

The Changes of and Attitude toward The Use of Electroconvulsive Therapy in Hungary and The Optimization of Timing of Anesthetics

Ph.D. Thesis

Márton Asztalos, MD

Semmelweis University
Doctoral School of Mental Health Sciences



Supervisor:

Gábor Gazdag, MD, Ph.D.

Official reviewers:

Oguz Kelemen, MD, Ph.D.
Beatrix Mersich, MD, Ph.D.

Chairman of the Final Examination Committee:

Dániel Bereczki, MD, D.Sc.

Members of the Final Examination Committee:

Anna Géczy, C.Sc.
Andrea Sárosi, MD, Ph.D.

Budapest
2019

Introduction

The first application of electroconvulsive therapy (ECT) celebrated its eightieth anniversary in 2018. The initially revolutionary treatment method has now become highly stigmatized, and the usage of treatment varies greatly. However, despite recent and new treatments, it is still one of the most effective therapies in certain psychiatric conditions.

The ECT Protocol in Hungary, published in 2005, contains the most important parameters of treatment, and provides recommendations for the everyday work of clinicians. However, the Protocol expired on 31 December 2008. One important and long term goal of our work is to provide new results for updating the protocol, which can provide more points of reference for colleagues than previously noted.

As a first step, the knowledge of local conditions is essential, so the first goal was to assess the practice of ECT treatment in Hungary (hereinafter referred to as Study 1).

In our another survey, which is the second pillar of the dissertation, we were interested in the attitude of lay people to ECT (2nd study). In Hungary, surveys of the attitudes of psychiatrists, anesthetist residents and medical students were performed, but the attitudes of the public have been hidden so far. Our questionnaire is meant to fill this gap.

The third pillar of the thesis examined the importance of the time elapsed between administration of the anesthetic agent/muscle relaxant and electrical stimulation (Study 3). Although some articles have been published on the subject over the past few years, this parameter is still a less researched area of practical application of ECT. With the help of our research I hope to contribute to the improvement of the implementation of the treatment.

At the same time, it is important that the treatment becomes not only more effective, but also more accepted and should reduce the negative attitudes and stigmatization that often surrounds it. I would like to contribute to the more effective use and acceptance of the ECT in our country, both by colleagues and lay

people, through the work that is the backbone of my thesis.

Objectives

The first study's objectives The aim of this study was to explore the use of ECT in Hungary in 2014 and compare the results to those of the previous survey conducted in 2002. An additional objective was to determine what were the reasons ECT was not used, and we also asked about the obstacles to using the treatment.

The second study's objectives In Hungary, neither ECT-treated patients nor public's attitude towards ECT were included in the previous surveys. Our research focuses on the knowledge and attitudes of the public to ECT.

The third study's objectives We investigated the effect of an increased time interval between the administration of thiopental and succinylcholine on one hand and initiation of the electrical stimulation on the other hand. Our hypothesis was that postponing the electrical stimulation would result in longer seizure

length, lower number of treatments per series, lower stimulation dose and a reduced need for re-stimulation.

Methods

The first study's methods Two semi-structured questionnaires were sent to all acute adult psychiatric units in Hungary. The first questionnaire contained 25 items concerning ECT use in Hungary in 2014. The second, 6-item questionnaire was compiled for the units and departments where ECT was not offered to explore the reasons for not using ECT and the future plans with the therapy.

The second study's methods We asked the participants to fill out a semi-structured questionnaire consisting of seventeen questions. In the first half of the questionnaire, we asked them about the demographic data of the respondent and then about their knowledge and attitude about ECT. Participation in the survey was anonymous.

The non-healthcare worker part of the Hungarian adult population considered as the population. We tried to

randomly select those to fill in the questionnaires, but our survey cannot be considered representative. The data collection took place between 8th of August and 8th of November 2017. We used descriptive statistics to process the data. For the comparison of groups, we used t-test for continuous variables, chi-square test, Wilcoxon test and multivariate General Linear Model for discrete variable.

The third study's methods A retrospective case record-based cohort study comparing two different ECT procedures took place at Aalborg University Hospital, Department of Psychiatry, Region North Jutland, Denmark.

In 2013, patients were treated according to the Previous Treatment Regimen, which means that ECT initiated 60–90 seconds after administration of succinylcholine. The period of time varied among patients, as when the effect of succinylcholine reached the toes, the stimulation occurred.

Based on the findings of existing literature and clinical observations by local clinicians, we have changed the method since the 1st January 2014. In 2014,

patients were treated according to the Present Treatment Regimen, which means that ECT initiated 120 seconds after administration of succinylcholine. No further changes were implemented in the treatment regimens.

The two cohorts defined by these two treatment regimens were compared on ECT related outcomes. We defined the primary ECT related outcomes as duration of seizures in seconds measured through clinical observation and by EEG. Secondary outcomes were defined as use of re-stimulations, number of ECTs, and mean energy delivered per treatment during the index series.

Case records from all patients receiving ECT between 1 January 2013 and 31 December 2014 were evaluated with respect to the inclusion- and exclusion-criterias. Data collection was initiated January 2015 and concluded November 2015. Initially, we performed descriptive statistics comparing the treatment regimens on various baseline measures. Second, we employed regression model analysis with ECT outcome measures, and with treatment regimen, gender and age as covariates. Furthermore, we used linear regression for

length of seizures (clinical and EEG) and stimulation dosage, logistic regression for risk of re-stimulation and negative binomial regression for number of treatments.

Results

The first study's results There were 58 acute psychiatric inpatient units in Hungary in 2014, 54 replied, yielding a final response rate of 93%. A négy, választ nem adó osztályról tudtuk, hogy nem használnak ECT-t. Twenty-seven (47%) of the units indicated that they used ECT, but in fact, only 22 (37,9%) had actually performed ECT in 2014. Thirty-one units (53,4%) did not offer ECT at all.

Data From the Units that Performed ECT in 2014

In 2014, 174 patients received ECT in Hungary, constituting 0.59% of all inpatients treated in the 27 units where ECT was offered; this equates to 0.176 patients per 10,000 population and 1.04 courses of ECT per 10,000 population.

The number of patients treated in one site was a wide range. The highest number of patients receiving

treatment was 52, while the lowest number was only one patient (the average for patients treated at one site was 6.5). Sixty-six percent of the patients who received ECT were female, and 102 (59%) were diagnosed with affective disorder, 66 (38%) with schizophrenia spectrum disorders, and 6 with other disorders.

Only one unit considered ECT for patients under the age of 18, nine units used ECT for patients over the age of 70, whereas three units used it for pregnant women. The number of sessions per course varied between four and twelve, with a mean of 5.9 (SD, 3.2). All except five units administered ECT three times a week. 21% of the units used sine wave machines (ICOMAT), the others used brief-pulse square wave devices. Convulsion was only visually observed in 18 units (81,8%), electroencephalographic monitoring was available in 47,5% of the units, but used only in three, and the cuff-method was used in only one unit to monitor motor seizure duration. Nine units achieved the desirable length of seizure activity according to the Hungarian guidelines (which is 20 seconds with visual observation).

In 2014, 8 patients (4.6%) received repeated

courses of ECT and a further 8 (4.6%) received maintenance ECT. Bitemporal electrode placement was the first choice in all units (one unit also used frontotemporal placement). Propofol was used in 84% of the units for sleep induction, whereas thiopental, etomidate were the favored agents in 10,3% and 5,3% of the units, respectively.

In 12 units (57,9%), fixed-dose stimulation was used for the seizure induction, in 15,8%-15,8% with half-life and life methods, whereas seizure threshold titration was performed in only two units (10,5%).

Before the first ECT session, routine laboratory tests and ECGs were performed in all units. The most common contraindication for ECT treatment was a severe medical condition, the second, if the patient refused the treatment. Two thirds of the sites reported that the ECT protocol issued in 2005 provided useful guidance for their work.

Data From Units that Did Not Perform ECT in 2014

In 2014, there were 31 psychiatric units where ECT was not used, of which 27 responded to our request. In addition, the Chiefs of Services of those five units

where all the conditions for the treatment were given but no one patient was treated with ECT in the given year also completed the second questionnaire. Thus, in this chapter I present the data of these 32 units in total.

The Chiefs of Services of 27 of the 31 units that did not offer ECT still considered ECT to be a valuable therapeutic method. However, 3 senior psychiatrists regarded ECT as generally out-dated owing to its severe adverse effects and, thus, only used it as a last resort.

Twelve (45%) units stated that they had no patients who would have benefited from ECT in 2014. Four of these units had all of the necessary conditions to perform ECT. In the other part of the units (55%), patients in need of ECT were treated. Thirteen units referred a total of 26 patients to other units for ECT. Four units admitted to having failed to refer suitable patients for ECT to another unit offering this treatment; however, no reasons were given.

In the second questionnaire we also asked about the obstacles to using the treatment. The most common reason for not using ECT was the lack of an ECT machine, and the second was the unavailability of an

anesthesiologist. 64% of the units would have performed ECT if these obstacles had not existed.

The second study's results A total of 306 persons completed the questionnaire; 66.3% (203 persons) of the respondents were lay people and 34.3% (103 persons) health care workers. 65 (32%) of the lay people heard about ECT and 138 (68%) did not. The proportion of health care workers was reversed, many more, 94 was the number of those who had heard about this treatment (91%), and only nine (9%) who did not. Those lay people, who have heard about the treatment, were significantly older and higher educated than the other part of the public, who has not heard about the ECT.

Those who had not heard of the treatment only answered the first six questions about demographic data. The other 159 respondents (65 lay people and 94 health care workers) answered all 17 questions that asked about their treatment knowledge and attitude.

From respondents who have already heard about ECT, we asked the source of the information, giving them the opportunity to mark multiple responses. The laymen were mostly informed through the Internet and

movies (60% and 49%), while the sources of information were different among health care workers, where colleagues and books were the primary sources of information (77% and 58%).

The knowledge of the lay people proved to be lower than that of the health care workers, and significantly fewer people thought the treatment was effective. However they were partially well informed regarding the side effect profile. The feelings of lay people about ECT were mostly negative or indifferent. Only less than one fifth of them are more positive about this treatment. One third of health care workers were more positive (34%), one third indifferent (33%) and the last third (32%) more negative for electroconvulsive therapy, although the difference between the two groups has not reached the level of significance.

If a close relative were a psychiatric patient, 27 percent of the lay people would support ECT treatment, 22 percent would not support it, and more than half of the respondents (51%) could not decide what to do. The following rates would be for health care workers; 56%

would support the ECT treatment, 14% would not support and 30% did not know.

Approximately 20 percent of both the public and health care workers considered the ECT as outdated as a treatment. In both groups, one-tenth of respondents thought the use of treatment should be prohibited. Three quarters of health care workers disagreed with this statement.

8.5% of lay people and 15% of health care workers have been treated by a psychiatrist but none of them have been treated with ECT.

The third study's results Ninety-three patients out of 153 eligible patients were included in the study population. A total of 40 patients were included in the 2013 cohort with a mean age of 57.7 years. On average, the patients received 8.5 ECT procedures during the index series. The mean duration of seizures was 31.3 seconds clinically, and 38.6 seconds on EEG. Ten patients received a restimulation during their series. Fifty-three patients were included in the 2014 cohort with a mean age of 54.3 years. On average, the patients received 9 ECT procedures during the index series. The

mean duration of seizures was 35.8 seconds clinically, and 42.6 seconds on EEG. Seven patients (four males and three females) received re- stimulation during their series.

Thiopental doses were weight adjusted with a mean dose of 286 mg in 2013, and a mean dose of 243.4 mg in 2014.

In both years, the vast majority of patients were diagnosed with some form of affective disorder, and both in 2013 and 2014 the majority of patients received antidepressant, antipsychotic and/or benzodiazepine treatment with ECT.

We showed that longer length of seizures after ECT, as measured clinically, was independently inversely associated with the higher age with a coefficient of -0.20, whereas treatment regimen and sex were not. Similarly, higher age was inversely associated to longer length of seizures as measured by EEG with a coefficient of -0.17. Length of seizure as measured by EEG was not associated to treatment regimen or sex.

The logistic regression analysis showed an association between being treated according to the

present treatment regimen and a lower risk of restimulation as compared to the previous regimen with an odds ratio (OR) of 0.23.

There was no correlation between number of treatments and treatment regimen, sex or age, and we showed that stimulation dosage was associated with sex, but not with treatment regimen or age. Mean stimulation dosage in 2013 was 151.9 mC, as compared to 143.2 mC in 2014.

Conclusions

The use of ECT in Hungary is decreasing and many factors can be assumed to be the cause of this decline. In view of the high frequency of depression and suicide in Hungary, it is very likely that a significant minority of patients who would benefit from ECT cannot have access to it.

It would be worthwhile to organize ECT into major centers with an intensive care unit and anesthesiologist. This would make treatments more efficient and cost-effective. The lower progressivity

psychiatric units could be assigned to these centers.

The responses to the questionnaires indicate that further training in the implementation of the application is needed to facilitate adequate use of ECT. In addition, regular training in and updating of the ECT protocol would also contribute to the improvement of quality. Developing and introducing an accreditation system - which exists in other countries - could further improve the quality of implementation.

Attitude studies show that the attitudes of ECT-treated patients and their relatives are the most positive to ECT. They are followed by psychiatrists' attitudes with varying results, which is followed by other health care professionals. The lay people have the least information about the treatment and the least positive attitude. This incomplete awareness and negative attitude was confirmed by my own research.

Therefore, the dissemination of credible information, the dissemination of knowledge, the dispersion of prejudices and doubts about electroconvulsive therapy would be fundamental; these are the key issues. In all these areas, both the media and

psychiatrists should play a crucial role.

The main strength of third the study is the use of a clinical sample treated under routine conditions and the use of broad selection criteria, thereby increasing generalizability of the results to clinical practice. Additionally, the use of a standardized time intervals increases the applicability of study results to clinical practice. By including 93 patients, this study is the largest to date investigating the use of increased time intervals from administration of muscle relaxants and anaesthetics to ECT initiation. In conclusion, we found an association between an increased time interval from administration of thiopental and succinylcholine to ECT and a lowered frequency of restimulation. The current study substantially strengthens the evidence on the benefits of delaying ECT after administration of anaesthetic agent and muscle relaxant.

Bibliography of the candidate's publications

Papers connected with the Ph.D. Thesis

1. Asztalos M, Könye P, Gazdag G. (2019) The Public's Attitude towards Electroconvulsive Therapy in Hungary. *Idegyogy Sz* (accepted for publication)
2. Gazdag G, Asztalos M, Ungvari GS. (2018) Accessibility to Electroconvulsive Therapy in Hungary. *Psychiat Hung*, 33 (3):266-269.
3. Asztalos M, Matzen P, Licht RW, Hesselund KB, Sartorius A, Nielsen RE. (2018) Delaying initiation of electroconvulsive treatment after administration of the anaesthetic agent and muscle relaxant reduces the necessity of re-stimulation. *Nord J Psychiatry*, Jul;72(5):341-346.
4. Asztalos M, Ungvari GS, Gazdag G. (2017) Changes in Electroconvulsive Therapy Practice in the Last 12 Years in Hungary. *J ECT*, 33(4):260-263.

Other publications

1. Takács R, Asztalos M, Ungvári GS, Gazdag G. (2019) The frequency of catatonic signs and symptoms in an acute psychiatric ward. *Psychiatr Pol* (accepted for publication)

2. Rohde C, Polcwiartek C, Asztalos M, Nielsen J. (2018) Effectiveness of Prescription-Based CNS Stimulants on Hospitalization in Patients With Schizophrenia: A Nation-Wide Register Study. *Schizophr Bull*, 13;44(1):93-100.
3. Takács R, Asztalos M, Ungvari GS, Gazdag G. (2017) Catatonia in an inpatient gerontopsychiatric population. *Psychiatry Res*, 255:215-2