

ELECTROCONVULSIVE THERAPY – GENERAL CONSIDERATIONS AND EXPERIENCE IN CROATIA

Alma Mihaljević-Peješ^{1,2}, Maja Bajs Janović², Ana Stručić¹, Marina Šagud^{1,2}, Milena Skočić Hanžek^{1,2},
Maja Živković² & Špiro Janović²

¹School of Medicine, University of Zagreb, Zagreb, Croatia

²Clinical Hospital Centre Zagreb, Zagreb, Croatia

SUMMARY

Despite controversy, ECT has been recognized as significantly effective for the treatment of mental disorders since 1938, when Cerletti and Bini introduced ECT in clinical psychiatric practice for treatment of schizophrenia. In the next period, indication for ECT switched more toward depression and catatonia. ECT was even banned from psychiatric training in 1960's, due to the anti-psychiatric movement, which were fortified by Oscar winning movie "One Flew over the Cuckoo's Nest". Due to its robust effectiveness, ECT revived in the early 1980's and today holds its position in clinical psychiatric practices around the world. Mechanism of ECT on brain and psychopathology is still not fully understood. Main theories have been neurotransmitter, post-receptor, neurophysiological and neuroendocrine theory. Regarding best clinical practices and evidence reported in the literature, ECT today is considered a treatment option for, traditionally, depression, suicidality and catatonia, and also schizophrenia, schizoaffective disorder, bipolar disorder, malignant neuroleptic syndrome, postpartal depression and psychosis, obsessive compulsive disorder, post-traumatic stress disorder, dementia, etc. Recent evidence of ECT efficacy is growing stronger also in the treatment resistant cases, for depression and psychosis. Great advantage of ECT is lack of absolute contraindications. ECT in Croatia was introduced in clinical psychiatric practice in 1960's in four institutions. Mainly due to stigma, but also a tendency for shifting toward hypothesized action mechanism, ECT in Croatia has been re-named to electrostimulative therapy or electroneuromodulatory treatment. In recent decades, the Department of psychiatry in the University Hospital Centre Zagreb (KBC Zagreb), has continuously been practicing ECT. Our department is considered a regional leader, regarding number of patient cases and overall experience in homeland and neighbouring countries. In the 2016, Croatian expert group, selected by the Croatian Psychiatric Association, proposed national guidelines for the ECT. Research in ECT at our department has shown predominance of the treatment for therapy resistance in depression and psychosis. The other research at our department also showed improvement in several cognitive functions of patients after ECT application.

Key words: ECT – history - mode of action – indications - Croatia

* * * * *

INTRODUCTION

ECT has been recognized as the most effective psychiatric therapy in the treatment of depression and schizophrenia, with acute efficacy rates higher even than pharmacotherapies. It is used in the treatment of depression, mania, catatonia and occasionally, schizophrenia (NICE 2010). Modern ECT is completely painless form of electric therapy, owing to better anaesthesia protocols (barbiturate and relaxant). Generally, an electric shock is applied for a fraction of a second through electrodes placed on the temporal region. ECT could be applied bilateral or unilateral – on non-dominant side of the head. The procedure today is safe and has no major complications and side-effects. Ethical procedures regarding ECT are strong and legally regulated by The Protection of Persons with Mental Illness Act (ZZODS).

HISTORY

ECT has been controversial partially due to a burden of a negative image in the history. It had been firstly introduced in 1938 when psychiatry professor Ugo Cerletti and his assistant Lucio Bini induced convulsions by

applying electricity directly to the brain (Cerletti 1950). For the patients with schizophrenia, their trials showed astonishing success. Their publications created a major turmoil in psychiatry. In 1940, psychiatrist Douglas Goldman, demonstrated ECT for the first time at the annual meeting of the American Psychiatric Association (Shorter 1997). During the time, the ECT technique has been modified. In 1940, curare was introduced to moderate the vertebrae-cracking force of the convulsions. Succinylcholine was introduced in 1952. In the early 1940's, common anaesthetic was barbiturate injection. In 1949, Goldman introduced unilateral ECT, placing the electrode over the right hemisphere. Abrams and Taylor (1976) introduced bi-frontal ECT by moving the electrodes forward over the forehead. In the 1950's, many patients, hospitalized for depression, had a chance of receiving ECT. The U.S. military made wide use of ECT during World War II, and by the 1950's, ECT had become one of the standard treatments for hospital depression, accepted also in European psychiatry. Suddenly, from 1960, ECT disappeared from psychiatric training.

The main reason for abandoning ECT was not growing power of the pharmaceutical industry and psychoanalysis, as expected. Problems started with the enthusiastic reception of Ken Kesey's antipsychiatry novel

“One Flew over the Cuckoo's Nest”, published in 1962. The main character in the same movie, performed by actor Jack Nicholson, had negative influence on the image of the psychiatric practice for years. There is an observation that the generation of “flower children” was hostile to psychiatry and to ECT in particular (Shorter 2004). Therefore, ECT use declined in the 1960's, but was re-introduced, starting in the early 1980's, due to its robust effectiveness in the treatment of severe depression. ECT came to be provided with consent, and the use of modified ECT became standard. Now, psychiatrists estimate that about 100.000 Americans received ECT during treatment. The history of ECT shows many controversies and turbulence around the treatment, but efficacy of the method gives hope to many patients in the treatment of their illness.

MECHANISM OF ACTION

Decades of ECT applications have not discovered mechanism of action in full. There is also a lack of controlled clinical trials with ECT. Most theories about the mode of action are focussed on its efficacy in depression.

Neurotransmitter theory

Neurotransmitter levels all change after the seizure. There is a transient increase of noradrenaline in plasma, which is more important on cardiac function and increase of HIAA and HVA, metabolites of serotonin and dopamine in cerebrospinal fluid (Papacostas 2005). ECT has an antipsychotic, and opposed to neuroleptics, an anti-parkinsons effect. Furthermore, the reduction of cholinergic function may be relevant to the cognitive side-effects of ECT. There is increase of GABA-ergic neurotransmission that may contribute to antidepressant, as well as, anticonvulsant action of ECT (Fosse & Read 2013).

Post-receptor theory

ECT increases the concentrations of the intracellular second messenger cAMP in the hippocampus and cerebral cortex. These increased concentrations in turn trigger other processes, such as an increase in protein kinase activity, and ultimately up-regulation of the Brain-derived neurotrophic factor (BDNF). By regulation of neurotrophic factors, ECT may reverse atrophy of neurons or protects them from further damage, and helps neuroplasticity (Holtzmann et al. 2007).

Neurophysiological theory

ECT have anticonvulsant properties. It increases in seizure threshold and decreases in seizure duration over the treatment course. It enhances transmission of inhibitory neurotransmitters, especially GABA. ECT has an anticonvulsant effect on intractable seizure disorder and status epilepticus in humans (Sackeim 1999).

Neuroendocrine theory

The rapid, strong and transient increase in plasma prolactin immediately after ECT is by far the most consist result of ECT-induced seizure. Definite conclusion regarding the mechanism of prolactin release and its correlation with the treatment outcome of ECT is still unknown. There are also evidences of ECT and HPT and HPA axes (Esel et al. 2004, Haskett 2014).

INDICATIONS

All the listed theories support the idea that ECT should have wider indication area. Therefore, ECT today should be considered as treatment option not only for depression and catatonia, but also for schizophrenia, schizoaffective disorder, bipolar disorder, suicidality, malignant neuroleptic syndrome, postpartum depression and psychosis, obsessive compulsive disorder, drug dependence, anorexia, hypochondria, delirium, chronic pain syndrome, extrapyramidal disorders, intractable seizure disorders, organic mental disorders, etc. Recent evidence of ECT efficacy is growing stronger also in the treatment resistant cases, for depression and psychosis.

CONTRAINDICATIONS AND ADVERSE EFFECTS

There are no absolute contraindications. Relative contraindications are myocardial infarction, hypertension, aneurysm, bleeding disorders, thrombophlebitis and sub-arachnoid haemorrhage, etc. Transient cardiovascular changes are expected in electroconvulsive therapy. Routine electrocardiograph should be performed to rule out baseline pathology. Headache, nausea, muscle soreness, drowsiness may occur after electroconvulsive therapy, but they usually respond to supportive management and nursing intervention. However, ECT is associated with a range of transitory cognitive side effects including a period of confusion immediately after the seizure and memory disturbance during the treatment course. Only a few patients report persistent problems.

ECT – EXPERTISE AND EXPERIENCE IN CROATIA

Guidelines and experiences with ECT treatments differ in various countries and clinical practices. ECT in Croatia was introduced in clinical practice in 1960's. In Croatia, due to stigmatisation of ECT, and focusing on possible mechanism of action, it is also called electrostimulative therapy or electroneuromodulatory treatment. In the past, there were several departments using ECT: KBC Zagreb, KBC Osijek, KBC Split and Department for psychiatry in Šibenik. Today, only the Department for psychiatry in the University Hospital Centre Zagreb (KBC Zagreb) has been continuously practicing ECT.

Table 1. Patients' data in ECT in the period 2010-2016 at the Department of psychiatry, KBC Zagreb

Gender	
Male	68 (51%)
Female	64 (49%)
Age at first ECT (y)	
Mean	43.16 (sd 12.429)
Range	19-71
Male	40.54 (sd 12.748)
Female	47.00 (sd 12.516)
	p=0.000*
Number of ECT applications	
Mean	10.00 (sd 3.497)
Range	2-18
ECT drop-out due to side effects	5 cases (drowsiness/memory impairment)
Number of previous hospitalization	
Mean	5.45 (sd 5.033)
Range	1-24
Life-time psychiatric treatment (months)	
Mean	124.43 (sd 111.928)
Pharmacotherapy	
Antipsychotics	100.00%
Antidepressants	39.50%
Mood stabilizers	35.40%
Anxiolytics	91.00%
Hospital treatment in the following year	
No	69.2%
Yes	30.8%
Diagnosis	
Schizophrenia and psychosis	77.11%
Recurrent depression	15.25%
Bipolar disorder	7.62%
ECT indications	
Sucidality	13.00%
Th. resistance	77.00%
NMS	1.00%
Catatonia	9.00%

Our department is considered as regional leader regarding number of patient cases and overall experience. ECT treatment is covered by the legal criteria following national The Protection of Persons with Mental Illness Act. In the 2016, national group of experts selected by Croatian Psychiatric Association, proposed guidelines for the ECT, which help psychiatrists in Croatia to make correct decision for ECT (HPD 2016).

In the 2017, we presented data for 132 patients treated with ECT in our Department in the period 2010-2016 at the 25th EPA Congress. Patients were either referred to ECT by department psychiatrist or sent from another institution in the country or region. Patients signed informed consent for ECT, and also institutional independent Ethical Board gave the permission for each individual case. Bi-temporal pulse ECT was administered three times a week at the intensive care unit at the psychiatric department. All the patients continued with pharmacological treatment during and after ECT treat-

ment. Leading diagnose for the patients receiving ECT at our department was in the range of psychoses (F20-F29), with predominantly schizophrenic patients with positive symptoms or treatment resistance. It was followed by recurrent depression and bipolar disorder. There were only few catatonia cases (N=6). Indications for ECT were partially different that generally expected. The leading indication for ECT in our department was psychosis and/or pharmacological treatment resistance in any given diagnose (psychoses, bipolar disorder, depression), followed by suicidality. Outcomes after the ECT were favourable in terms of better controlling the symptoms and lowering exacerbation frequency that was shown for the 2/3 of the patients without further psychiatric hospitalizations in the year following ECT (Mihaljević-Peješ et al. 2017). Another group of researchers from our Department, conducted open prospective study, in 31 patients with treatment resistance schizophrenia, regarding the impact of ECT on cognitive functions. Improved immediate and delayed verbal memory and executive functioning, with statistical trend being observed for visual memory and psychomotor speed, had been found. There was no worsening in other cognitive domains (Vuksan Čusa et al. 2018). More emphasis has also been put on the education of medical students and residents regarding ECT, including introducing obligatory clinical practical at our department.

CONCLUSION

The history of ECT shows many controversies considering the treatment, but efficacy of the method gives hope to many patients in the treatment of their illness. Evidence shows ECT has high efficacy rates for the treatment of depression and psychosis, and also other mental disorders, with evidence growing stronger also in the treatment resistant cases. In Croatia, we have more than 50 years of experience in ECT. ECT is applied in Croatia at the highest ethical standards and national guidelines have been developed. Department for psychiatry of Clinical Hospital Centre Zagreb is a regional leader regarding number of patient cases and overall experience. Research at our Department shows therapy resistance in depression and psychosis as the leading indication for ECT in the last 7 years. More emphasis has also been put on the education of the medical students, residents and other mental health professionals.

Acknowledgements: None.

Conflict of interest: None to declare.

Contribution of individual authors:

Research initiative and study design: Alma Mihaljević-Peješ, Maja Bajš Janović, Ana Stručić, Špiro Janović
Manuscript parts writing: Alma Mihaljević-Peješ, Maja Bajš Janović, Ana Stručić, Marina Šagud, Milena Skočić Hanžek, Maja Živković, Špiro Janović

References

1. NICE guidance: *The use of electroconvulsive therapy*, 2010
2. Cerletti U: *Old and new information about electroshock*. *Am J Psychiatry* 1950; 107:87-94
3. Shorter E: *A History of Psychiatry: From the Era of the Asylum to the Age of Prozac*. John Wiley & Sons, New York, 1997
4. Shorter E: *History of electroconvulsive therapy*. *Psychiatric Times* 2004; 21:1-3
5. *Electroconvulsive therapy: A history of controversy but also of help*, 2017. <https://theconversation.com/electroconvulsive-therapy-a-history-of-controversy-but-also-of-help-70938>
6. Papacostas YG: *The clinician and the mode of action of ECT*. Athens, 12 March 2005, oral presentation
7. Fosse R & Read J: *Electroconvulsive Treatment: Hypotheses about Mechanisms of Action*. *Front Psychiatry* 2013; 4:94
8. Holtzmann J, Polosan M, Baro P & Bougerol T: *ECT: from neuronal plasticity to mechanisms underlying antidepressant medication effect*. *Encephale* 2007; 33:572-8
9. Sackeim HA: *The anticonvulsant hypothesis of the mechanisms of action of ECT: current status*. *J ECT* 1999; 15:5-26.
10. Haskett RF: *Electroconvulsive therapy's mechanism of action: neuroendocrine hypotheses*. *J ECT* 2014; 30:107-10
11. Eselić E, Kilic C, Kula M, Basturk M, Ozsoy S, Turan T et al.: *Effects of electroconvulsive therapy on the thyrotropin-releasing hormone test in patients with depression*. *J ECT* 2004; 20:248-53
12. *Croatian Psychiatric Association - expert group: Guidelines for the electroconvulsive therapy (ECT) treatment of Croatian Psychiatric Association*, Zagreb, 2016
13. Mihaljević-Peješ A, Bajs Janović M, Stručić A, Janović Š: *Analysis of ECT Indications in the Hospitalized Psychiatric Patients*. 25th European Congress of Psychiatry, Florence, Italy 01.-04.04.2017
14. Vuksan Čusa B, Klepac N, Jakšić N, Bradaš Z, Božičević M, Palac N et al.: *The Effects of Electroconvulsive Therapy Augmentation of Antipsychotic Treatment on Cognitive Functions in Patients With Treatment-Resistant Schizophrenia*. *Journal of ECT* 2018; 34:31-4

Correspondence:

Prof. Alma Mihaljević-Peješ, MD, PhD
University Hospital Centre Zagreb, Department of Psychiatry
Kišpatićeva 12, 10 000 Zagreb, Croatia
E-mail: apeles@mef.hr