

Satisfaction and attitude of bipolar patients regarding electroconvulsive therapy: modified or unmodified

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ABSTRACT

Objective: Ministry of Health of Turkey issued a legislation to use only modified electroconvulsive therapy (ECT) in 2005, and this study aimed to assess satisfaction and attitude of bipolar patients regarding modified and unmodified electroconvulsive therapy.

Methods: A total of 100 patients (50 treated with modified electroconvulsive therapy (M-ECT) and 50 treated with unmodified ECT (UM-ECT) with a diagnosis of Bipolar Disorder (depressive or manic episode) were invited to participate in this study. Patients with euthymic mood were included. Satisfaction and attitude towards ECT were evaluated with a structured attitude questionnaire, and M-ECT and UM-ECT patients, and their subgroups (depressive vs. manic) were compared.

Results: No significant differences were found between M-ECT and UM-ECT groups regarding age, sex, marital status and occupation. The majority of all patients (78%) were satisfied from treatment with ECT and with the outcome (88%), without significant differences between modified and unmodified groups. Forgetfulness (70%) and headaches (57%) occurred in all groups, with the only significant difference in forgetfulness being reported by more manic patients treated with UM-ECT. Depressive and manic patients treated with UM-ECT reported concerns of brain damage and physical harm significantly more frequently. While 86% of patients treated with M-ECT consented to a future treatment, this was significantly less in patients treated with UM-ECT (50%).

Conclusions: Bipolar patients report a high degree of satisfaction treated either with modified or unmodified ECT but there was a significant difference in perception of adverse effects and willingness for receiving ECT in future.

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Introduction


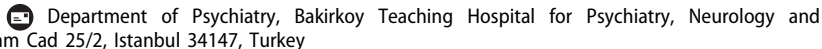
Electroconvulsive therapy (ECT) is one of the oldest biological treatment modalities and it has been used since 1938 for the treatment of psychiatric disorders and especially in depression. This modality is based on the electrical stimulation of the brain tissues and creation of an epileptic seizure. It was done unmodified, without muscle relaxants and anaesthesia until the end of 1940s. Muscle relaxants reduce musculoskeletal morbidity with electroconvulsive therapy (ECT) but need to be administered under general anaesthesia [1 (pp: 1–16),2–11]. Recent data of a large retrospective study and two prospective studies suggest that the risks with unmodified ECT may be lower than was formerly believed [5,7,12,13]. During the past three decades or so, the practice of unmodified ECT has been reported from developing and developed countries, alike.

Electroconvulsive therapy is regarded by almost all psychiatrists as being a safe and highly effective treatment, considerable stigma still surrounds it [14,15]. It still remains one of the most controversial treatments used in medicine, especially in

the eyes of the lay public [16,17]. Another contributing factor is the role of the media in shaping attitudes toward treatment [18]. Conventional research from developed countries has suggested that most patients (50–100%) perceive electroconvulsive therapy helpful, most express positive attitudes (60–90%), and are willing to repeat the treatment (53–98%) if required. However, a sizeable percentage also has negative views [11,19]. Attitudes towards unmodified ECT have also been studied in patients, medical students and psychiatrists. There are no controlled studies on attitudes towards unmodified ECT in any population [6,20].

It is seen that mere clinical efficacy of ECT does not necessarily predict patients' perceptions or satisfaction. In a recent depression study by Krech assessing the influence of pre-treatment expectations, responders and non-responders did not differ in their rather high expectation of ECT effectiveness prior to treatment [21].

Forgetfulness and headache are the most common complaints for ECT treatment. In a review study by Rose et al. forgetfulness was identified at least in one third (29–79%) of

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the patients after ECT [22,23]. Memory disturbances (11%) were only reported by patients in the ECT group in a recent case-control study on remission rates of Transcranial Magnetic Stimulation (TMS) and ECT [24].

Attitude toward and satisfaction with electroconvulsive therapy have also been found to be a transcultural issue. In many developing countries, a paternalistic model of patient care still predominates, and therefore, any treatment option recommended by the doctor is generally viewed as an inevitable matter of necessity [25]. Electroconvulsive therapy (mainly unmodified) is used quite frequently in many of the developing countries [6,26,27]. Electroconvulsive therapy without anaesthesia was a standard approach in Turkey, until 2005. With the new regulation of the Ministry of Health, modified electroconvulsive therapy became the standard. Within a year, which is quite a short time, all psychiatric hospitals switched from unmodified electroconvulsive therapy to modified ECT [28–31]. Clinical studies in Turkey reported rates of ECT use in inpatient units ranging between 12.4% and 16.4%, somewhat higher than Western countries. Few studies examined knowledge of and attitudes toward ECT among healthcare professionals, medical students, or lay people. Aki et al. in a study on attitudes toward and knowledge about ECT in Turkish medical students, psychology students and a sample of the general public, reported that 3 groups differed in their level of knowledge of ECT, and that a higher-than-expected proportion of participants in each group had a positive attitude toward ECT compared with similar studies. [32]. A study from Turkey examining bipolar patients who underwent ECT and their relatives reported that attitudes toward ECT were generally positive among both patients and their families [33].

In this study we aim to assess the contentment and attitude of patients regarding modified and unmodified ECT. As healthcare professionals working at a psychiatric facility treating a large number of psychiatric patients, some with ECT, we believe that information on attitudes toward ECT can guide efforts to improve the image [34].

Subjects and methods

This prospective study was conducted between December 2005-March 2007, in Bakirkoy and Erenkoy Teaching Hospitals, tertiary care neuropsychiatric centers and training hospitals located in Istanbul, Turkey. Institutional Ethics Committee approval was obtained before the onset of the study. All patients were informed about the study and have signed the informed consent. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practices.

Participants

Consecutive patients aged 18–65 years, with bipolar manic or depressive episodes according to DSM IV [35], who were treated with modified or unmodified electroconvulsive therapy were invited for participation in this study. Patients with euthymic mood (50 patients treated with modified and 50

patients with unmodified ECT) were included in the study. They were assessed within the first month (at least 2 weeks after the last treatment) The description of euthymic mood was having less than 7 points in Hamilton Depression Scale (HAM-D) and less than 6 points in Young Mania Scale as well as not having mood symptoms according to DSM- 4R*. Patients with organic brain disorder, comorbid psychiatric and medical illness were excluded. The assessments were carried out by the same investigators (SB and HU). Sociodemographic and clinical features of the patients who participated in the study can be seen in Table 1.

ECT procedure

The decision on ECT indication was made by the patients' attending psychiatrists. A written informed consent is obtained from the patient if he or she is capable to do so. If the patient cannot give consent, it is obtained from his or her legal representative or first degree relatives. The attending psychiatrist routinely provides information about the procedure, expected benefits and adverse effects to patients on the wards before their first ECT session. The consent for modified ECT also includes consent for general anaesthesia. In general, patients undergo 7 to 10 ECT sessions, 2 or 3 times a week. Psychiatric, physical, and neurological examinations and laboratory workup are performed in each patient. An ECT administration form and observation form are filled.

Unmodified ECT was administered in an ECT room (in the psychiatric ward) with trained nursing staff and electroconvulsive therapy was administered by a resident, under supervision of the attending psychiatrist. Patients fasted overnight. Intramuscular atropine at 0.5 mg was given routinely to reduce the risk of pulmonary aspiration or arrhythmias. Before the procedure, vital signs were checked by nurses and electrodes for recording were placed. Electroconvulsive therapy electrodes were placed in the bilateral fronto-temporal manner, half-age method was used in determining the initial intensity. The patients were restimulated at a higher intensity when seizure duration was less than 25 s in EEG recording. A brief-pulse square-wave ECT device (Thymatron system IV device; Somatics, Inc., Lake Bluff, IL, USA) was

Table 1. Sociodemographic and clinical features.

		Modified ECT Patients		Unmodified ECT Patients		
		37,34 (SD ± 14,16)		40,84 (SD ± 12,59)		
		n	%	n	%	
Age	39					.195*
	(SD ± 13.4)					.167 [†]
Sex	Female	25	50%	34	68%	
	Male	25	50%	16	32%	
Marital status	Unmarried	13	26%	11	22%	.886 [†]
	Married	29	58%	30	60%	
	Widow	8	16%	9	18%	
Occupation	Has a job	34	68%	25	50%	.067 [†]
	Jobless	16	32%	25	50%	
Diagnosis	Bipolar depression	18	36%	11	22%	.093 [†]
	Bipolar mania	32	64%	39	78%	

n: number of patient.

*Student t test.

[†]Chi-square test.

used. Patients were discharged from the ECT room when their vital signs were stable.

Modified ECT is administered at the ECT Center. After a preoperative evaluation by an internist and an anaesthesiologist, the patient is scheduled for the intervention. The patient is transferred to the ECT Center after a 6-hour fasting period. In the preparation room, vital signs are checked; the intravenous line is checked; and electrodes for recording are placed by nurses. Electroconvulsive therapy is administered by a resident, under supervision of the attending psychiatrist. Electroconvulsive therapy electrodes are placed in the bilateral fronto-temporal manner. General anaesthesia is induced by an anaesthesiologist by intravenous administration of propofol (0.75–1 mg/kg) and succinylcholine (0.5 mg/kg). A brief-pulse square-wave ECT device is used (Thymatron system IV device; Somatics, Inc., Lake Bluff, IL, USA). Half-amp method is used in determining the initial intensity. The patients are re-stimulated at a higher intensity when seizure duration is less than 25 seconds by EEG recording. Respiration is maintained using positive pressure ventilation with 100% oxygen. Patients are discharged from the post-recovery room when their vital signs are stable.

Sociodemographic and clinical data form

The sociodemographic data form which included data such as the age, sex, marital status, psychiatric illness and electroconvulsive treatment history of the patients was filled out by the investigators.

Satisfaction and attitude questionnaire

This is a self-administered comprehensive and structured questionnaire in Turkish language and contains 20 items to

assess the patients' contentment and attitude regarding ECT. This questionnaire, which was used by Freeman and Kendell [36] in their study has been translated to Turkish by an English-speaking psychiatrist and adapted by taking into consideration the sociocultural factors. For each question the possible answers are either "true" or "false". The questionnaire is in three parts: general contentment regarding electroconvulsive therapy, contentment regarding the treatment results of ECT, and attitude towards adverse effects of ECT.

Statistical analyses

The data was analysed using Statistical Package for the Social Sciences (SPSS) 20.0. Sociodemographic data for age examined with Student *t* test is shown in Table 1. Chi-square was used for other sociodemographic variables in Table 1. Chi-square and Fisher's exact test were used for the comparisons of the questionnaire between modified and unmodified patients in Table 2 and between depressive and manic patients; and between manic modified-unmodified and between depressive modified-unmodified patients in .

We compared also 'headache' and 'forgetfulness' regarding age with Student *t* test.

Statistical significance was accepted as $p < .05$.

Results

Sociodemographic and clinical features

No significant differences were found between M-ECT and UM-ECT groups regarding age, sex and marital status. Sociodemographic and clinical features of the patients are presented in Table 1.

Table 2. Attitudes and thoughts regarding ECT.

	ECT patients $n = 100$, (%)		Modified ECT patients $n = 50$, (%)		Unmodified ECT patients $n = 50$, (%)		<i>p</i>
	TRUE	FALSE	TRUE	FALSE	TRUE	FALSE	
Overall satisfaction							
ECT is a treatment modality	81	19	37 (%74)	13 (%26)	44 (%88)	6 (%12)	.074 [§]
ECT helps people (get well)	78	22	37 (%74)	13 (%26)	41 (%81)	9 (%19)	.334 [§]
People shouldn't be afraid of ECT	65	35	35	15	30 (%60)	20 (%40)	.295 [§]
A lot of people have benefited from ECT	70	30	39 (%78)	11 (%22)	31 (%62)	19 (%38)	.081 [§]
Contentment about results							
I'm content about being treated (with ECT)	78	22	41 (%82)	9 (%18)	37 (%74)	13 (26)	.334 [§]
ECT has increased my quality of life	83	17	45 (%90)	5 (%10)	38	12	.062 [§]
I'm content about ECT results	89	11	47 (%94)	3 (%6)	42	8	.200 ^Ω
ECT increased my functionality	83	17	42 (%84)	8 (%6)	41	9	.790 [§]
ECT is good for my illness	92	8	47	3	45	5	.715 ^Ω
ECT made me get well rapidly	86	14	47 (%94)	3 (%6)	39	11	.041 ^Ω
ECT increased my relationship (with other people)	80	20	46 (%92)	4 (%8)	34 (%68)	16 (%32)	.005 ^Ω
Adverse effects							
ECT is a painful procedure	34	66	16 (%32)	34 (%68)	18 (%36)	32 (%64)	.674 [§]
I remember what I go through ECT	49	51	25 (%50)	25 (%50)	24 (%48)	26 (%52)	.841 [§]
ECT causes forgetfulness	70	30	31 (%62)	19 (%38)	39 (%78)	11 (%22)	.081 [§]
ECT causes headaches	57	43	29	21	28 (%56)	22 (%44)	.840 [§]
Negative Thoughts							
ECT causes brain damage	51	49	12 (%24)	38 (%76)	39 (%78)	11 (%22)	.000 [§]
ECT is physically harmful	45	55	12 (%24)	38 (%76)	33 (%66)	17 (%34)	.000 [§]
ECT damages people	44	56	13 (%26)	37 (%74)	31 (%62)	19 (%38)	.000 [§]
ECT disrupts flow of thought	43	57	17 (%34)	33 (%66)	26 (%52)	24 (%48)	.069 [§]
Treatment in the future							
I agree to be treated with ECT in the future	68	32	43 (%86)+	7 (%14)	25 (%50)	25 (%50)	.000 [§]

N: indicates number of patients; §: chi-square test; Ω: fisher's exact test.

Table 3. Attitudes and thoughts regarding ECT.

	Patients		Depressive Patients		Manic Patients		<i>p</i>	Depressive patients				<i>p</i>	Manic patients				<i>p</i>	
	<i>N</i> = 100		<i>N</i> = 30		<i>N</i> = 70			M-ECT = 18		UM-ECT = 12			M-ECT = 32		UM-ECT = 38			
	T	F	T	F	T	F		T	F	T	F		T	F	T	F		
Overall satisfaction																		
ECT is a treatment modality	81	19	25	5	56	14	.697§	14	4	11	1	.622 ^Ω	23	9	33	5	.119§	
ECT helps people (get well)	78	22	24	6	54	16	.752§	14	4	10	2	1.000 ^Ω	23	9	31	7	.335§	
People shouldn't be afraid of ECT	65	35	21	9	44	26	.493§	13	5	8	4	1.000 ^Ω	22	10	22	16	.349§	
A lot of people have benefited from ECT	70	30	24	6	46	24	.153§	15	3	9	3	.660 ^Ω	24	8	22	16	.133§	
Contentment about results																		
I'm content about being treated with ECT	78	22	26	4	52	18	.199 ^Ω	15	3	11	1	.632 ^Ω	26	6	26	12	.221§	
ECT has increased my quality of life	83	17	24	6	59	11	.601§	14	4	10	2	1.000 ^Ω	31	1	28	10	.009 ^Ω	
I'm content about ECT results	89	11	28	2	61	9	.497 ^Ω	16	2	12	0	.503 ^Ω	31	1	30	8	<i>p</i> < .05 .033 ^Ω	
ECT increased my functionality	83	17	26	4	57	13	.772 ^Ω	15	3	11	1	.632 ^Ω	27	5	30	8	<i>p</i> < .05 .561§	
ECT is good for my illness	92	8	28	2	64	6	1.000 ^Ω	16	2	12	0	.503 ^Ω	31	1	33	5	.209 ^Ω	
ECT made me get well rapidly	86	14	26	4	60	10	1.000 ^Ω	16	2	10	2	1.000 ^Ω	31	1	29	9	.017 ^Ω	
ECT increased my relationship with others	80	20	24	6	56	14	1.000§	16	2	8	4	.184 ^Ω	30	2	26	12	<i>p</i> < .05 .014 ^Ω <i>p</i> < .05	
Adverse effects																		
ECT is a painful procedure	34	66	9	21	25	45	.580§	3	15	6	6	.102 ^Ω	13	19	12	26	.431§	
I remember what I go through ECT	49	51	11	19	38	32	.106§	7	11	4	8	1.000 ^Ω	18	14	20	18	.762§	
ECT causes forgetfulness	70	30	19	11	51	19	.341§	12	6	7	5	.643§	19	13	32	6	.020 <i>p</i> < .05	
ECT causes headaches	57	43	17	13	40	30	.965§	12	6	5	7	.176§	17	15	23	15	.533§	
Negative Thoughts																		
ECT causes brain damage	51	49	12	18	39	31	.150§	4	14	8	4	.024 ^Ω	8	24	31	7	.000§ <i>p</i> < .05 <i>p</i> < .001	
ECT is physically harmful	45	55	10	20	35	35	.125§	2	16	8	4	.004 ^Ω	10	22	25	13	.004§ <i>p</i> < .05	
ECT damages people	44	56	8	22	36	34	.022§	1	17	7	5	.003 ^Ω	12	20	24	14	.032§ <i>p</i> < .05	
ECT disrupts flow of thought	43	57	11	19	32	38	.402§	5	13	6	6	.216§	12	20	20	18	.206§ <i>p</i> < .05	
Treatment in the future																		
I agree to be treated with ECT in the future	68	32	23	7	45	25	.224§	15	3	8	4	.392 ^Ω	28	4	17	21	.000 ^Ω <i>p</i> < .001	

N: number of patients; §: chi-square test; ^Ω: fisher's exact test; M-ECT: Modified ECT; UM-ECT: Unmodified ECT.

Satisfaction and attitude

Majority of all patients considered electroconvulsive therapy beneficial (70%) a treatment modality (81%), which helps people to get well (78%), improving their quality of life (84%). There were no differences between M-ECT and UM-ECT groups, and no differences were found between manic and depressive patient subgroups. No differences were found for manic and depressive patients treated with modified either unmodified ECT.

Majority of patients (M-ECT + UM-ECT) expressed contentment with ECT (78%) and with the results (88%). They also expressed that electroconvulsive therapy was good for their illness (89%) and helped them get well (84%) rapidly; and increased their functionality (82%) and sociability (80%). The only significant difference between unmodified and modified groups was presence of more patients in the modified group reporting that ECT helped them get well rapidly and increased their sociability and reported contentment about the results. (*p* < .05).

There were no significant differences between manic and depressive patient subgroups. No differences were found for depressive patients treated with modified or unmodified ECT. More manic patients in modified group were significantly

more positive than unmodified patients for items of quality of life, sociability, treatment results and speed of recovery.

Two third (65%) of all patients reported no fear from ECT treatment. There were no differences between UM-ECT and M-ECT groups. No differences were found between manic and depressive patients. No differences were found for manic and depressive patients treated with modified or unmodified ECT.

Adverse effects – negative thoughts

Forgetfulness was reported by 70% of all patients and there were no differences between UM-ECT and M-ECT groups. No differences were found between manic and depressive patients. Significantly more manic patients treated with unmodified ECT reported forgetfulness. (*p* = .020). No differences were found regarding age between patients who did or did not report forgetfulness and also between patients treated with modified or unmodified ECT.

Headache was reported by 56% of all patients. There were no differences for all group comparisons. No differences were found regarding age between patients who did or did

not report headache and also between patients treated with modified or unmodified ECT.

One third of all patients (34%) described electroconvulsive therapy as a painful procedure and half (49%) reported remembering it. There was no difference between any groups.

Negative thoughts Half of all patients (51%) believed in a possibility of brain damage and fewer of them reported that ECT was physically harmful and damages people with a significant difference ($p < .001$) between UM and M groups. More manic patients believe that ECT damages people ($p < .05$). Significantly more manic and depressive patients treated with UM-ECT believe that ECT causes brain damage ($p < .001$) and it is physically harmful and damages people ($p < .05$).

Future treatment

If ECT treatment was to be repeated, two thirds of all patients (68%) consented but M-ECT group was significantly more willing to accept future ECT treatment in comparison with the UM-ECT group ($p < .001$). Manic patients treated with unmodified ECT were significantly less consented. ($p = .000$)

Attitudes and thoughts regarding electroconvulsive therapy are presented in [Tables 2 and 3](#).

Discussion and conclusion

Bipolar patients report a high degree of satisfaction, irrespective of treatment with M or UM-ECT. Our results are similar to those reported by similar studies, and are in accordance with the views of Grover who emphasized that the positive assessment of a treatment is primarily the result of getting treated [22]. Krech et al. in a recent prospective study on the influence of depressed patients' expectations prior to ECT, report that responders' rating of ECT effectiveness remained stable on a high level, non-responders' rating decreased significantly [21]. We interviewed the patients within the first month after the treatment. In studies with a shorter interval between treatment and interview, with simple questionnaires, taking place in the hospital where they were treated, higher satisfaction scores are reported [37].

In the present study one third of the patients expressed fear from ECT treatment. Although electroconvulsive therapy is a safe and effective treatment modality, the society and patients have concerns and anxiety towards ECT [38]. A number of Western studies have reported that 47% to 75% of the patients are extremely fearful of electroconvulsive therapy whereas others have concluded that most patients do not find ECT frightening or upsetting [19]. Early studies of unmodified electroconvulsive therapy documented high rates of fear and anxiety, whereas in a historical study Havens (1959) comparing modified and unmodified electroconvulsive therapy, did not find a significant difference either in fear and anxiety before the treatment or afterwards. Gallinek reported that patients rarely spoke spontaneously about their fear and required intense direct questioning [39]. James

reported that only 36% of patients perceived the procedure in some way stressful [40]. It may be a possible expression of unspoken fear. It is important for clinicians to acknowledge patients' concerns and negative feelings toward the treatment, even in the event of a "good outcome" [41].

Similar to previous studies, forgetfulness and headache were the most common complaints [22]. Rose et al. identified forgetfulness at least in one third of the patients [23]. Krech et al. found that the patients' tolerability was not influenced by responder status, and patients with high vs. low expectations did not report differences in the severity of subjective side effects [21]. Headache was similar in all groups in our study, but forgetfulness differs significantly between modified and unmodified manic patients (Unmodified: 84% and Modified: 60%, ($p < .05$)). Most of studies from Western countries addressed on unipolar or bipolar or schizoaffective depressive patient populations [42]. There are few modern studies on attitudes and satisfaction of manic patients treated with M-ECT or UM-ECT and thus it is difficult for us to discuss the significance and importance of these findings. In an attitude study in bipolar patients treated with bilateral modified ECT authors reported forgetfulness in 39%, acknowledging that unfortunately, no data were obtained on which episode (mania, depression, or mixed) ECT was taken as an important limitation [33]. James reported forgetfulness in 30% of all patients (35% bipolar) treated with UM-ECT. [40]. In the position statement and guidelines on unmodified ECT, Andrade [6] referring to this study states that headache and memory impairment may predict negative attitudes towards ECT. High rates of subjective memory impairment in our group (70%) may be explained by the relatively short time interval (within the first month) between treatment and assessment. Also, preference of bilateral electrode placement may have played a role. Another influencing factor may be effects of the drugs which was not included in the design of the study.

About half of all patients (significantly more in the group treated with UM-ECT) have concerns of brain damage and physical harm with ECT treatment. The findings of a very recent and large study revealed that many members of the general public who screened positive for depression were frightened about ECT and had concerns that it was a painful procedure and could cause brain damage [15].

If ECT treatment was to be repeated, two thirds (68%) of the patients consented, similar to many other studies [16,40,42,43,47]. The proportion of patients choosing ECT as a future treatment option is considered as a measure for the overall satisfaction with treatment and varies from 36% to 98% [23,36,44]. Sestoft et al. reported that ECT-treated patients are more likely to prefer ECT in case of future illness, especially those with a high degree of satisfaction [45]. Unmodified ECT patients were less consented for future ECT as well as manic patients treated with unmodified ECT. Gazdag pointed that willingness to consent to ECT is another sensitive indicator of attitude toward the treatment [46]. As Sienaert et al. stated patient satisfaction with treatment is not a clear concept and many other unknown factors may play a crucial role and the degree of the complaints such as

memory complaints and headache does not seem to predict satisfaction with the treatment [41].

Conclusion

Bipolar patients report a high degree of satisfaction treated either with modified or unmodified ECT but there was a significant difference in perception of adverse effects and willingness for receiving ECT in future.

Limitations

Our study groups consisted of patients in remission after ECT. As we emphasized in our discussion, the positive assessment of a treatment may be primarily the result of getting treated. Non-responders to ECT might have been less satisfied with the treatment they had [37]. We think that it is important to share the results of this study carried out in the transition period, since unmodified electroconvulsive therapy is no longer used as a treatment modality. However, it is the main restriction of this study, since it cannot be repeated under same circumstances.

Geolocation information

Bakirkoy Teaching Hospital for Psychiatry, Neurology and Neurosurgery and Erenkoy Teaching Hospital for Psychiatry and Neurology are tertiary care neuropsychiatry centers and training hospitals located in Istanbul, Turkey.

The catchment area has a population of approximately 16 million.

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Disclosure statement

The authors do not have any conflicts of interest or financial disclosures to declare.

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