



# Headache Associated with Electroconvulsive Therapy

Selçuki D<sup>1</sup>, Batum M<sup>1,†</sup>, Ayşın Kısabay<sup>1</sup>, Kömürcülü N<sup>2</sup>, Aydemir Ö<sup>3</sup>, Esen-Danacı A<sup>3</sup>

## ABSTRACT

### Objective

The electroconvulsive therapy (ECT) is a treatment method used in major depression, mania, schizophrenia, and mixed affective conditions. The side effects of this therapy include arrhythmia, hypertension, headache, prolonged seizures, amnesia, muscle pain, and nausea. The characteristics of post-ECT headache and the effect of pre-ECT headache on post-ECT headache were investigated in our study.

### Methods

After obtaining the approval of the ethics committee, we retrospectively reviewed 337 patients aged between 18 and 70 who had an ECT indication and were applied ECT due to one of the diagnoses of major depression, psychosis, or bipolar affective disorder as per the DSM V criteria. The localization, severity and duration of post-ECT headache, the conditions accompanying it and the need for its treatment were evaluated in line with the International Classification of Headache Disorders 2018 criteria. Headache was questioned immediately after the ECT, and at the 2<sup>nd</sup> and 4<sup>th</sup> hours.

### Results

From the 337 patients, 96 female (28.5%) and 241 male (71.5%), 33 patients (9.8%) were found to have pre-ECT headache and 49 patients (14.5%) post-ECT headache. While pre-ECT headache was more common among women ( $p=0.004$ ), no difference was found between the genders in post-ECT headache ( $p=0.853$ ). While there was also no difference between the severities of pre-ECT and post-ECT headaches ( $p=0.66$ ), 10 (30.3%) out of 33 patients with pre-ECT headache also had post-ECT headache ( $p<0.001$ ). The mean duration of post-ECT headache was  $1.87 \pm 3.55$  hours and the mean severity (VAS) score was  $4.61 \pm .56$ . Only 9 (18.3%) of the patients with post-ECT received treatment.

### Conclusion

The post-ECT headache in our study was mostly bilateral, more of a throbbing nature, mild to moderate in severity, tolerable, and not accompanied by conditions such as nausea, vomiting or dizziness. There was an association between pre-ECT and post-ECT headaches. Contribution was made to the characteristics of the headache in excess of the current criteria.

### Keywords

Electroconvulsive therapy (ECT), Side effects, post-ECT headache, Pre-ECT headache, Psychiatric diseases, Criteria

<sup>1</sup>Department of Neurology, Medical School Hospital, Celal Bayar University, Manisa, Turkey

<sup>2</sup>Manisa Psychiatric Hospital, Manisa, Turkey

<sup>3</sup>Department of Psychiatry, Medical School Hospital, Celal Bayar University, Manisa, Turkey

<sup>†</sup>Author for correspondences: Batum M, Celal Bayar University, Medical School Hospital, Department of Neurology, Manisa, Turkey

### Introduction

Since the beginnings of the twentieth century, electroconvulsive therapy (ECT) has effectively kept its position in the treatment of major psychiatric diseases [1-3]. Having been used for nearly 80 years, this method is based on formation of a typical grand mal epileptic seizure by way of electrical stimulation [2]. Its commonly known indications include major depression, mania, schizophrenia, mixed affective conditions, catatonia and schizoaffective disorders [1]. ECT is also used in uncontrollable seizures, Parkinson's disease and neuroleptic malignant syndrome [1,3].

Since ECT is widely used in psychiatric diseases, the rate of side effects associated with it is also high.

The ECT-related side effects have a broad spectrum consisting of serious side effects such as prolonged seizures, confusional periods and amnesia as well as milder ones such as headache, muscle pain and nausea. The most common side effects are arrhythmia, hypertension and headache as evidenced by studies [4-7]. Severe cardiovascular and pulmonary side effects and complications during the course of ECT has been reported as 0.92% in a retrospective review [8]. Cognitive impairment and memory loss, affects 30% of the patients who were underwent ECT [9].

It is important to recognize the side effects and to select, assess and treat patients in consideration of these side effects [2,10].

It has been reported in a study conducted in the United States that ECT is being administered to approximately ten thousand patients every year and headache is seen as a side effect in 45% of these patients [11]. Although seen so often, there are only a few studies dealing with post-ECT headache [12-17]. For this reason, the recognition of post-ECT headache and clinical approach to it are still ambiguous. Post-ECT headache is included in Appendix A7.6.3 of the International Classification of Headache Disorders (ICHD-3) criteria for 2018 [18]. They have not been verified in a satisfactory way in the studies carried out so far and have been referred to as potential criteria based on the data of such studies. Since the information on the description of post-ECT headache is limited, its recognition and treatment can remain inadequate today.

There is a need for further studies where both the characteristics of post-ECT headache and the

methods for treating it are investigated, so that it can be removed from the appendix section.

In our study, we planned to assess the characteristics of pre-ECT and post-ECT headaches and to investigate the effect of pre-ECT headache on post-ECT headache.

### Materials and Methods

After obtaining the approval of the ethics committee of our university, we retrospectively reviewed 337 patients who had an electroconvulsive therapy (ECT) indication and had one of the diagnoses of major depression, psychosis or bipolar affective disorder as per the DSM V criteria. Our study was conducted in line with the Helsinki rules and consents were obtained from the patients and their relatives before the procedure. The diagnoses and characteristics of the headaches suffered by our patients were assessed according to the International Classification of Headache Disorders (ICHD-3 2018) criteria.

The International Classification of Headache Disorders (ICHD-3) diagnostic criteria for post-ECT headache (appendix A7.6.3):

- A. Recurrent headache fulfilling criterion C
- B. A course of electroconvulsive therapy (ECT) has been given
- C. Evidence of causation demonstrated by all of the following:
  1. Headache has developed after 50% of ECT sessions
  2. Each headache has developed within 4 hours after ECT
  3. Each headache has resolved within 72 hours after ECT
  4. Not better accounted for by another ICHD-3 diagnosis (18).

Routine questionnaires are filled out for patient complaints and clinics for all patients receiving the electroconvulsive therapy (ECT). The routinely completed questionnaires were reviewed retrospectively in our study. Patients aged between 18 and 70 years who had one of the diagnoses of depression, psychotic disorder or bipolar disorder as per the DSM-V criteria, who had an ECT indication and agreed to undergo the therapy, and who signed the subject consent form were included in the study. Patients whose ejection fraction was below 50%, those

who had Class 3/4 heart failure, uncontrolled hypertension, history of hypotensive attack, rhythm disorders, epilepsy, neuromuscular disease, intracranial space-occupying lesions or aneurysm, those who had ischemic stroke or intracerebral hematoma within the last 3 months, those with intellectual disability and pregnant patients were excluded from the study. Patients with a very severe psychotic disorder were also excluded due to limited cooperation.

The first section in the ECT questionnaire administered to the patients in our study was related to the demographic information of the patient, the second section to the characteristics of pre-ECT headache and the third section to those of post-ECT headache. The questions on demographic information were related to the name and surname, age, education status and place of residence of the patient. The education statuses of the patients were classified as unable to read or write, literate, private school graduate, high school graduate and university graduate. Their clinical diagnoses were assessed under psychotic disorder, bipolar disorder and depression. The patients were administered a questionnaire inquiring the characteristics of their headache by a neurologist before and after their ECT. Prepared in line with the ICHD-3 criteria, the questionnaire included questions about the type, localization and severity of the headache, whether it was accompanied by nausea, vomiting, photophobia or phonophobia, whether any treatment was administered, whether it was under control through treatment, and the temporal relationship between ECT and headache. The severity of headache was assessed using the visual analog scale (VAS). Headache was questioned immediately after the ECT, and at the 2<sup>nd</sup> and 4<sup>th</sup> hours, and the patients were observed until the 72<sup>nd</sup> hour. Before their ECT, the patients were consulted to the Department of Anesthesia and Reanimation. During the ECT, all patients were administered a 1 mg/kg dose of propofol, an intravenous anesthetic, and a 0.75 mg/kg dose of neuromuscular blocker succinyl choline. The pre-ECT and post-ECT pulse and blood pressure measurements were recorded. A Somatic Thymatron II brand four-channel ECT device (Class I, type BF, 0.9 ampere constant current, 0.25 through 1.5 MS pulse width, 0.14 through 7.99 seconds of duration, 4 recording channels, 220 ohm maximum output and 504 Mc impedance-USA) was used during the procedure. The electrodes were placed bitemporally.

### ■ Statistical methods

The data obtained from the study were entered into the database formed on the SPSS program and analyzed statistically. The means, standard deviations, medians, minimum and maximum values of the continuous variables were presented. The variables were checked for normal distribution. The independent groups were compared by way of non-parametric correlation tests and/or chi-square test as appropriate. In all statistical comparison tests, if the “*p*” value turned out less than 0.05, the intergroup differences were accepted to be statistically significant.

## Results

Our study included 337 patients, 96 female (28.5%) and 241 male (71.5%). The demographic data and psychiatric diagnoses of the patients who had headaches before and after their ECTs are summarized in **Table 1**.

### ■ Pre-Ect headache

Pre-ECT headache was seen in a total of 33 patients (9.8%), 17 females and 16 males. Pre-ECT headache was more frequent in women ( $p=0.004$ ). While 32 of the 33 patients with pre-ECT headache described the characteristics of their headache, 1 patient was not able to give a satisfactory answer due to prolonged confusion. Of the patients, 8 (25%) described their headache as migraine, 16 (50%) as tension type headache (TTH), 3 (9.4%) as vascular headache and 5 (15%) a type of headache consisting of at least two of the mentioned headaches. When the severity of pre-ECT headache was assessed using VAS, 8 (25%) patients were observed to have mild (VAS: 1-3), 12 (37.5%) patients moderate (VAS: 4-6) and 12 (37.5%) patients severe (VAS: 7-10) headaches. The characteristics of pre-ECT headaches are summarized in **Table 2**.

### ■ POST-ECT headache

To assess their post-ECT headache, the patients were questioned immediately after their ECT, and at the 2<sup>nd</sup> and 4<sup>th</sup> hours. Out of the 337 patients participating in the study, 49 (14.5%) had post-ECT headache. No difference was found between the genders with respect to post-ECT headache ( $p=0.853$ ). The temporal relationship of the post-ECT headache with the ECT, the type of the headache, at which ECT it occurred, its severity as per VAS, its localization, its character, conditions accompanying it and its duration were questioned. The characteristics of post-ECT headache are summarized in **Table 2**.

**Table 1: Demographic data of patients with pre-ECT and post-ECT headaches.**

Variable	Median (minimum-maximum)	Pre-ECT Headache N=33 (9.8%)	Post-ECT Headache N=49 (14.5%)
Age	36 (17-70)	34.9 ± 8.8 (20-54)	32.7 ± 7.6 (20-51)
Gender			
Female	96 (28.5%)	17 (17.7%)	15 (15.6%)
Male	241 (71.5%)	16 (6.6%)	34 (14.1%)
Psychiatric diagnosis			
Psychosis	289 (85.8%)	26 (78.8)	38 (77.6%)
Bipolar	30 (8.9%)	3 (9.1)	3 (6.1%)
Depression	18 (5.3%)	4 (12.1)	8 (16.3%)
Education			
Literate	32 (6.5%)		
Primary school	219 (65%)		
High school	83 (24.6%)		
University	13 (3.9%)		

**Table 2: Headache characteristics of the patients who had pre-ECT and post-ECT headaches.**

	Pre-ECT Headache N=33 (9.8%)	Post-ECT Headache N=49 (14.5%)
Gender (F/M)	17/16 (p=0.004)	15/34 (p=0.853)
Type of headache		
Migraine	8 (24%)	4 (8.1%)
TTH	16 (48%)	12 (24.4%)
Vascular type headache	3 (9%)	29 (59.1%)
Mixed type headache	5 (15%)	2 (4%)
Undefined	1 (3%)	2 (4%)
VAS		
Mild (1-3)	8 (24.4%)	22 (44.8%)
Moderate (4-6)	12 (36.3%)	15 (30.6%)
Severe (7-10)	12 (36.3%)	10 (20.4%)
Undefined	1 (3%)	2 (4%)
Condition accompanying headache		
Nausea-Vomiting		1 (2%)
Dizziness		1 (2%)
All of the above		1 (2%)
No accompanying condition		44 (89.7%)
Undefined		2 (4%)
Temporal relationship of headache with ECT		
Immediately after		43 (87.7%)
1 hour later		4 (8.1%)
Undefined		2 (4%)
Remission of headache		
Receded spontaneously		38 (77.5%)
Receded with medication		9 (18.3%)
Unanswered		2 (10.8%)

ABB: TTH: Tension Type Headache; VAS: Visual Analog Scale

The mean duration of headache suffered by the patients was 1.87±3.55 hours (min: 0.1-max: 24) and the mean severity of their headache was 4.61 ± 2.56 (min: 2-max: 10). Only 9 (18.3%) of the patients with post-ECT headache needed treatment. These patients were given 500 mg of acetaminophen within the first half an hour and they were observed for 2 hours; 4 patients with continuing headache were given a 50 mg dose of diclofenac potassium as a second medication. After giving the second medication, headaches were observed to resolve except in 2 subjects who responded to it partially.

**■ The relationship between pre-ECT and post-ECT headaches**

When 10 patients who had both pre-ECT and post-ECT headaches were questioned whether the characteristics of these headaches were similar or different, half of the patients stated that it was a pain similar to their previous headaches. No difference was found in the severity of pre-ECT and post-ECT headaches (p=0.66). Out of 33 patients who had pre-ECT headache, 10 (30.3%) also had post-ECT headache in our study (p<0.001).

In conclusion, we defined the post-ECT headache in our study as a headache that; occurs immediately after an ECT most of the time, is moderate in severity, of vascular nature, not accompanied by other conditions such as nausea, vomiting or dizziness, and usually recedes spontaneously within two hours without any treatment. Although no difference was found in the severity of pre-ECT and post-ECT headaches, the presence of headache before ECT was found as a risk factor for post-ECT headache ( $p < 0.001$ ).

### Discussion and Conclusion

The electroconvulsive therapy (ECT) is agreed today to be one of the effective options in the treatment of particularly severe depressions not responding to pharmacological therapies as well as other diseases such as mania, schizophrenia, schizoaffective disorder, catatonia, Parkinson's disease and neuroleptic malignant syndrome (NMS) [19].

ECT is thought to show its effect by enhancing the theta and delta rhythms on the frontal and temporal lobes, activating brain inhibitor processes and anticonvulsant mechanisms and promoting neuroactive hormone (ACTH, cortisol, prolactin and vasopressin) neuropeptide release, subcortical dopamine increase and hippocampal BDNF (brain-derived neurotrophic factor) formation [20-22]. It is reported that the effect of serotonergic system plays a role, which is similar to the pathophysiology of migraine headache, in development of headache as the side effect of ECT [23]. While desensitizing 5HT<sub>1A</sub> (hydroxytryptamine) auto-receptors, ECT upregulates 5HT<sub>2</sub> receptors and produces headache. Antidepressants, however, downregulates the 5HT<sub>2</sub> receptors. Sensitivity of 5HT<sub>2</sub> receptors have an important role in production of headache. This may explain why ECT causes headache but amitriptyllin relieves [24].

ECT is a widely used treatment, but involves minor or major side effects secondary to the frequency of its use. The electroconvulsive therapy has some serious side effects including cognitive (anterograde and retrograde amnesia), cardiovascular (arrhythmia, hypertension) and epileptic attacks as well as mild ones such as muscle pain, nausea and headache. Other side effects of ECT include hypotension, apnea and hypoxia associated with the anesthetics used, muscular fasciculation associated with muscle

relaxants, intracranial and intraocular pressure increase associated with attacks and fractures-dislocations. Muscle pain and headache are usually mild complications responding to simple analgesics [4,25].

Although the cause of the headache occurring after ECT is not fully known, the contractions in the masseteric and temporal muscles, and cerebral vasodilatation are thought to play an important role in its pathogenesis [26,27].

In addition to determining the frequency and characteristics of post-ECT headache, this study also investigated the relationship of pre-ECT headache with post-ECT headache.

In the studies assessing post-ECT headache, Haghighi et al. found the prevalence of post-ECT headache to be 22% [12], Weiner et al to be 37% [24] and Wang et al to be 46% [28]. We found the prevalence of post-ECT headache to be 14.5% in our study, which was lower than those in other studies. The reason for this broad discrepancy in the prevalence of post-ECT headache may be the differences in the time when the headache was questioned in those studies. For example, while Haghighi et al. questioned headache 6 hours after the ECT, Sariççek et al. questioned it at the 2<sup>nd</sup>, 6<sup>th</sup>, 12<sup>th</sup> and 24<sup>th</sup> hours [7]. We assessed our patients' headaches immediately after the ECT and at the 2<sup>nd</sup> and 4<sup>th</sup> hours in our study. Since we did not question headache at the 6<sup>th</sup>, 12<sup>th</sup> and 24<sup>th</sup> hours as in some other studies, this was interpreted as the reason for our rate of headache turning out lower.

It has also been argued that pre-ECT headache increases the prevalence of post-ECT headache [29]. Besides this, the presence of unknown and unattended pre-ECT headache in the studies included in the literature can be interpreted as the reason for the increased prevalence of post-ECT headache. In our study, identification of just a few pre-ECT headaches could be another reason for the low prevalence of post-ECT headache.

There are not a sufficient number of studies defining the characteristics of post-ECT headache in detail. Kertesz et al. have stressed in their study the presence of a diffuse, compressive type headache after ECT in more than half of their patients [16]. The post-ECT headache in our study was usually a mild to moderate, tolerable, bilateral headache more of a throbbing nature without any accompanying conditions (e.g. nausea, vomiting, dizziness).

Dinwiddie and Haghghi reported that post-ECT headache was mild in their experiences [12,26] and Markowitz et al. that 46.2% of their patients had a severe and 53.8% had a moderate headache [15]. Ferreira-Valente et al. pointed out that the headache became severest 2 hours after an ECT and returned to its former state a day after the therapy [30].

We observed in our study that 44.8% of the patients with post-ECT headache had mild, 30.6% moderate and 20.4% severe headaches. The mean severity of post-ECT headache was [VAS:  $4.61 \pm 2.56$  (min: 2 max: 10)], which could be considered moderate. Since the rating of pain severity is a personal and subjective finding, it may play a role in obtaining differing results. Additionally, the characteristics of the population taking part in the study, the psychiatric diseases they have and the time at which headache was questioned were interpreted as the other factors playing a role in having varying results.

Weiner et al. reported that post-ECT headache was seen in 7% of the patients who had pre-ECT headache and its severity was higher than pre-ECT headache [24]. In a study assessing patients suffering migraine before their ECT, it could not be explained fully whether or not migraine was a predisposing factor for post-ECT headache [29].

In our study, 30.3% of the patients with pre-ECT headache had also post-ECT headache. Unlike the literature, we found the presence of headache before ECT as a risk factor for post-ECT headache even though the number of subjects with pre-ECT headache was 10 ( $p < 0.001$ ). However, there was no significant difference in the comparison of the severity of pre-ECT and post-ECT headaches ( $p > 0.05$ ).

The first limitation of our study was that no responses could be obtained from one patient and ambiguous responses from two other patients due to the confusing condition arising from both ECT and premedication. Another limitation was the exclusion of patients with severe psychosis due to their inability to communicate.

The International Classification of Headache Disorders (ICHD 3-2018) criterion stating that a headache occurring after an ECT should develop within 4 hours and resolve within 72 hours following the ECT is compatible with the results of our study.

The Appendix Criteria do not include the aspects we have assessed such as localization, character and severity of the headache. Alongside the characteristics of the headache we mentioned in our study, the results of further similar studies will clarify the criteria for post-ECT headache, enabling removal of the post-ECT headache criteria from an Appendix (A7.6.3) section.

We should also bear in mind that the presence of pre-ECT headache can be a risk factor for post-ECT headache and for this reason premedication (preemptive analgesic therapy) should be administered accordingly. In this way, the patients in need of treatment will be selected and the likelihood of those who had previously received ECT and those who had experienced post-ECT headache to refuse the treatment will be reduced.

A great responsibility rests with both the neurologists and psychiatrists in recognizing the characteristics of post-ECT headache and determining the treatment approach for it.

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