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Dose Electroconvulsive Therapy as the First Choice in Treatment for Psychiatry Disorder?

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ABSTRACT

Electroconvulsive Therapy (ECT) is the oldest biology treatments in psychiatry. It has been still in use over 80 years. It is a safe well-tolerated, highly effective treatment option for mental disorder especially depression and schizophrenia. Although the development of psychotropic drugs decreased the application of ECT. There are some controversies about its efficacy, and some concerns on inconvenience, side effects, course of treatment, indication and efficacy, which limit the extensive application of ECT. ECT was proved to be effective in mental disorder expect for depression and schizophrenia from numerous studies. It's embarrassing that ECT has been not suggested as the first-line treatment. The mechanism of ECT is still unknown. Although there is no absolute indication for ECT, there is no guideline on specific guidance on treatment parameters, course of treatment to help doctors in clinical practice. ECT was used based on doctors' experience. So more research needed to provide more evidence for ECT use in practice.

Keywords: Electroconvulsive therapy; Adverse effects; Mortality; Indication; Mental disorder

INTRODUCTION

Electroconvulsive Therapy (ECT) is the oldest biology treatments in psychiatry. It plays a very important role in psychiatry. It has been still in use over last 80 years since 1938. It is a safe, well-tolerated, highly effective treatment option for depression and schizophrenia, especially when there is an acute exacerbation of psychotic symptoms. The development of psychotropic drugs has a certain impact on the clinical application of ECT. Compared with the relatively complex operation of electroconvulsive therapy, drugs have become the mainstream treatment method for mental diseases due to their convenience and relatively few side effects. And because the mechanism of ECT has not yet been clarified, there are still many controversies about its efficacy, but ECT plays an irreplaceable role in the treatment of psychosis. Therefore, this article will review the electroconvulsive therapy in order to provide better help for clinical treatment.

HISTORY of ECT

In the past decades, ECT remains controversial for its side effect or misuse in treatment for mental disorder. Traditional ECT will bring some adverse reactions, including epilepsy induction, cognitive side effects, memory impairment and effects on brain physiology, thus reducing the opportunity to use ECT. Modified ECT replaced the traditional ECT after 1952, oral fracture and injury decreased significantly under general anesthesia [1]. There will still be some unavoidable side effects, including headache, nausea, myalgia, and confusion, which are minor and self-limiting. General anesthesia and ECG monitoring improve the safety of modified ECT, even if cardiovascular, pulmonary, and cerebrovascular events happened which may be minimized by physiologic monitoring [2]. Modified ECT is safe and effective with fewer side effects, even for elderly patients, adolescents and pregnant women [3]. But examples of both success and failure, especially failure, and cognitive side effects, especially amnesia, although temporary, made some

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scholars skeptical to ECT.

In the 1950s, ECT faced new challenges with the development of antipsychotics and antidepressants. Drug treatment has gradually become the first choice for psychiatry treatment. The development of antipsychotics including traditional antipsychotics (chlorpromazine, haloperidol, etc.) in the 1950s and atypical antipsychotics (clozapine, risperidone, olanzapine, quetiapine) after the 1960s provide a safe, effective therapy for patients with mental disorders. Especially atypical antipsychotics were recommended as first-line pharmacological treatments for psychiatry therapy attributed to significant improvement of positive symptoms, negative symptoms and cognitive symptoms. Antidepressants including traditional antidepressants such as Monoamine Oxidase Inhibitor (MAOI), Tricyclic Antidepressants (TCAs), etc. and new antidepressants such as Selective Serotonin Reuptake Inhibitor (SSRI), Serotonin and Norepinephrine Reuptake Inhibitor (SNRI), etc. are effective for most patients. Drugs became the mainstream treatment for psychiatry disorders. Safe, effective, economic and convenience is prominent of drug therapy make reduction in use for ECT. The extensive use of antipsychotics has gradually replaced ECT in the treatment of mental disorders. At the same time, modified ECT reduced the adverse reactions due to the introduction of anesthesia. Even so, the use of ECT in patients with psychotic disorders gradually went into the glooms in the developed countries and its use was restricted to affective disorders [4]. In England, there has been a reduction in its use over the past few decades. In 1999, 2835 patients received ECT over a 3 months period, equating to an annual estimated total of 11,340 patients. By 2002, this annual figure had dropped to an estimated 9088 patients. A more recent study in 2006 confirmed a further decline in ECT administrations overall. Possible reasons for the decline in its use include the availability of newer antidepressants, improved care in the community and earlier recognition of mental illness [5]. In the US, the use of ECT has also declined since the 1970s but there are still an estimated 100,000 ECT procedures conducted each year [6].

ECT faced a dilemma, although ECT can quickly alleviate symptoms, it seemed that ECT was not usually as the first choice for treatment. It is usually an end-stage therapy, recommended for those who failed to respond to other therapies and whose severity of illness may be life-threatening (National Institute for Health and Clinical Excellence, 2003). However, guidelines of the American Psychiatric Association task force state that ECT should not be reserved for use as a “last resort” but promotes its use as a first-line treatment when there is a need for a prompt and definitive response, when patients have responded well to previous ECT administrations, and when the treatment is preferred by the patient (Task Force on Electroconvulsive Therapy, 2001).

ECT was as a first-choice for those refractory or serious patients by doctor, especially when patients were under in some emergency crisis. In fact, patients with severe major depressive disorder received short term ECT, the symptoms alleviate quickly [7]. There is good evidence that ECT is more effective than antidepressants in reducing depression and suicidal intent among patients with severe depression [8]. However, there is still controversial about the efficacy between the suicide and ECT that is another reason for reduction in ECT use. The incidence of suicide attempt has also been found to be lower in patients treated with ECT compared to antidepressants [9]. In Finland, for example, Isometsa and colleagues found that, over a 12 months period, only 2 of the 1397 suicide cases had received ECT within 3 months of death, accounting for 0.14% of all suicide cases [10]. These data were obtained from suicide related studies, particularly as the proportion of those who die by suicide who have received ECT is very low. The impact of ECT on completed suicide, however, is less clear, especially lack of large sample research between ECT and suicide. The majority of studies have found no relationship between ECT and completed suicide [11,12]. For example, of 30 patients who died within 14 days of receiving ECT between 1993 and 1998, reported 8 cases (27%) had died by suicide, but that there was no association with the treatment the rate of suicide being high in those with severe depression [13]. However, Munk-Olsen and colleagues reported an increased risk of suicide (relative risk=4.82, 95% CI 2.12-10.95) in patients who had received ECT in the week before death compared to non-ECT patients [14]. The authors acknowledged this finding was based on a small sample (6 suicide cases) and may have been explained by selection bias in that patients treated with ECT were already at high risk of suicide. In addition, this finding may be related to early treatment response mechanisms that have been suggested with drug therapies. For example, antidepressants are known to improve depressive symptoms but they may also possibly increase suicidal thoughts and behavior in the early stages of treatment [15,16]. Explanations include a delay in any therapeutic effects until later in the treatment phase, or that antidepressants are prescribed at a time when depressive symptoms are acute and therefore the risk of suicidal behavior is already increased. Alternatively, it may be that for some patients receiving pharmacological treatment a rise in energy levels precedes an improvement of depressive symptoms and they therefore may have the motivation to carry out suicidal acts [17]. Suicides following ECT may also be an indication of treatment failure.

Benefits of ECT from Short-Term or Long-Term

Self-Injurious Behavior (SIB) and suicide are common symptoms occurs in various psychiatric disorders such as major depression, schizophrenia, personality disorder, bipolar disorder, personality disorders (especially borderline personality disorder), mental retardation, post-traumatic stress disorder, trichotillomania, and others. Although ECT is not considered as a treatment for suicidal behavior, it may decrease or prevent suicidal behavior, presumably due to its effectiveness in treating the illnesses characterized by suicidal symptoms. Although there are few studies on the application of ECT in the treatment of SIB and suicide, substantial clinical experience indicates that ECT often exerts a profound short-term beneficial effect on suicidality. This effect is often rapid, and is particularly marked in patients whose psychiatric disorder responds favorably to ECT. So ECT should be given particular consideration when suitable patients present with acute suicidality. There is no doubt about the efficacy of ECT. However, it is not clear how long the clinical efficacy of ECT can be maintained. For a long time, it seems that ECT is more likely to be used to solve clinical crisis situations. So it is often used in short-term in clinical practice, and more attention was paid to whether the crisis

situation can be quickly controlled. In recent years, more and more studies have focused on whether the efficacy of ECT is sustainable. The study found that up to 50% of patients with depression who received short term ECT had relapsed within 6 months even if they maintained drug treatment, even if they accepted appropriate continuation or maintenance pharmacotherapy strategies [18-20]. High recurrence rates of between 42% and 95% were observed in long-term follow-up studies. The study found that the effect of continuous application of ECT was equivalent to that of continuous application of drugs, which proved that ECT can be used for long-term treatment like continuous treatment of drugs [21,22].

The American Psychiatric Association's guidelines propose that continuous ECT/ECT may be indicated to reduce the risk of relapse/recurrences, especially those patients who respond to short-term ECT or show resistance or intolerance to drug treatment. Patients who received continuous ECT plus drug therapy showed lower rates of depressive relapses than those patients treated with pharmacotherapy alone [23]. And it might improve the outcome of those patients with an especially severe condition. Even though some studies showed no difference between continuous ECT and maintained drug treatment. Short-term ECT treatment can improve the response to other therapy methods and ultimately improve the course of the disease. The inconsistent results of the study can't explain the poor efficacy of maintenance electroshock treatment. It is important to find the appropriate population who need continuous ECT to obtain greater benefits from ECT. Therefore, like other treatments, ECT can be used as a long-term treatment. Whether or not to choose a long-term treatment depends on the patient's efficacy, acceptability, benefit and other factors. Individualized evaluation may help doctors and patients make decisions, how to get better benefits from long-term or short-term ECT.

Clinical Indications of ECT

ECT plays a very important role in treatment for mental disorder attributed by no absolute contraindications, although it is not the mainstream treatment. It was recommended as a treatment for major depression and schizophrenia. In fact, it was used widely in various psychiatric diseases in clinical practice especially when other treatments failed. Except for major depression and schizophrenia, many cases have reported that the patients get benefit from ECT therapy. Feridun Bu¨lbu¨l ect report a case of depressive episode of bipolar disorder with OCD comorbidity treated successfully by ECT. A 33 years old man experienced 3 manic and 8 depressive episodes in the last 16 years, with cleaning compulsive behaviors, sexual obsessive thoughts, thoughts of death and suicide, loss of appetite, and sleep disorder. Failure to achieve a complete response with pharmaco-therapy, coupled with suicidal thoughts, he accepted 13 sessions of ECT therapy. A significant improvement was found in the depression and OCD symptoms as well, Clinical Global Impression (CGI) score reduced to 3 from 6 before ECT, Hamilton Depression Scale (HAM-D) score reduced to 7 from 17, and Yale-Brown Obsessive-Compulsive Scoring Scale score reduced to 10 from 33 [24]. Lee Elizabeth Wachtel ECT report a 19 years old man with autism and mild mental retardation who developed severe depression with repeated suicide attempts, multiple symptoms of catatonia, and life-threatening repetitive self-injurious behaviors after 3 years of failed psychotropic and behavioral interventions, and the patients get remission treated by ECT therapy [25]. Two men with self-injurious behavior who met criteria for catatonia, one of them met criteria for autism. ECT combined with drugs was used for improvement in symptoms [26]. 16-years-old patient was diagnosed by autism and bipolar disorder comorbidity. The patient displayed very complicated symptoms such as severe insomnia, hyper sexuality, expansive and agitated affect, aggression, self-injury, and property destruction. Many treatments were failed after hospitalization; he had to accept ECT for a history of poor response to multiple antipsychotics. After 3 weeks of weekly maintenance ECT, a marked positive response was identified, so the patient was discharged to a community residential care setting [27].

Although the validated evidence for its use in Eating Disorders (EDs) is limited, ECT had to be used as a last resort due to the crisis situation of patients in clinical practice. A 30-years-old American woman was presented to the emergency room with suicidal ideation. She has a history of AN, depression, anxiety, PTSD, and multiple suicide attempts. When a variety of treatment modalities failed, ECT was recommended because of the urgency of her condition and need for immediate intervention for her suicidality and restricting behavior, she accepted 11 times ECT therapy, her mood had improved significantly, and she was no longer reporting a desire to self-harm [28]. A 70-years-old white man with diagnoses of major depressive disorder and Frontotemporal Dementia (FTD), he was accepted ECT therapy for severe depression, psychosis, and acute suicidal ideation. ECT was applied 3 times a week, after 6 times ECT treatment, his depressive and psychotic symptoms resolved, with no worsening in cognition as demonstrated by the lack of change in his Montreal cognitive Assessment score [29]. In our previous study, we report a case that an 18-years-old male with Obsessive Compulsive Disorder (OCD) and Body Dysmorphic Disorder (BDD) comorbidity successfully treated by ECT. He accepted the ECT treatment for repeated self-injury when he failed to drug treatment [30]. ECT was also used as a novel treatment for PTSD to improve the PTSD symptoms and showed a dramatic reduction in mortality from suicide in patients with depression and PTSD comorbidity [31]. When used safely and appropriately, ECT has been shown to be useful in conditions as varied as Obsessive-Compulsive Disorder (OCD), Parkinson disease, and Post-Traumatic Stress Disorder (PTSD), dementia, autism; it can be effectively used more broadly than indicated according to literature and research reports.

Applicable Population for ECT

There is no rigid restrict in age for ECT. So ECT was applied for patients from child to older patients under rigorous clinical evaluation. Even if drug treatment is mainstream in psychiatry disorder, but sometimes psychiatrist feel embarrassed and troublesome for some special groups. Pregnancy will increase the risk for psychiatric disorders, it is estimated the prevalence of 15%-29% in pregnant women [32]. And it may bring profound consequences for both mother and her future child. Depression is the leading cause of disease-related disability. The prevalence of depression during pregnancy range from 3.1%-4.9% approximately 14.5% of pregnant women having a new

episode of depression during pregnancy [33]. Pharmacotherapy during pregnancy may also carry risks for both mother and fetus. Less impact on reproduction was administered in numerous psychotropic medications. Psychotropic drugs may cross the placenta and enter the fetal circulation at varying degrees based on characteristics of the drug and maternal physiology. Some drugs have maternal and fetal side effects. Valproic acid is among the greatest teratogens and associated with neurodevelopmental abnormalities. Benzodiazepine is related to preterm birth and low birth weight [34].

ECT is safe and effective for many psychiatric disorders in pregnancy. And the risks, adverse reactions, length of treatment, and response in pregnancy are similar to those of ECT in any individual [35]. It is a good choice for minimizing potential adverse effects, maternal and fetal. Especially when pregnant women are in severe depression with suicide or acute psychosis during pregnancy, resulting in the impairment of the mother's ability to take care of herself or causing danger to herself or others, or their symptoms are ineffective for drug treatment [36]. Older psychiatric patients are prone to drug-induced side effects because of their slow metabolism and their poorer medical condition. ECT is considered to be an effective and safe method for the treatment of older psychiatric patients for better treatment outcomes, few side effects than pharmacotherapy and low incidence of complications [37]. One-third older psychiatric inpatients received ECT. ECT can short hospitalization for taking effect quickly. So it is viewed as a more cost-effective treatment [38]. The US Food and Drug Administration propose that antidepressants can increase suicidal thoughts and behaviors in adolescent depressed patients [39]. Severe side effects caused by psychotropic medications such as such as tardive dyskinesia, weight gain, elevated blood sugar, and blood lipids maybe harmful to developing adults. So it is an alternative treatment option in adolescents. However, there is still controversy about the use of electroconvulsive therapy in adolescents. ECT should be strictly regulated due to the ethical concerns and risk of significant cognitive impairment. In the past decades, ECT has been rarely used for adolescents in western populations. However, ECT is a highly efficient option for treating several psychiatric disorders in adolescents with few and relatively benign adverse effects [40]. ECT is mainly recommended for the treatment of major depression, bipolar disorder, and schizophrenia, particularly for patients with suicidal or aggressive behavior, and catatonia. Treatment-resistant mood disorders and high risk of aggression are the main indications of ECT in China.

Mortality and Adverse Effects of ECT

ECT is a safe and effective treatment for psychotic disorder. However, ECT is still an irreplaceable classical treatment especially in treat resistant patients. In the last years, it was used widely in the world for its efficacy and effectiveness. And it was a safe treatment confirmed by some retrospective study. The overall mortality rate from natural causes was lower among ECT than other in-patients from the study of Denmark national registers. Some scholars suggested that the reduction of the risk of natural death in ECT patients may be the result of selection bias, because patients with poor health are unlikely to receive treatment. However, there is no absolute medical contraindication of ECT. It is sound unreasonable for its lower mortality. But there was slightly increased but statistically insignificant mortality rate from unnatural causes among ECT patients. Patients treated with ECT had a marginally significant trend towards an increased risk of dying by suicide compared with other in-patients, especially in those patients whom had unipolar or bipolar affective disorder [41]. Those patients had a higher risk of suicide than others. Another reasonable explanation for increased mortality is due to the poor response of patients to ECT treatment or the severity of disease. ECT had proved to be a safe treatment due to no significantly increased risk of mortality from the observed data. It was found that those patients who may be effective for ECT increased suicide mortality in some suicide related studies. Given the findings of the large database studies, as well as the evidence that ECT is associated in decreased long-term mortality for a wide variety of causes, the death rate attributable to ECT is likely much lower than 18/100,000 treatments [42]. And it seemed safer than antidepressant medications, especially in young patients; some agents will enhance the risk for suicide. Like drug therapy, there will be unavoidable Adverse Effects (AEs) after ECT, dry mouth; nausea, headache, and myalgia are common in patients after ECT. These AEs are usually mild and transient [43]. Some studies have reported that post-ECT delirium and fever could be observed in patients after ECT [44]. These AEs mostly occur during or shortly after an ECT session which related to the anesthesia, anticholinergic drug, muscle relaxant, electrical stimulus, or seizure. Cardiovascular complications is one of the severe AEs, the commonest cause of morbidity and mortality with ECT, have decreased with the institution of continuous heart rate, blood pressure, and electrocardiogram (ECG) monitoring, and improved anesthesiological technique [45]. Transient, benign brain edema, aspiration pneumonia rarely occur under careful care. In recent years, researchers paid more attention to cognitive impairment, even with the modified-ECT; cognitive side effects are still an important issue, although their nature and extent have not yet been fully clarified [46]. Cognitive function is very complicated. However, the risk of cognitive side-effects of ECT is related to the domain of cognitive function, ECT treatment parameters and individual patient factors. Non-memory cognition especially in executive function and processing speed maybe impaired significantly in short-term, but few influence in long-term. Loss of memory is very common in patients of ECT. Individual studies show that there was impairment on tests of anterograde memory from early in a course of ECT and meta-analyses suggest that this was still impaired sub-acutely (0-3 days) but returned to baseline after the end of the course of ECT. The degree of initial impairment depends on treatment and patient factors. Retrograde memory was influenced by ECT especially autobiographical memory (i.e. loss of memory for events that the person has experienced) involved in distressing and functionally impairing, there is evidence that females and those receiving bilateral ECT are more at risk [47]. ECT treatment parameters maybe related to cognitive function. The other important factor is treatment parameters; in general, the impairment of cognitive function was more closely with stimulation intensity, location of electrode stimulation and treatment duration. High stimulation intensity, bilateral stimulation and long-term treatment are more prone to aggravate cognitive impairment. Individual patient factors

play an important role in cognitive function [48]. The severity of the disease, gender, age, what kind of disease, whether to combine drug therapy, and which drug to combine will be associated with the degree of cognitive impairment [49]. Hippocampal volume change is related to cognitive impairment confirmed by imaging study. Strategies to reduce the impact of ECT on the hippocampus may be clinically useful and bring little cognitive function impairment [50]. Generally, ECT is a safe procedure in which complications are minor and manageable.

ECT ALONE OR COMBINATION ECT AND DRUGS?

There is a controversial about the treatment of mental disorders with ECT alone or ECT combined with psychotropic drugs. Attributed to little evidence of enhanced efficacy and concerns about increased side effects, the American Psychiatric Association Task Force on ECT discouraged combination drug treatment. Combination drug treatments is recommended and considered routine for many practitioners in the US and other parts of the world, and the reasons are as follows: First, ECT is the most effective acute treatment for psychiatric disorder, but it is rarely used as the first-line treatment. Drug resistance has become its main indication. And relapse during the early weeks after ECT treatment alone remains common. Considering the observed delay in the onset of therapeutic action after initiation of drug, it has been hypothesized that early relapse after ECT may be a consequence of delaying resumption of pharmacotherapy until after completion of acute ECT. It has been suggested that concurrent pharmacotherapy during the course of acute ECT might decrease the frequency of early post-ECT relapse. Second, although the current research results are inconsistent, concurrent pharmacotherapy with ECT rarely increase side effects in most studies. Moreover, the increased incidence of side effects is more related to which drugs are used, and shows certain dose dependence.

ECT combined with antidepressant drugs is used to treat depression. An unexpected finding was a higher incidence of transient cardiovascular and cognitive side effects in patients receiving venlafaxine (VEN). And the adverse cardiac effects including asystole, associated with the administration of high dose venlafaxine during ECT. Subsequent studies confirmed that treatment with venlafaxine during acute phase ECT can improve short-term antidepressant efficacy without increasing adverse reactions, and can reduce the recurrence rate after ECT. Current guidelines suggest lithium or anticonvulsants as first-line treatments for mania, while ECT has been used effectively to treat acute mania since its introduction. Previous studies found that 80% of patients benefit from ECT and achieved marked clinical improvement and evidence supporting the augmenting effects of adjunctive antipsychotic treatment in patients with mania. although the literature dose not identify specific hazards associated with the combination of ECT and antipsychotic medication, considering cognitive impairment maybe associated with combination ECT and lithium, discontinuation of lithium during ECT would still appear to be the appropriate practice. ECT had been used to treat schizophrenia since its introduction. According to report from the study on the combination of ECT and antipsychotic medications in the treatment of schizophrenia, combination treatment with ECT was more effective than pharmacotherapy alone. So combination ECT and antipsychotic medications can be considered an option for people with schizophrenia when the goal is rapid global improvement and symptomatic reduction. And its side effect does not appear different from that seen with ECT alone, especially for those patients with poor response to medication alone.

Third, although the evidence for the effectiveness of ECT in patients with mental disorder was inconclusive, that antipsychotic medication may be more effective than ECT alone, especially for those poor responses to medication alone. The results from large sample report by Baghai et al. showed improved efficacy with concurrent administration of several classes of antidepressant during ECT. ECT combined with antipsychotic drugs is more effective and benefit from remission that antipsychotic drugs alone or ECT alone, especially in schizophrenic patients resistant to antipsychotic drugs. A large amount of evidence showed patients would benefit more from combination ECT with antipsychotic medication, and that combination drug treatments would be preferred to recommended for many practitioners as routine therapy. But it is worth noting that maybe some potential risks of combination therapy would increase by large dose drugs or changes in epileptic threshold. It is undoubtedly that reducing the dosage of antipsychotics in combination therapy is a good choice for fewer side effects.

DISCUSSION AND FUTURE DIRECTIONS

ECT is one of the oldest and irreplaceable therapies in psychiatry disorder. Although there is misunderstanding about its efficacy, treatment procedures, mortality rates, cardiovascular complications and cognitive impairment, it was proved to be a safe therapy more than 80 years of application. ECT was has no absolute contraindication. It plays a very important role in the treatment of refractory psychiatry disorder and critical situations such as self-injury, suicide or patients in extreme excitement, and it seems to be a routine.

CONCLUSION

Although its efficacy has been confirmed by numerous studies, it is prone to be the last sort for many psychiatrists, and it cannot be used as a first-line therapy in psychiatry disorder. There are many concerns such as inconvenience, side effects, course of treatment, indication and efficacy, which limit the extensive application of ECT. Therefore, application of ECT should be more widely used in mental disorder, more evidence would be obtained to make guidelines and benefit more patients.

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CONFLICT OF INTEREST

The author's declared that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

Xiaoyan Ma is responsible for original idea and writing article, Chaoran Ding, Shujie Chai and Ying Wang are responsible for research literature; Feng Jia and Ranli Li are responsible for

check and revision. All authors contributed to the article and approved the submitted version.

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