Electroconvulsive therapy: old acquaintance for the youngster or new opportunity for the elder? Review of the literature and applications in the geriatric population

Massimo Palleschi,* Davide Trubian,1 Anna Palleschi2
1Geriatric Division, San Giovanni-Addolorata Hospital, Rome; 2University of Padua, Padua; 3Psychiatrist and Forensic Psychiatrist, Padua, Italy

Abstract

Electroconvulsive therapy (ECT) is among the most controversial and mythicized therapies in the psychiatric and medical clinical context. Historically, this practice was used in some contexts as a torture or a coercive method and the lay public as well as the collective imaginary (books, motion pictures and cultural agencies, etc.) has always considered and represented this treatment as inhuman. Prejudices and limited knowledge of this therapeutic tool have contributed to consider this procedure as a violent act and an assault to human dignity, progressively reducing its employment in time. Despite these prejudices, in the international literature several studies have demonstrated a considerable evidence in support of the use of ECT for some psychiatric diseases, considering it among the safest and most effective treatments. Especially in case of life-risk diseases, such as major depression, ECT proved to be necessary in dealing with pharmaco-resistance and bringing to remission psychotic depression with high risk of suicide. Furthermore, to date ECT results to be the treatment of choice in depressed patients that cannot be treated with pharmacotherapy, e.g. in pregnant women, in which the use of antidepressant drugs exposes the fetus to a teratogenic risk, or in elder patients, in which multiple-drug treatments and interactions have to be carefully considered.

The purpose of this work is to provide a review of the literature regarding ECT and concise guidelines for this treatment and its clinical outcomes, with special reference to geriatric population.

Introduction

Electroconvulsive therapy (ECT), commonly named electroshock, is probably among the most controversial and mythicized therapies in the psychiatric and medical clinical context. It consists in passage of electric current through the brain, deliberately triggering a brief seizure. Historically, this practice was used in some contexts as a torture or a coercive method and the lay public as well as the collective imaginary (books, motion pictures and cultural agencies, etc.) has always considered and represented this treatment as inhuman. The limited knowledge of this therapeutic tool - the whole mechanism of action is still only partially known - combined with the use of unmodified ECT (former technique administered without anesthesia and myorelaxant therapy, causing a shocking reaction on the patient) have contributed to consider this procedure as a violent act and an assault to human dignity, progressively reducing its employment in time.

Despite these prejudices, in the international literature several studies have demonstrated a considerable evidence in support of the use of ECT for some psychiatric diseases, considering it among the safest and most effective treatments. Especially in case of life-risk diseases, such as major depression, ECT proved to be necessary in dealing with pharmaco-resistance and bringing to remission psychotic depression with high risk of suicide. Furthermore, to date ECT results to be the treatment of choice in depressed patients that cannot be treated with pharmacotherapy, e.g. in pregnant women, in which the use of antidepressant drugs exposes the fetus to a teratogenic risk, or in elder patients, in which multiple-drug treatments and interactions have to be carefully considered.

The purpose of this work is to provide a review of the literature regarding ECT and concise guidelines for this treatment and its clinical outcomes, with special reference to geriatric population.

Data and methods

This paper adopts the problem intervention outcome (PIO) and aims to answer the following question: What limits the diffusion of the electroconvulsive therapy (I) in light of its proven efficacy (O) to treat elderly patients in Italy (P)?

The data consists of all pertinent studies and meta-analyses conducted so far without any time limits. We gave, however, preference to more recent data points.

As authors we hope that this paper serves the dual aim of critically summarizing the available empirical evidence on ECT and of stimulating a debate on its most appropriate use.
first line treatment options, the method was progressively abandoned and limited to few severe clinical conditions (ex: severe suicidal symptoms or catatonia).

Today, this method is known with the name of electroconvulsive therapy (ECT). It remains the most effective treatment for severe depressive episodes and, by virtue of its rapidity in action, it has to be considered in life-threatening psychiatric conditions.2

Despite this, ECT is being perceived as an old fashioned approach by the lay public as well as by many Authors.4 The way it was used in the initial stage (when high doses of electricity were administered without anesthesia, leading to memory loss and death) and its political employment in some context (it was named electroshock) have increased prejudices on this treatment.

Today, ECT is administered in a very different way, such as approximately half of the psychiatric clinics in Germany apply ECT4 and, although complications and side effects are still observed, all the various parameters are controlled so as to achieve the most benefit with the fewer possible risks.

To date, in Italy ECT is still a stigmatized treatment option and it is underused so that only few psychiatric hospitals in our country currently use this treatment option: only 14 centers dispose of the instrumentation for ECT, 7 are structure of the SSN (Servizio Sanitario Nazionale - National Health Service) and the others 7 are private centers.6 However, it is important to note that no data about the availability of ECT in Italy exist and often the number of structures that provide this technique are discordant. However, ECT is used in USA and in several European Countries. Precisely, provision of ECT in Europe goes from 100% in Denmark to 22% in Belgium,8 through 23% in the Netherlands,9 34% in Poland,10 46% in Spain and Russia,11,12 51% in France,13,14 57% in Hungary,14 59% in Germany15 and 72% in Norway.16,17 Its rapid effect and low side effects make some patients ask for this treatment to reduce social and personal limitations.

**Indications**

ECT is indicated for patients affected by major depressive disorder, schizophrenia, catatonia and acute mania, non-responsive ness to other traditional therapies or if the use of other therapies is contraindicated, when a rapid response is needed.18 Also, Parkinson’s Disease patients may be good candidates to ECT treatment: in an editorial of Medical Hypothesis the Authors collected few and old studies in which ECT was described as useful in treatment PD patients, but more studies have to be done.19 Moreover, ECT can be useful in treating drug-induced psychosis in PD patients.20

ECT should be considered as first line treatment, in case of less risk for the patient than medication, when there is a clear history of medication resistance or a history of favorable response to ECT, or when the patient prefers ECT to medication.7

Baghai and Möller21 recommend the use of ECT as first-line treatment for other pathologies, namely psychotic depression (remission rate around 90%), depressive stupor and inanition, severe psychomotor retardation or refusal of food and drink, delirious mania, malignant catatonia, and neuroleptic malignant syndrome (NMS). Authors also indicate that ECT becomes a useful treatment option, when depression, mania, and psychotic symptoms accompany systemic illnesses or are present during early pregnancy or the post-partum breast-feeding period (when the administration of medications is often precluded).1,22,23

Conca, Pycha, Giupponi et al.24 suggest, instead, that ECT can be used both in standard and in extraordinary populations, such as pregnant women, elders and even infants and adolescents, although these latter cases are limited by social dislike and laws.

**Major depressive disorder**

This is the most common indication, mostly because ECT is fast and most effective available treatment. ECT should be considered in cases who failed with drugs, do not tolerate medications, with severe psychotic symptoms, agitation or stupor, suicidal or homicidal ideation.25

Kennedy, Miley, Giacobbe et al. found evidence of effectiveness of ECT for all type of major depressive disorders, although there are very few comparisons between ECT and first-line antidepressants.26 Higher response rates have been reported (80%-90%) when ECT is used as first-line treatment, demonstrating that ECT is a superior acute antidepressant compared to pharmacotherapy.26 Rabheru and Persad27 reported that ECT is a good choice for acute episodes of severe major depression. According to Antunes et al.,28 no other treatment up to now has shown to be superior to ECT in the treatment of major depression in controlled studies.

For other Authors,29 in case of pharmacotherapy non-responsiveness, ECT is recommended as fifth step of five (after optimization, switching, combination and augmentation).

However, despite the considerable antidepressant power of ECT, its benefits may not persist without one form of maintenance treatment. For this reason, two large studies support the combination of nortriptyline plus lithium for relapse prevention in patients who responded to ECT.26

As far as efficacy is concerned, this is demonstrated by the scientific evidence in some cases, by the clinical and test evidence in others, but there are also cases of application, which are supported only by the clinical evidence.24 In any case, efficacy of ECT vs placebo and antidepressants has been demonstrated.18

The efficacy of ECT in treating depressive disorders varies depending on the diagnosis, in patients with unipolar depression, ECT has a major efficacy in comparison with antidepressant pharmacotherapy: response rate is over 80% and remission rate is 75% in patients treated with optimized ECT. Khalid Saad al-Harbi reports a response ratio of 50%-70% in patients with treatment-resistant depression.29 Most patients show faster treatment response during ECT in comparison with pharmacotherapy,20 mostly in case of patients with depression31 and in severe cases. ECT is the treatment with the highest rates of response and remission of any form of antidepressant treatment, with 70%-90% of patients treated showing improvement.

Recent evidences show a good efficacy also in the depressive phase of a bipolar depression, suggesting to consider ECT in those non-respondent-to-drugs patients,32 but a risk of switch to mania phase is observed.21

**Schizophrenia**

ECT did not shown more effectiveness than pharmacotherapy, but ECT acts faster so can be indicated in treatment patients at their first episode or with catatonia or suicide tendency. ECT is now commonly indicated in schizophrenic patients to strengthen action of antipsychotics and for acute symptoms.33 ECT is particularly useful in association with antipsychotics both in acute and chronic disease.24

**Manic episodes**

In these patients, ECT is generally limited since pharmacological treatment is very effective in the short term. It finds possible employment in patients with specific contraindications to pharmacotherapy or dangerous level of exhaustion.

**Other conditions**

Ray-Griffith et al.34 considered the use of ECT in pregnancy, reporting that the foundation of the risk/benefit assessment for treatment options during pregnancy is based on the premise that maternal mental illness poses at risk to the mother and/or fetus. If the goal of treatment is the rapid resolution of such maternal symptoms and minimizing risk to the fetus, then it is rea-
reasonable to consider ECT much earlier in the treatment course - particularly in women with suicidal ideation. The results showed that only one documented case of fetal loss directly related to ECT has been reported, otherwise, ECT is only associated with transient, spontaneously resolving bradycardia of no known clinical significance. According to Spodnioková et al.,

ECT represents a promising option for treating serious psychiatric disorders in pregnant women. Prospective studies with a much larger sample sizes are still needed. More reviews should focus on the long-term sequel of ECT as they relate to the neonate.

ECT is reported as effective in episodic psychosis, atypical psychosis, obsessive-compulsive disorder and delirium. Several other medical conditions find ECT useful: Parkinson’s disease, neuroleptic malignant syndrome, hypopituitarism, intractable seizure disorders.

Finally, ECT may be considered the treatment of choice, thanks to his safety and efficacy for this age, for geriatric and medically ill patients who cannot take drugs safely, due to chronic conditions or multiple drug therapy interactions.

Pretreatment recommendations

ECT administration should be preceded by a pretreatment evaluation, including clinical and instrumental assessment (physical and neurological examination, pre-anesthesia examination, medical history; blood and urine lab testing, chest X-ray, electrocardiogram, dental examination especially for elder patients).

For patients with seizure a space-occupying lesion should be excluded with specific neuroimaging (CT scan and MRI).

All ongoing medication should be carefully assessed, searching for possible interactions or absolute contraindications, both for positive/negative effects on seizure threshold and for drug interaction with medications used during ECT administration. Accepted drugs include tricyclic and tetracyclic drugs, MAO-inhibitors and antidepressants. Due to their influence on seizure or on cardiopulmonary function, the following drugs should be withdrawn prior ECT: i.e. benzodiazepines, lithium, clozapine, bupropion, lidocaine, theophylline and remerpine.

Patients must have fasted for 6 hours before administration.

Immediately before ECT, an intravenous line should be established and mouth should be checked (foreign bodies, dentures). To prevent dental and tongue injury, clinician should insert a bite block in the mouth, administer 100% oxygen (rate of 5L/min) and have immediately available emergency equipment for establishing an airway.

Pretreatment drugs include: i) muscarinic anticholinergic drugs, to minimize oral and respiratory secretions and to block bradycardias and asystoles, especially in patients treated with beta-adrenergic receptor antagonists and with ventricular ectopic beats. The most used are: atropine and glycopyrrolate; ii) anesthesia, which should be as light as possible. Several drugs are currently available and the choice depends on patient clinical history;  iii) muscle relaxants, to minimize the risk of bone fractures or other traumatic injuries. Succinylcholine is the treatment of choice, excluding some exceptions (i.e. known pseudo-cholinesterase deficiency) which require other drugs (curare or atracurium).

The patient is monitored during and after the treatment and the procedure supervised by a psychiatrist and an anesthesiologist. The patient must be ventilated, but not intubated.

Electroconvulsive therapy administration

Electrode placement

Standard positions bifrontal configuration and asymmetrical placement. Electrodes can be placed bilaterally or unilaterally (typically, on the right side - RUL). RUL seems to cause less cognitive impairment than bilateral, but, for some patients, bilateral is more effective (response rates for low-dose and moderate-dose RUL ECT were 17% and 43%, respectively, compared with 65% and 63% for low-dose and moderate-dose bilateral treatment).

Electrical stimulus

The stimulus must be enough strong to reach the seizure threshold. According to the most recent evidences, the stimulus parameters are: current 500-800 mA, frequency 20 to 120Hz, pulse width 0.25 to 2 milliseconds and duration 0.5 to 8 or more seconds. Seizure threshold influences both efficacy and side effects in RUL, whereas electrode position does not affect cognitive side effects.

Number and spacing of treatments

Studies show that when ECT is administered 3 times a week, it can cause a more rapid improvement compared to 2 times per week, the number of total treatments necessary to achieve the result remains unchanged: twice-weekly administration may be optimal schedule for bitemporal ECT in elderly. The total number of ECT treatments necessary to obtain results is very variable: among elderly patients with major depression, 6 to 12 treatment are often required to achieve maximal benefit. In case of no response or minimal response, many Authors recommend at least 10 to 12 bitemporal treatment before the depressive episode is labelled nonresponsive.

The treatment protocol consists of a series of 10 single treatments on average, applied at an interval of several days.

Electroconvulsive therapy mechanism of action

Although 100 years of use and testing, no definitive theory regarding the ECT mechanisms of action is fully accepted and there is a gap in our knowledge of exactly how it works. According to Conca, the generalized seizure constitutes the therapeutic agent of...
ECT, leading to an increase release of nerve growth factors, which stimulates the neuroformation of nerve cells and synapses. This result in increased plasticity and regeneration of neural networks.

ECT seems to enhance serotonergic neurotransmission and activate the mesocorticolimbic dopamine system. Moreover, it seems that these effects are evident at various levels, including neurotransmitter release, receptor binding, and overall neurotransmission. In major depressive patients, tryptophan plasma levels change, and studies that investigated the correlation between tryptophan plasma levels and ECT effectiveness notice that a reduction of tryptophan may be associated with a good response to the therapy.

An increase of γ-aminobutyric acid (GABA) neurotransmission has been considered as well: after ECT, GABA concentrations in occipital cortex are increased in depressed patients. ECT has been shown to enhance activity of inhibitory circuits in human motor cortex, further indicating that ECT has marked effects on GABAergic neurotransmission.

Other substances involved are ACTH and cortisol, suggesting an involvement of hypothalamic-pituitary-adrenal (HPA) axis; BDNF mRNA and tyrosine kinase B (TrkB) mRNA, indicating a possible effect on neurogenesis and neuromplasticity. In depressed patients, the cerebral blood flow (CBF) is reduced briefly after ECT but increases and normalizes after a course of ECT.

It has been observed that Dehydroepiandrosterone sulphate (DHEAS), a potent negative modulator of GABA-A receptor, increases after ECT, this may be used as a predictive marker of non-responsiveness to ECT; moreover, responders compared to non-responders had reduced cerebral glucose metabolism in the frontal region.

According to Conca, Pycha et al., the antidepressant effect of ECT may be due to the reduction of β1-receptor density and of mRNA of β1-receptor concentration. Whereas antipsychotic and animac effect can be read in the light of the modulation of D1-receptor and of density of post-synaptic 5-HT2-receptor.

A certain fact is that a generalized tonic-clonic seizure is necessary for ECT to exert its antidepressant effect, in comparing real ECT with sham ECT, where all attempts to modify the core element, i.e. the seizure, no therapeutic impacts were observed.

**Side effects and risks**

As all medical treatments, ECT has some side effects and risks, but many side effects are temporary and improve with time (in general a rapid improvement is reached within 1 and up to 4 weeks); thus, ECT is one of the best-tolerated biological therapies. ECT does not cause any damage to the brain at a structural or cellular level.

**Mortality**

Death caused by ECT is an extremely rare event. According to a recent systematic review the mortality rate was estimated at 2.1 per 100,000 treatments (95% CI: 1.2-3.4). In nine studies, published after 2001 (covering 414,747 treatments), there was only one reported ECT-related death. Deaths are due to cardiovascular complications, mostly in patients already compromised in the cardiac system.

**Central nervous system effects and neurologic impairment**

Cognitive side effects are the main limitation of ECT. Memory loss and delirium are the most common neurologic sequelae. Memory loss can be retrograde, anterograde or both, but there is no evidence of brain damage. An important aspect of neurologic impairment is that it generally resolves in the weeks and months after the treatment and only some patients complain long-term impairment.

Cognitive effects are the most relevant side effects, but their frequency is up to 30% of patients treated, and only 5%-7% of those are severe (on the total that is 1.5-2.1%). The Authors report that the parameters responsible of cognitive effects are the electrode position, the modulation of impulse, the width of the impulse and the dose. A complete loss of memory does not occur in general. The intensity and frequency of some side effects - such as memory disturbances, concentration or attention deficits - is influenced by the parameters through which ECT is administered. Patients treated under twice a week regimen are safer than those treated with a three times weekly regimen. Moreover, side effects can be reduced by reducing the frequency of treatment, by using a particular ECT machine that produce brief pulse rather than sine wave, or by reducing the dose of stimuli.

**Cardiac complications**

Individuals with cardiovascular disease have been treated safely with ECT. ECG performed during ECT frequently shows abnormalities, but it is not clear how sensitive or specific are as indicators of heart dysfunction. On echocardiography, temporary left ventricular dysfunction has been observed, but the same Authors indicate that neither clinical nor ECT variables were associated with development of ECT-associated LV dysfunction and patients who developed new LV dysfunction did not have any short-term adverse events. ECT has no cumulative effects on heart; rather it seems that tolerance to ECT is developed.

Another study reported that no adverse cardiac or cardiovascular event was observed during maintenance-ECT (M-ECT), despite the fact that 50% of their subjects had abnormal electrocardiograms at baseline and this supports the idea that heart is affected by seizure during ECT, but after the end of the treatment there are no sequelae.

According to a recent review, the increasing heart rate after a successful ECT course may be involved with symptom improvement; furthermore, the relationship between cardiac autonomic modulation and major depression may be crucial in elderly patients in whom major depression disease (MDD) could aggravate their already age-related reduced autonomic modulation, exposing them to the risk of sudden cardiac death.

**Other side effects**

Other side effects include nausea, headache (up to 45% can be treated symptomatically), muscle pain, oral injuries, persistent myalgia, vomiting, very rarely fractures.

**Contraindications**

No absolute contraindications for ECT are described. Relative contraindications are cranial lesion occupying space or endocranial hypertension, recent myocardial infarct with functional heart instability, recent cerebral bleeding, vascular anomalies, aneurism, pelvis bone veins thrombosis, retinal detachment, pheochromocytoma, arterial hypertension not well treated and increased anesthetic risk.

In patients with relative contraindications, ECT can be administered, but with special attention, considering adequate pre-medication.

**Electroconvulsive therapy in the elder**

Since ECT is a safe technique to achieve a rapid and strong antidepressant effect, it can be very useful in old-age-patients who, nowadays, increasingly use many drugs for other comorbidities, thus increasing the risk of drugs interaction. Having a powerful method to treat depression without using other drugs, is extremely significant.
Especially in light of the fact that untreated depression can have severe medical consequences in older people and increased risk of mortality. The technique and the administration schedules are like the ones used for the general populations, with the care to pay special attention to particular conditions of this segment of population.

In their review, Baghai and Möller reported that ECT has also been shown to have excellent effectiveness in geriatric patients. Efficacy was generally greater in geriatric than in young patients and greater in patients. Efficacy was generally greater in patients treated with ECT and, more importantly, old people do not incur worst side effects, while mixed-age population does. Within 5 weeks, 64% of patients treated with ECT remitted according to the MADRS scores. Within 5 weeks, 64% of patients treated with medication and the final remission rates of 64% after 6 weeks in the ECT group and 33% after 12 weeks in the medication group underlines the superiority of ECT even more. ECT seems to be a good option in old patients with depressive psychosis, schizoaffective disorder, or depression with dementia who are treatment-refractory, medication-intolerant, medically ill, or frail. As regards patients depressed with dementia, few trials are available, but appear that ECT may be useful, also because the use of ECT allow to avoid the use of drugs and it is very fast in the results.

Obviously, several recommendations can be made about the administration of ECT to older patients, because age is also a risk factor, rates of cardiovascular complications among patients older than 80 years of age are higher than those among patients who are 65 to 80 years of age (36% vs 12%).

In the first place, the dose of electricity must be optimal; secondly, case-by-case the choice of high-dose RUL or low-dose bitemporal ECT should be take, even though further research in order to help this choice is needed; thirdly, the optimal schedule for bitemporal ECT seems to be the twice-weekly administration. Bjølseth et al. noted that the speed of recovery from disorientation may supplement EEG characteristics in tailoring stimulus dosing for elderly patients.

Regarding the position of electrodes, in another study, Bjølseth et al. indicate that in the context of relatively small sample of elderly patients, randomly allocated to formula-based BR and RUL ECT, there were no significant differences in improvement from major depression and no detectable differences in cognitive side-effects, using the MMSE.

Furthermore, Rabheru and Persad show that relapses are common with missed treatment, and after 10 weeks without ECT, as many as 80% of patients may relapse, particularly the elderly. In this field, some studies suggest the use of continuous/maintenance-ECT (C/M-ECT) to prevent relapse.

Properly, van der Wurff et al. highlighted that the studies on the effects of ECT, both in general and with elderly people, are rare and not always performed with the right approach. Evidence on the efficacy and safety of ECT in depressed elderly with concomitant dementia, cerebrovascular disorders or Parkinson’s disease is sparse. Moreover, it has been noted that, despite the efficacy of ECT in older people, elderly people tend to be under-represented in trials, which limits the confidence with which results can be used to lend support to clinical practice in this subgroup.

Legal aspects

Nowadays, in Italy ECT is banned as a mean of achieving rapid remission of symptoms in psychiatric diseases. In general, the use of ECT is restricted to disorders such as major depression with psychotic symptoms and psychomotor inhibition, only when drug treatment is contraindicated, ineffective, or precluded by its side effect.

There are no legal problems if the patient is capable of understanding, able to take a decision about his or her treatment, and, more importantly, able to subscribe the informed consent free, aware, current and evident. If this is not the case, the authorization of the Court is required.

In Italy, the only national legal document regarding ECT is a Statement issued by the Ministry of Health (on February 15th, 1999). The document analyses efficacy and contraindications and indicates the cases in which ECT can be used. The patient candidates to ECT are those who have severe depressive episodes with psychotic symptoms and psychomotor slowing, when the pharmacotherapies are not administrable, i.e. a clear and sure pharmacological therapy and when the use of drugs is contraindicated. In general, the use of ECT must be restricted only to indication previously mentioned.

Limitations

The main limit of our work is represented by the poor number of original articles about this method: the bulk of articles available are reviews of non-recent works (often non randomized) and, even though using the best statistics methods, they cannot be accurate in considering every variables like a double-blind research can do.

Conclusions

The above analysis of the literature on this topic allows us to conclude that the data support the efficacy of ECT in selected cases, mainly those who cannot benefit of other treatment options such as the elder and pregnant women. Further research is required to fully understand the mechanism of actions and how to avoid side effects. Further research would allow adequate methodological evaluation, thus avoiding incoherence and the immoral consequences of the rhetorical stigmatization of ECT - a biased rhetoric that is neither humanistic nor scientific - which affects patients by prolonging their wait for appropriated therapy. The clinical practice, although very useful, cannot be the only base on which a treatment is used.

There are no ethical reasons for doubling the licit nature of ECT. However, because of politically and ideologically based conflicts, public ECT centers are still lacking. Efforts must be done to sensitize the public opinion and the lawmakers on this issue. The main target is to approach to this controversial matter without prejudice in order to offer patients the best and safest possible evidence-based treatment. Lawmakers are not alone in deciding the indications to provide, but they must be supported by the scientific community because, as reminded by Pallanti, therapeutic choice cannot be acceptably be the result of purely political and ideological decisions. Crucial is the training of the new generations of specialists, as ECT therapy should be systematically included in the psychiatric training of medical student. What all of us always have to remember is that the main aim of medicine is to achieve the state of health of the Person. This target has to be reached without prejudice and ideological walls.
References


