Predictors for the Efficacy of Electroconvulsive Therapy: Chart Review of a Naturalistic Study

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Background: Several variables have been suggested that can predict the efficacy of electroconvulsive therapy (ECT) in patients suffering from depression. The results of studies into these predictors for ECT efficacy are not consistent.

Method: In a retrospective chart review of patients suffering from major depressive disorder and bipolar disorder according to DSM-IV criteria who have been given ECT in a psychiatric hospital in the Netherlands, predictors for ECT efficacy were explored. Information was gathered for predictors including sex, age, diagnosis, presence of psychosis, duration of index episode, medication treatment failure prior to ECT, medication during ECT course, and ECT variables. ECT was given twice weekly from November 1997 to June 2002. The 17-item Hamilton Rating Scale for Depression (HAM-D) was applied at baseline and weekly during the course.

Results: Seventy-three patients suffering from unipolar or bipolar depression were given ECT in the study period, with 56 patients (77%) meeting antidepressant treatment history form criteria for medication treatment failure. With remission defined as a reduction of depressive symptoms of at least 60% from baseline and a HAM-D end score of less than 8, 48 patients (65.8%) remitted. Forward stepwise logistic regression analysis selected only duration of index episode as a significant predictor for ECT efficacy. Medication treatment failure was not found to be a significant predictor. The concurrent use of psychotropic medication during ECT did not influence the efficacy.

Conclusion: Duration of index episode was the only variable found to significantly predict the efficacy of ECT.

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Compared to antidepressive medication, electroconvulsive therapy (ECT) has been shown to be more efficacious for the treatment of depression.[1,2] However, due to the side effects, of which memory impairment can be a major problem,[3] clinicians in several countries do not view ECT as a first line of treatment for depression. Predictors for the efficacy of this treatment can facilitate a more adequate prescription of ECT and improve the risk-benefit ratio. In the past decades, several variables have been found to be associated with the efficacy of ECT. There is evidence that medication treatment failure can be an important predictor. Three controlled studies[4–6] have found an association between higher levels of medication treatment failure and lower levels of ECT efficacy. These studies suggest that ECT should be applied earlier in the treatment of depressive disorder.

Many studies have found that the duration of index episode (defined here as the period between the first sign of depression noted in the medical record and the first ECT session) has an influence on the response to ECT. Several studies found that a long duration compromised the efficacy.[6–13]

Few studies have compared medication treatment failure and duration of index episode as predictors. A study by Pluijms and colleagues[14] did not find a significant relationship between medication treatment failure and duration of index episode with ECT efficacy, whereas Prudic and colleagues[6] and Shapira and colleagues[13] both found a negative association between medication treatment failure and duration of index episode with change from baseline depression scores during ECT. These 2 variables may be correlated, as the study by Prudic and colleagues[5] found that patients who had inadequate medication treatment prior to ECT had been ill for a shorter period of time.

The association between remission status and baseline Hamilton Rating Scale for Depression (HAM-D) score is less consistent. Fraser and Glass[15] and Prudic and colleagues[6] found an association between higher baseline HAM-D scores and ECT-remission likelihood, whereas Sackeim and colleagues[16] and Andrade and colleagues[9] did not find an association. Kindler and colleagues[11] and Sackeim and colleagues,[17] however, found an association between a lower baseline HAM-D score and ECT-remission.

Few modern studies have explored the efficacy of the combination of ECT and antidepressive medication.[1] The studies by Nelson and Benjamin[18] and Lauritzen and colleagues[19] report a superior outcome with the combination of ECT and a tricyclic antidepressant (TCA), whereas Mayur and colleagues[20] failed to find an advantage for adjunctive treatment with antidepressants during ECT compared to ECT only.

This study compares the predictive ability of these variables (sex, age, diagnosis, duration of index episode, severity of depression, psychosis, and medication treatment failure) for the efficacy of ECT as treatment for depression in a retrospective chart review. The results of a study into predictors for the speed of response to ECT using the current study population have been reported elsewhere.[21]

METHOD

Patients who received ECT between November 1997 and June 2002 in GGZ Delfland, a general psychiatric hospital in the Netherlands, were screened for inclusion. The medical records of patients with a clinical diagnosis of major depressive disorder and bipolar I disorder, most recent episode depressed, according to DSM-IV criteria were selected for a retrospective chart review. Patients were considered to suffer from a bipolar disorder if the records showed that at least 1 manic or hypomanic phase had occurred in the past. Patients suffering from other diagnoses were excluded from analysis. Also, patients who had an ECT course of 4 or fewer sessions without a significant improvement were excluded from analysis. These patients were considered to have terminated the course prematurely. Diagnoses were made by consensus reached in team discussions. The 17-item HAM-D[22] was applied prior to ECT (baseline), weekly during ECT, and after the ECT course (end score) by the clinicians.

Information on sex, age, diagnosis, presence of psychosis, duration of index episode, medication treatment failure prior to ECT, medication during ECT course, and ECT variables was collected. The duration of the index episode was defined as the period between the first sign of depression noted in the medical record and the first ECT session. The antidepressant treatment history form (ATHF)[23] was used to score the level of medication treatment failure. With the ATHF, the level of treatment failure to different groups of antidepressants can be scored (0–5). A total medication treatment failure score can be calculated using the separate scores. Medication treatment failure was defined as a score of 3 or more. As some patients continued treatment with psychotropic medication during ECT, information on the concurrent use of antidepressants, antipsychotics, and mood stabilizers during the course was also collected. Patients were classified in 2 groups for each medication: no medication and continuation of medication during the course. Information on the number of ECT sessions, and the number of unilateral or bilateral electrode applications, was collected. We defined remission as a HAM-D end score less than 8 with a reduction of at least 60% from baseline.

ECT Procedure

Anesthesia was induced with intravenous thiopentone sodium (4–5 mg/kg) and succinylcholine (0.5–1 mg/kg). The blood oxygen level was kept above 95%. Seizures were induced with the Thymatron DGx (Somatics, LLC, Lake Bluff, Ill.) twice weekly. Treatment was started with unilateral electrode placement, which was changed to bilateral placement if there was an insufficient response after several sessions. In life-threatening conditions, patients were given bilateral treatment from the onset. The stimulus settings were initially based on age[24] and adjusted for the concurrent medication used; the stimulus setting was adjusted 5% to 10% upward with the use of benzodiazepines and antiepileptics. The length of the seizures measured by the electroencephalogram (EEG) was kept above 20 seconds. If seizure duration fell below 20 seconds, the stimulus setting was raised at the next session. ECT was stopped when remission was achieved, if there was a lack of further improvement, or if intolerable side effects occurred.

Statistical Analysis

Analyses were conducted using the Statistical Package for Social Science software, version 10 (SPSS Inc., Chicago, Ill.). A stepwise forward logistic regression analysis was used to explore the relation of remission status (yes/no) with duration of index episode, sex, age at initiation of ECT, diagnosis (unipolar or bipolar depression), baseline HAM-D score, psychosis (yes/no), and medication treatment failure. Duration of index episode, age at initiation of ECT, baseline HAM-D score, and medication treatment failure scores were dichotomized using the median value as cutoff point. The medication treatment failure score was separated in treatment failure to selective serotonin reuptake inhibitors (SSRIs), TCAs, other antidepressants, combination therapies (antidepressants + lithium or antidepressants + triiodothyronine [T3]), and total medication treatment failure. The association between variables that were available after the start of ECT (medication during ECT and ECT variables) and remission status were analyzed separately using the Mann-Whitney U test.

RESULTS

One hundred patients received ECT in the study period. Eighty-five were treated for unipolar (N = 73) or bipolar (N = 12) depression. Fifteen patients were excluded from analysis because they suffered from other diagnosed

Table 1. General Results From Analysis of Predictors for the Efficacy of Electroconvulsive Therapy (N = 73)

Characteristic	Value
Male:female ratio, N	24:49
Age, mean (SD), y	57.7 (14.6)
Unipolar:bipolar ratio, N	62:11
Duration of index episode, mean (SD), y	4.4 (6.5)
Baseline HAM-D score, mean (SD)	26.5 (7.6)
Psychosis:nonpsychosis ratio, N	34:39
Medication treatment failure patients, N (%)	56 (77)

Abbreviation: HAM-D = Hamilton Rating Scale for Depression.

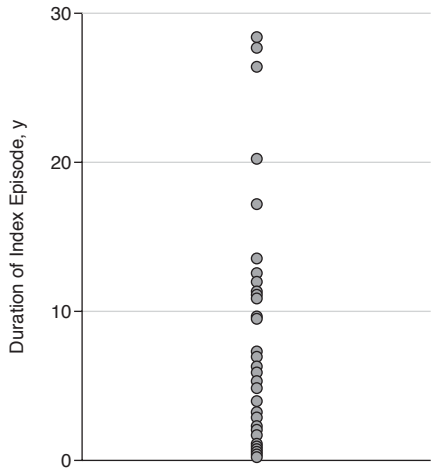
disorders (7 schizophrenia, 3 schizoaffective disorder, 5 bipolar mania or hypomania). Of the 85 patients suffering from unipolar or bipolar depression, 12 were excluded from analysis because the ECT course was terminated prematurely (2 severe headache, 1 severe confusion, 2 no apparent reason), and due to missing HAM-D scores (7 patients). Table 1 shows the 73 patients included in the analysis. Sixty-two suffered from unipolar depression and 11 from bipolar depression. There were 24 male and 49 female patients, with a mean age of 57.7 years (SD = 14.6) at start of ECT. The mean duration of index episode was 4.4 years (SD = 6.5) with a range of 2.6 weeks to 28 years. The median duration of index episode of 1.5 years with a range of 0.6 month to 28 years and the scatterplot (Figure 1) show the skewness of distribution. Few patients had extremely long index episodes.

The mean baseline HAM-D score was 26.5 (SD = 7.6). Fifty-six depressed patients (77%) were considered to be medication treatment failures according to ATHF criteria (total ATHF score of 3 or more).

Table 2 shows details on the ECT course. The mean electrical stimulation during the first 10 sessions was 348 mC (SD = 109 mC). The mean number of ECT sessions was 7, mostly given with unilateral electrode placement (66 patients). Twenty patients received bilateral ECT. In 13 patients, unilateral electrode placement was switched to bilateral during the course.

Forty-eight patients (65.7%) achieved remission (Table 3). For the forward stepwise logistic regression analysis, sex; age; diagnosis (unipolar vs. bipolar depression); duration of index episode; baseline HAM-D; psychosis; scores of treatment failure to SSRIs, to TCAs, to other antidepressants, and to combination treatments (antidepressant with lithium or with T3); and total medication treatment failure score were used as independent variables with remission status as dependent variable. Only duration of index episode was selected for entry into the model (N = 73; regression coefficient $\beta = -1.367$, Wald = 6.547, df = 1, p = .011; odds ratio 0.26, 95% CI = 0.09 to 0.73). Thirteen percent of the variation in remission can be explained by this variable. A longer index episode reduces the chance to achieve remission. Table 3 shows the odds ratios for all variables. Entering the total number of ECT sessions during the course, the number of unilateral and bilateral sessions into the model did not influence the results.

Figure 1. Duration of Index Episode in a Study of Predictors for the Efficacy of Electroconvulsive Therapy (ECT) (N = 73)[a]



[a]Duration of index episode: the period between the first sign of depression noted in the medical record and the first ECT session.

Table 2. Details on the ECT Courses

Variable	Value
Charge during first 10 ECT sessions, mean (SD)	348 mC (109)
No. of ECT sessions in a course, mean (SD)	7 (3)
Patients receiving unilateral ECT, N	66
No. of unilateral ECT sessions, mean (SD)	6 (3)
Patients receiving bilateral ECT, N	20
No. of bilateral ECT sessions, mean (SD)	5 (3)
Patients switching from unilateral to bilateral ECT, N	13
No. of unilateral ECT sessions prior to switch, mean (SD)	3 (2)

Abbreviation: ECT = electroconvulsive therapy.

Logistic regression analysis excluding patients suffering from bipolar depression also selected duration of index episode for entry into the model (N = 62; regression coefficient $\beta = -1.386$, Wald = 5.76,; df = 1, p = .016; odds ratio 0.25, 95% CI = 0.08 to 0.78) as well as analysis excluding the 5 patients with a prior history of ECT (N = 69; regression coefficient $\beta = -1.178$, Wald = 4.704, df = 1, p = .030; odds ratio 0.31, 95% CI = 0.11 to 0.89).

During the ECT course, 47 of 73 patients used psychotropic medication, 19 patients used TCAs, 12 patients used SSRIs, 7 used combination treatment, 12 used lithium, and 30 used antipsychotic medication. There was no significant difference in remission between patients using psychotropic medication (68.1%) or not (61.5%; p = .61), TCA (57.9%) or not (68.5%; p = .41), and antipsychotic medication (76.7%) or not (58.1%; p = .13). Analysis on

Table 3. Univariate Association Between Prognostic Variables and Remission After ECT

Patient Group	N	Remission, N (%)[b]	No Remission, N (%)[b]	OR (95% CI)	p Value[a]
Male gender	24	15 (63)	9 (37)	0.81 (0.29 to 2.24)	.79
Age > 55.7 y	37	25 (68)	12 (32)	1.18 (0.45 to 3.10)	.81
Bipolar depression	11	8 (73)	3 (27)	1.47 (0.35 to 6.10)	.74
Duration of index episode > 1.46 y	37	19 (51)	18 (49)	0.26 (0.09 to 0.73)	.01
HAM-D score > 25	36	23 (64)	13 (36)	0.85 (0.32 to 2.24)	.81
Psychosis	34	26 (76)	8 (24)	2.51 (0.91 to 6.92)	.09
SSRI ATHF score ≥ 3	13	9 (69)	4 (31)	1.21 (0.33 to 4.41)	1.00
TCA ATHF score ≥ 3	35	22 (63)	13 (37)	0.78 (0.30 to 2.06)	.63
Other ATHF score ≥ 3	22	14 (64)	8 (36)	0.88 (0.31 to 2.49)	.80
Combined ATHF score ≥ 3	23	18 (78)	5 (22)	2.40 (0.77 to 7.51)	.19
Total ATHF score ≥ 3	56	38 (68)	18 (32)	1.48 (0.48 to 4.52)	.56

[a]Fisher exact test (2-sided).
[b]Of the 73 patients included in the analysis, 48 achieved remission; 25 did not.
Abbreviations: ATHF = antidepressant treatment history form, ECT = electroconvulsive therapy, HAM-D = Hamilton Rating Scale for Depression, SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant.

the use of other medication during ECT was not done, as the numbers were too small. Using the median as cutoff point for the total number of ECT sessions and percentage of bilateral electrode applications during the course, no significant differences in remission were found between short courses (66.7%) and long courses (65.2%) and between low percentage of bilateral sessions (64.2%) and high percentage of bilateral sessions (70%).

DISCUSSION

In this retrospective chart review, we found that the majority of patients (77%) who had been given ECT satisfied the ATHF criteria for medication treatment failure (total ATHF score of 3 or more). This is consistent with the view that ECT should be used after several failed trials with antidepressants, which is common practice in the Netherlands. Our patient sample had a long mean index episode of 4.4 years, even in comparison to other Dutch samples. Pluijms and colleagues[14] reported a mean index episode of 1.9 years, and Lemstra and colleagues[25] reported a median index episode of 1 year with a range of 1 month to 5.5 years. This long mean index episode limits the generalizability of our results to other samples.

The distribution of duration of index episode was skewed, with few patients having extremely long index episodes. These were patients who had been ill for many years and could not receive ECT prior to the introduction of ECT in our hospital, as they declined to be referred to another hospital where ECT was available. Probably, other psychiatric centers that still do not offer ECT house patients with long-term illnesses who could benefit from ECT. Despite the evidence that offering ECT in an earlier stage can significantly reduce suffering for depressed patients, this unfortunately still is not common practice in the Netherlands. Our patients were severely ill as suggested by the high percentage of psychosis (47%) in comparison to other ECT samples; Sackeim and colleagues[26] reported 36% psychosis and Husain and colleagues[27] reported 30% psychosis in their samples.

Studies have shown that depressed patients suffering from psychosis are at significantly higher risk for committing suicide.[28] Fortunately the latest Dutch ECT guidelines[29] recommend the use of ECT as preferred treatment for depression with psychosis. The latest data available on the use of ECT in the Netherlands showed that in 1999, 328 patients received ECT in 20 ECT centers, i.e., an average of 16 patients a year for each center.[30] These numbers suggest another possible explanation for the reluctance of psychiatrists to offer ECT apart from concerns about memory problems following ECT. The limited opportunity that residents and psychiatrists have to gain experience with ECT may contribute to the lack of knowledge of this treatment and its benefits and adverse effects, resulting in low numbers of patients offered ECT. This is in sharp contrast with the vast resources of the pharmaceutical industry for educating physicians on the use of psychotropic medication, resulting in a much more frequent use of medication.

Using an end score HAM-D of less than 8 with a reduction of at least 60% from baseline as definition for remission resulted in remission rates of around 66% irrespective of medication treatment failure status. Our study found only duration of index episode as a significant predictor for remission. A shorter index episode increases the chance to respond to ECT.

Further analyses were done to exclude the influence of confounders. The efficacy of ECT could be influenced by the unipolar/bipolar distinction,[31,32] so a separate analysis was done using only unipolar depressed patients. This analysis also found duration of index episode as predictor for remission. Another analysis excluding the few patients with a prior history of ECT was done also, as a successful previous ECT course could bias the clinician into more readily offering this treatment to these patients. This analysis gave the same result. A limitation of our analysis is the relatively small number of patients available for the

number of variables used to explore the presence of predictors for achieving remission. Analysis using a larger population is necessary before more definite conclusions can be drawn.

Adjunctive treatment with medication during ECT did not contribute to a higher efficacy, contrary to the retrospective study by Nelson and Benjamin,[18] which suggests that the concurrent use of TCAs increases the efficacy of ECT. This is not supported by our study. The retrospective nature of our study, however, does not allow formulations of firm conclusions, as it is not possible to determine in retrospect why some patients continued the use of antidepressants during ECT and others did not. Possibly patients who were relatively more ECT resistant continued their medication, which contributed to treatment efficacy. The prospective, randomized study by Mayur and colleagues[20] is consistent with our findings, as this study also did not find evidence for the beneficial effect of continuing antidepressants during ECT. Neither the length of the ECT course nor the percentage of bilateral electrode placements used during the course was associated with the outcome.

The recognition of medication treatment failure or duration of index episode as predictor(s) for remission could be theoretically and clinically relevant. If medication treatment failure is an important predictor for ECT efficacy, as suggested by Prudic and colleagues[6] and Shapira and colleagues,[13] it could be used to define a group of patients that does not respond to pharmacotherapy or ECT. It would be important to recognize as soon as possible such patients so that other specific treatments, which should be developed for this group of patients, could be given. A search for markers for medication and ECT treatment failure would be warranted. If, on the other hand, duration of index episode predicts the results of ECT and not medication treatment failure, the search for that particular group of patients is not relevant. A search for markers would not be productive. All patients should receive pharmacotherapy and ECT instead. It would, however, be important not to wait too long before applying ECT to prevent a reduction in efficacy.

Contrary to the finding by Petrides and colleagues[33] and O'Connor and colleagues[34] that ECT was more efficacious in older compared to younger patients, we did not find a significant association between age and efficacy. Sackeim and colleagues[26] found that high-dose unilateral ECT, defined as stimulation at 6 times seizure threshold, was more efficacious than moderate-dose unilateral ECT, defined as stimulation at 2.5 times seizure threshold. Because age-based stimulus setting results in relatively higher electrical stimulation in the older compared to younger patients,[17,35] we expected to find an exaggeration of the finding by Petrides and colleagues[33] and O'Connor and colleagues[34] that age significantly predicts the efficacy of ECT. This, however, is not the case. These 2 studies used stimulus titration and bilateral ECT, whereas we used age-based stimulus setting, and most of our patients were treated with unilateral ECT. The patient sample from the 2 studies[33,34] had a shorter index episode than ours. These differences hamper an adequate comparison with our study.

More studies are necessary to explore the association between several variables and ECT efficacy. This study adds to the existing literature. It is possible that no clear picture can emerge, as diverse ECT populations across studies result in varying significant associations between relevant variables and ECT efficacy. It is possible that the results of our study are typical for the Dutch ECT population and cannot be easily compared to studies from other countries with a different use of ECT.

Drug names: lithium (Eskalith, Lithobid, and others), succinylcholine (Anectine, Quelicin, and others).

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