



# Maintenance ECT in Recurrent Depression and Treatment Resistant Schizophrenia

## Yineleyici Depresif Bozukluk ve Tedaviye Dirençli Şizofrenide İdame EKT

Sinem Zeynep METİN

Üsküdar University Faculty of Medicine, Department of Psychiatry İstanbul, Turkey

### ABSTRACT

**Objective:** Electroconvulsive therapy (ECT) has been used for treatment of depression and psychosis for a long time. A less known way of use is as a maintenance treatment for keeping patients stable during remission. Recently ECT has been increasingly used for schizophrenia and depression after remission of the acute exacerbation.

**Methods:** In this study, we examined files of 24 patients diagnosed as having treatment-resistant schizophrenia (14) or recurrent depression (10) who were treated with ECT on an outpatient basis.

**Results:** Patients with depression and schizophrenia were followed up for minimum 2 months and maximum 54 months with ECT. The remission rate in both groups were 70%. None of the patients quitted treatment due to adverse effects.

**Conclusion:** Biases and stigmatization cause a decreased rate of use of ECT in outpatient settings. However, the literature indicates that the morbidity and morbidity due to ECT are negligible. Although our data were collected retrospectively, they showed that ECT might be an option for a maintenance or continuation treatment of recurrent depression and treatment-resistant schizophrenia. Our findings should be supported by randomized studies.

**Keywords:** ECT, maintenance, recurrent depressive disorder, treatment resistant schizophrenia

### ÖZ

**Amaç:** Elektrokonvülfik terapi (EKT) depresyon ve psikozun akut tedavisinde uzun süredir kullanılan bir nöromodülasyon tedavisidir. Bununla birlikte, hastaların iyilik hallerinin devam etmesi için farmakoterapiye oranla uygulaması daha az bilinen ve tercih edilen bir sürdürüm tedavi şeklidir. Son yıllarda, akut alevlenme tedavisi sonrası sürdürüm tedavisinde de yineleyici depresif bozuklukta ve tedaviye dirençli şizofrenide kullanılmaya başlanmıştır.

**Yöntem:** Bu çalışmada 2015-2018 yılları arasında yineleyici depresif bozukluk (10) ve tedaviye dirençli şizofreni (14) tanısı ile idame EKT tedavisi alan 24 hastanın verileri retrospektif olarak incelenmiştir.

**Bulgular:** Remisyon oranları her iki grupta %70 olarak tespit edilmiştir. Hiçbir hasta EKT'ye bağlı yan etkiler nedeniyle tedaviyi bırakmamıştır.

**Sonuç:** EKT tedavisi hakkındaki ön yargılar ve hastaların damgalanma yaşaması özellikle ayaktan hastalar için az tercih edilen bir tedavi olmasına neden olmaktadır. Ancak literatür verileri incelendiğinde EKT'nin morbidite ve mortalitesinin oldukça düşük olduğu görülmektedir. Bizim bulgularımız retrospektif bir analiz sonucu elde edilmiş olsa da idame EKT'nin yineleyici depresif bozukluk ve tedaviye dirençli şizofreninin sürdürüm tedavisi için bir seçenek olabileceğini göstermektedir. Ancak bulguların gelecek randomize kontrollü çalışmalarla da desteklenmesi gerekmektedir.

**Anahtar Sözcükler:** EKT, idame, yineleyici depresif bozukluk, tedaviye dirençli şizofreni

**Address for Correspondence:** Sinem Zeynep METİN, Üsküdar University Faculty of Medicine, Department of Psychiatry İstanbul, Turkey

**E-mail:** sinembaser@gmail.com **ORCID ID:** orcid.org/0000-0002-0511-2867

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## Introduction

Electroconvulsive therapy (ECT) continues to be used as the most effective somatic, non-invasive treatment in psychiatry for nearly a century. This process of experience has proven the reliability and effectiveness of ECT in many psychiatric disorders, especially depression, bipolar disorder, and schizophrenia, which no other somatic treatment can reach (1). Although it is an elective treatment option in many patients that do not respond to pharmacotherapy and psychotherapy, it is the first choice when it is necessary to achieve rapid treatment in patients in whom there are affective, psychotic and catatonic symptoms, who have a risk of suicide, in whom there is worsening in general health, or in whom the use of drugs is not found safe (for example, pregnancy) or cannot be tolerated (1,2).

Contrary to common negative opinions, ECT is a safe and comfortable treatment method. The most common indication for ECT, known to all psychiatrists, is treatment-resistant and severe depression. Major depression is a recurrent disease with a lifetime prevalence of 7-12% for men and 20-25% for women. If left untreated, the possibility of becoming chronic, and the mortality and morbidity are high (3).

ECT can also be seen as the first choice especially in patients with psychotic symptoms, accompanied by suicidal tendencies, and emergency situations such as catatonia and neuroleptic malignant syndrome (4). Although the most well-known indication of ECT is depression, its effectiveness is also known in clinical practice in many non-depressive conditions. In controlled studies, the effectiveness of ECT has also been reported in conditions such as schizophrenia, mania, and catatonia (2). The use of ECT in manic episodes has been established in the literature and treatment guidelines (4). Today, it is applied in patients who have not responded to anti-manic drug therapy or who are in life-threatening manic excitations or catatonic conditions. There are supportive findings in the literature with the administration of maintenance ECT in patients whose acute period of manic episode has been treated with ECT, but whose well-being cannot be maintained with medication (4). In addition to these, there are publications showing that it can also be used in obsessive compulsive disorder (5). Although its effectiveness is known in severe, suicidal and psychotic depression, its use is limited due to widespread stigmatization and misinformation about side effects. In recent years, especially anesthetized ECT has significantly reduced the risk of complications. For example, in large case series, morbidity and mortality associated with ECT have been found to be much lower than previously thought (6,7).

Conservation therapy is generally accepted after a successful ECT response. The most important reason for this is the high rate of relapse in psychiatric disorders. It is still unclear whether the high relapse rate after ECT is related to abrupt termination of ECT, maintenance therapy, or the course of the disease itself. Sackeim et al. treated one group with placebo, one group with nortriptyline, and another group with nortriptyline and lithium following index ECT in their study performed with 84 patients with unipolar depression. They reported that relapse rate was

60% in the group using only nortriptyline, 39% in the group using nortriptyline and lithium, and 84% in the placebo group within 6 months (8). In the nortriptyline and lithium group, all but one relapse occurred in the first 5 weeks after ECT.

Maintenance ECT is an important option to prevent recurrence in the maintenance treatment of patients who have benefited from ECT in acute treatment. Despite the use of ECT for more than eighty years, studies and applications related to maintenance ECT are limited. It is still not known to whom, how often and when maintenance ECT should be administered. More descriptive studies are needed (9,10). Prudic et al. conducted a study to understand the effect of adding drugs at the start of ECT in preventing relapse. Placebo, nortriptyline or venlafaxine were added to the patients at the beginning of ECT. After ECT, lithium was added to all three groups. Even when aggressive pharmacotherapy was applied, relapse rate was reported 50%, and it was thought that adding medication at the beginning of ECT had no effect on relapse. At the end of this study, it was recommended to examine not abrupt but gradual discontinuation of ECT (11). In the CORE (Consortium for research in ECT) studies that started in 1997, patients with depression were randomly divided into groups. The efficacy of maintenance ECT, lithium and nortriptyline in maintenance therapy was compared. While no difference was found between the relapse rates of the two groups, it was reported that relapse was delayed in patients receiving maintenance ECT (12).

In the first phase of the PRIDE studies of the 2010s, 61.7% remission was achieved with the combination of unilateral ECT and venlafaxine in patients with geriatric depression (13). In the second phase, the effectiveness of pharmacotherapy (lithium and venlafaxine) group and both ECT and pharmacotherapy group in the maintenance treatment was compared, and the decrease in the Hamilton Depression Rating scale (HAM-D) scores of the ECT and pharmacotherapy group was found to be statistically higher (14). In these studies, the STABLE algorithm, which was used to determine the frequency of maintenance ECT, was used to determine the individual frequency. In this algorithm, the frequency is determined by applying HAM-D and the Mini Mental State Exam (MMSE) (15).

Nordenskjöld et al. (16), on the other hand, compared only pharmacotherapy with ECT and pharmacotherapy, and found the relapse rates to be significantly lower in the second group. It was also reported that 4 patients who attempted suicide were in the pharmacotherapy group. Cognitive side effects were also evaluated in this study, and they were not found to be statistically significant.

Contrary to maintenance ECT applications in recurrent depression, studies related to maintenance ECT application in treatment-resistant schizophrenia are limited in the literature. Maintenance ECT can also be combined with antipsychotics for maintenance therapy in patients with schizophrenia who have achieved remission with ECT (17). Due to limited literature, there is no consensus on maintenance ECT applications. Patients

with treatment-resistant schizophrenia in whom clozapine and ECT are frequently used together are also reported. These two are the most used combination and most beneficial (18,19). The combination of clozapine and maintenance ECT was found to be effective in patients with catatonic schizophrenia, aggression, suicidal ideation, unresponsiveness to pharmacotherapy, or a previously known ECT response (20). In another study, cognitive side effects did not differ in acute or maintenance ECT (21,22).

In their retrospective study, Krepela et al. found that maintenance ECT was not effective in hallucinations and delusions in 19 patients with chronic pharmacotherapy-resistant schizophrenia; however, they found that maintenance ECT affected behavioral symptoms such as suicidal thoughts/behaviors, aggression, refusal to eat, and catatonia, and that increased social functionality (23).

In our study, we tried to examine the effectiveness of maintenance ECT in these 2 diseases by including patients with recurrent depressive disorder and patients with treatment-resistant schizophrenia who were admitted to a reference psychiatric hospital in Istanbul between 2015-2018 and received maintenance ECT. Considering that there are few studies on maintenance ECT in the literature, it is anticipated that the findings will contribute to the literature on the effectiveness of the method.

## Method

In this retrospective study, the data of patients who received maintenance ECT between 2015 and 2018 in a reference center hospital (NP İstanbul Brain Hospital, İstanbul) were retrospectively analyzed. All of the patients received ECT during hospitalization and were followed up with maintenance ECT to prevent recurrence after discharge. Diagnostic groups were recurrent depressive disorder and schizophrenia groups, and both diagnoses were made by a psychiatrist through clinical evaluation according to DSM-4 TR and 5 criteria. The study was designed retrospectively. With the archive scanning method, patients who were given maintenance ECT in the hospital records in 2015-2018 were determined. It was required that the patient was followed up with maintenance ECT for at least 2 months and received at least 2 ECTs. The patients were observed to remain in remission or to relapse during maintenance ECT, and the remission/relapse assessment was made by psychiatrist in the follow up.

### Outpatient ECT Method: Findings

The mean age of the group was 35 and the standard deviation was 10.7. Seven of the patients were women. The patients received an average of 5.2 sessions of maintenance ECT (minimum 2, maximum 18). Fourteen of the patients were diagnosed as having schizophrenia and 10 patients were diagnosed as having recurrent depressive disorder, and they received maintenance ECT. Although there were 2 women in the schizophrenia group and 2 women in the depression group, the gender distribution did not reach significance in the chi-square test ( $p=0.14$ ). The characteristics of the patients can be seen in Table 1 in detail.

According to the results, 10 of 14 patients with schizophrenia were followed up with remission, while 4 of them relapsed. Recurrence was detected in 3 out of 10 patients with depression. When the recurrence risk in the groups was compared with the chi-square test, there was no significant difference ( $p=0.25$ ). When the two groups were compared in terms of the number of maintenance ECT, no significant difference was found ( $p=0.22$ ). When the ECT number of the patients who remained in remission and who did not remain in remission during the follow-up was compared, no significant difference was found ( $p=0.48$ ). When the number of ECT received during hospitalization by patients in remission and patients without remission was compared, no significant difference was found ( $p=0.48$ ). When the number of ECT received during hospitalization by patients in remission and patients without remission was compared, no significant difference was found ( $p=0.08$ ).

## Discussion

In this study, the effectiveness of maintenance ECT was investigated retrospectively in patients with treatment-resistant schizophrenia and recurrent depressive disorder. In the study, the efficacy criterion was remission/relapse, and a similarly low number of relapses was observed in both groups (remission rate approximately 70%). These findings show that maintenance ECT can be used as an alternative to medication in treatment-resistant schizophrenia and recurrent depressive disorder. Publications on maintenance ECT in the literature mostly consist of case reports, case series and retrospective analyzes (24). Except for the few studies mentioned in the introduction, the number of randomized controlled studies, specifically examining cognitive side effects, is limited. However, psychiatrists frequently apply this treatment only to their patients who are resistant to treatment or who have relapsed. Studies in the literature mostly focus on depression and schizophrenia. The lack of statistically significant difference in relapse rates between the two groups in our study suggests that maintenance ECT can be used more frequently in treatment-resistant schizophrenia, like its widespread use in depression.

An important uncertainty relates to determining the frequency and number of maintenance ECT. Although the general practice in clinical practice is application of ECT as often as the physician deems necessary, there is no standardized decision-making algorithm. The STABLE algorithm is a practical algorithm that proposes to determine the frequency by evaluating the cognitive side effects and change in depressive symptoms (25). In the follow-up workshop held by the participants of the CORE study in 2017, it was suggested that maintenance ECT could be preferred when there were episodic recurrent severe depressive episodes, presence of psychotic features, resistance to previous maintenance drug therapy, bipolar depression, the usefulness of index ECT applied for the second time, cognitive side effects of previous ECTs tolerated by the patient, response to maintenance ECT in the past, the patient's preference, the patient's ability to continue regular psychiatric follow-up, and the patient's medical and cognitive well-being (especially for the elderly) (13,14).

**Table 1.** Clinical and demographic characteristics of the patients

Patient ID	Diagnosis	Number of index ECT	Number of maintenance ECT	Remission	Age	Gender
1	RDD	11	14	2	31	M
2	RDD	7	6	2	38	F
3	RDD	14	18	1	45	F
4	RDD	12	7	1	45	F
5	RDD	8	3	1	54	F
6	RDD	10	2	1	28	M
7	RDD	7	2	1	69	F
8	RDD	10	5	2	40	M
9	RDD	7	7	1	33	M
10	RDD	10	2	1	33	M
11	SCH	10	13	2	37	M
12	SCH	12	2	2	26	F
13	SCH	10	2	2	27	M
14	SCH	7	2	2	27	M
15	SCH	12	7	1	25	M
16	SCH	11	7	1	33	M
17	SCH	10	6	1	23	M
18	SCH	10	4	1	38	M
19	SCH	10	3	1	23	M
20	SCH	8	2	1	44	M
21	SCH	10	2	1	35	M
22	SCH	10	2	1	27	M
23	SCH	7	2	1	41	M
24	SCH	10	4	1	30	F

RDD: Recurrent depressive disorder, SCH: Schizophrenia, Remission, 1 yes, 2 no index, ECT: ECT applied sequentially at the start of treatment

An important limitation of our study was that it was a retrospective study. In this study, patient files were scanned retrospectively, and evaluation of remission was also done retrospectively. Therefore, structured diagnostic tools such as SCID-I could not be used, and diagnostic reliability was limited to clinician evaluation. Likewise, the inability to include clinical scales to objectively evaluate remission and relapse to the design of our study reduced its power. However, the number of prospective maintenance ECT studies is very few in the literature, and to our knowledge, the number of controlled studies is also limited. Limited objective study data on a clinically known treatment also prevent prejudices from being demolished. The most important reason for this is perhaps the difficulty of maintenance ECT and the difficulties encountered in finding patients for studies.

### Study Limitations

Another limitation of our study was that cognitive problems, one of the most important known side effects of ECT, were not measured. Since the confusion and amnesia seen in the acute exacerbation period of the disease can also be seen during maintenance ECT, it will be useful to measure the memory performance of patients during maintenance ECT in future studies.

### Conclusion

As a result, although ECT is generally accepted by all physicians, it is a less preferred treatment method due to prejudices about stigmatization and side effects. In this study, we did not observe that any patient discontinued the study due to side effects related to ECT. Therefore, the findings suggest that maintenance ECT can be safely applied in outpatients as well.

### Ethics

**Ethics Committee Approval:** Üsküdar University Non-Interventional Research Ethics Committee Presidency (date: 27.05.2020/no: 61351342/2020-257).

**Peer-review:** Externally and internally peer reviewed.

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