure is circumscribed to a focal area and does not target the medio-temporal structures such as the hippocampus whose nonoptimal stimulation could trigger cognitive side effects such as various forms of memory impairment. Kayser *et al* (41) compared RUL ECT to MST by randomly assigning into the two treatment groups 20 patients diagnosed with major depression disorder (treatment-resistant) who had experienced a current depressive episode. The main results included the findings that MST was associated with antidepressant effects and also reduced symptom severity to an extent comparable to ECT. Improved compliance and tolerability were observed in MST, i.e., patients took less time to recover and regain orientation as assessed by neuropsychological measure.

Repetitive transcranial magnetic stimulation (rTMS) does not require anesthesia nor does it induce therapeutic seizures. The stimulation targets various areas of the brain: bilateral, left prefrontal and right prefrontal. Chen *et al* (3) compared rTMS and ECT in multiple-treatment meta-analysis based on data from 25 articles that included 1,288 patients randomly assigned to one of the four treatment modalities. The results revealed no significant superiority of one treatment forms over the others. However, ECT came out as being the most efficacious as compared to the least efficacious left prefrontal transcranial magnetic stimulation. Furthermore, right prefrontal magnetic stimulation showed improved tolerability than ECT.

7. ECT in epilepsy

ECT has anticonvulsant properties and may be useful in the treatment of patients with grand mal epilepsy. It can generally be used safely in patients with epilepsy, but there have been cases of spontaneous seizures seen in patients receiving ECT, including tonic-clonic seizures (the most common) and/or simple partial seizures. In a survey conducted in 1945 on more than 500 patients, it was found that in two individuals who had no seizures prior to treatment, they appeared two months after ECT (42). Consistent with the anticonvulsant properties of ECT, it was further observed that the incidence of spontaneous seizures among patients receiving ECT was, in fact, lower than the incidence of epilepsy in the general population (0.5%). A 1983 study of all known cases of seizures found that there was no correlation between seizures and ECT (43). Although some patients experienced more seizures after receiving ECT, there was no evidence that ECT caused epilepsy. Antiepileptic drug treatment does not prohibit the use of concomitant ECT, although in some cases it has been found necessary to reduce the dose of the drug.

Bryson *et al* (44) described five patients who received ECT and who developed temporal epileptiform discharges on electroencephalography (EEG), despite the absence of a previous history of epilepsy. Those authors reported that three patients had seizures. After cessation of ECT, their EEG recordings normalized and no clinical seizures occurred. Those authors concluded that maintenance of ECT is potentially dangerous and recommended that EEG be performed regularly for patients receiving long-term ECT (44).

In other studies, ECT was not correlated with epilepsy in two large studies. For 166 patients who received ECT, the prevalence of epilepsy did not differ significantly from that in the general population (45). In another study of 619 patients, there were no reports of spontaneous seizures (46). Other findings suggested otherwise, however, and are consistent with Bryson's observation. It is probably fair to say that epidemiological data do not suggest that ECT causes epilepsy. However, when a patient receiving ECT develops spontaneous epileptic seizures, the question arises as to whether ECT was the cause. To answer this question, we should consider the possibility of coexisting epilepsy and psychiatric disorders, the risk of seizures as side effects of psychiatric medications, and other potentially confusing factors, *i.e.*, factors that can mislead (*e.g.*, family history of epilepsy) (47).

In short, it is premature to suggest that ECT is potentially dangerous, but routine EEG should be performed for patients receiving this therapy based on these observations. Well-designed studies are needed to establish any potential relationship between ECT and epilepsy.

8. Conclusions

This narrative review of the literature investigated the variables included when efficacy of ECT on MDD is analyzed. Our findings support the hypothesis that there is an overall consensus regarding the efficacy of ECT. There is consistent evidence that there are low to mild side effects and most of them are transient and remit usually before the second treatment. Moreover, there are cognitive outcomes

that improve beyond baseline. There is a low relapse rate compared to other treatments and it can be prevented and/or reduced by continuation of treatment with medication and/or psychotherapy.

There are no consistent randomized trials to consider all variables. Randomized trials often differ in the way the technique itself is used, as well as other variables. There are inconsistent studies on efficacy or side effects when comorbidities appear and consequently other medication than antidepressants are used. Finally, and most important there is a great need for long term effect follow up and more investigation on relapse.

In summary, our conclusion is that ECT is effective and relatively safe with specific monitoring and benefit/risk considered. This type of intervention has suffered great changes and improvement over time and presently it is performed with the support of anesthesia. In severe cases of depressive disorders, it may be a first-choice treatment if sufficient information is provided both to the patient and the caregivers.

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All information included in this review is documented by relevant references.

Authors' contributions

ST and MS designed and drafted the initial review. AS and AMD gathered the medical information and conducted the final view and structure of the article. AS and MS investigated the present area of research and gathered the important information. ST and MBC finalized the work, analyzed the results and approved the final version of the work for publication. All authors read and approved the final manuscript.

Ethics approval and consent to participate

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Patient consent for publication

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Competing interests

The authors declare that they have no competing interests.

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