One-Year Follow-Up After Successful ECT: A Naturalistic Study in Depressed Inpatients

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Background: The aim of this study is to examine both long-term efficacy of electroconvulsive therapy (ECT) and the predictive value of adequate pre-ECT pharmacotherapy and the presence of delusions in relation to post-ECT relapse in patients who suffered from DSM-III-R major depression.

Method: Forty responders (a decrease in Hamilton Rating Scale for Depression score ≥ 50%) to ECT were followed for 1 year, the majority (N = 28) prospectively and the remainder (N = 12) retrospectively. Relapse was defined as readmission, an obvious decline in social functioning, or a change of antidepressant medication caused by a clear worsening of depressive symptoms.

Results: Both 6- and 12-month post-ECT relapse was significantly lower in patients with delusional depression compared with nondelusional patients: 3/24 (12%) versus 8/15 (53%) and 5/24 (21%) versus 11/15 (73%), respectively. Relapse rates for the whole sample were 11/39 (28%) at 6 months and 16/39 (41%) at 12 months. Regarding the impact of adequate pre-ECT antidepressant trials on relapse, our data are inconclusive, because only a few patients did not receive adequate pharmacotherapy prior to ECT.

Conclusion: The remarkable finding of the present study is the favorable 1-year outcome for patients with delusional depression. The relapse rate for patients adequately pretreated with antidepressants (45% over 1 year) is somewhat more favorable than expected.

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Electroconvulsive therapy (ECT) is highly effective in severe depression, but since ECT is typically discontinued after successful treatment, relapse is a major problem. Follow-up studies show that relapse rates in the first 6 to 12 months after successful ECT are high, probably above 50%.[1–3] In most countries, ECT is usually performed in depressed patients that have been adequately pretreated with antidepressants. These are the patients who seem to be prone to relapse as Sackeim et al.[2] demonstrated in a naturalistic follow-up study. Continuation treatment with tricyclic antidepressants may reduce post-ECT relapse, but certainly not to the level of 20% during the first 6 months, as early studies suggested.[4]

It is common practice to administer as continuation post-ECT pharmacotherapy the same class of antidepressant that was ineffective prior to ECT. The effectiveness of this strategy appears to be doubtful; Sackeim et al.[2] found a 64% relapse rate in adequately pretreated patients during the first year post-ECT. In a randomized controlled double-blind study,[3] nortriptyline-lithium combination was superior over both nortriptyline and placebo in preventing relapse, but 6-month post-ECT relapse rates were fairly high (39% vs. 60%).

The results of the referred studies may not be applicable to the population of depressed patients in the Netherlands. In our country, little research has been done regarding the long-term efficacy of ECT, although 2 studies[5,6] have found a high relapse rate as well.

In the Netherlands, ECT is an exceptional treatment administered almost exclusively to severely depressed inpatients in a limited number of hospitals; 300 patients received ECT nationwide in 1999[7] in a population of 16,000,000 inhabitants.

Aim of the Study

The present study is partially retrospective and evaluates the long-term efficacy of ECT in a setting in which patients receiving ECT are inpatients exclusively, the majority show a high degree of medication-resistance, and many suffer from delusional depression.

Furthermore, we wondered whether the possible predictive value of illness characteristics regarding post-ECT relapse could be replicated in our patient sample. We examined the impact of adequate pharmacotherapy

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prior to ECT[2] and the presence of delusions[1,8,9] on post-ECT relapse.

METHOD

Patient Selection

We reviewed the case records of 69 consecutive inpatients that were successively treated with ECT between December 1993 and December 2000 at the inpatient unit for patients with severe depression of Parnassia Psychomedical Center, The Hague, the Netherlands. Eight patients with schizoaffective or bipolar disorder were excluded as well as 6 patients that had received a prior course of ECT.

Thus, 55 patients met the DSM-III-R criteria for major depression, fulfilling the inclusion criteria prior to ECT, and received their first ECT course. Because some patients were admitted and treated before the introduction of DSM-IV, we had to use DSM-III-R criteria for the whole sample. To participate in this follow-up study, patients had to be classified as responders to ECT. Response to ECT was defined a priori as a reduction in the 17-item Hamilton Rating Scale for Depression (HAM-D)[10] score of at least 50% and a HAM-D score of ≤ 14.

Forty (73%) of 55 patients responded to ECT and entered the follow-up study. For a more detailed description of the acute treatment phase, the reader is referred to a previous article.[11]

The adequacy of pre-ECT antidepressant trials was evaluated independently and rated by a psychiatrist (T.K.B.) and a resident (E.M.P.) using the Antidepressant Treatment History Form (ATHF).[2,12] Patients scoring 3 or more on this 0 to 5 scale are classified as having received adequate treatment with antidepressants. A diagnosis of delusional depression was made only when the patient had expressed, either spontaneously or on inquiry, definite mood-congruent delusions. Strong feelings of hopelessness and worthlessness were not considered sufficient for inclusion in the delusional sample. When the case records of an individual patient left any room for doubt about the presence of delusions, the patient was included in the nondelusional group. The relapse status was assessed by the second author (J.-W.R.).

Electroconvulsive Therapy

Patients were withdrawn from all psychotropic medication at least 1 week before ECT, and they were maintained drug-free during the course of ECT in all but 5 cases. These patients received 5 mg of droperidol prior to ECT for severe anxiety. Two of them also received haloperidol, 1 to 3 mg daily, to control severe agitation. Eleven patients received right unilateral (d'Elia) ECT only; another 11 patients initially received right unilateral ECT and were crossed over to bilateral ECT, because of insufficient response after 3 to 11 treatments; and 18 patients received bilateral ECT from the start, because of the severity of the illness based on clinical observation.

ECT was administered with a brief-pulse, constant-current apparatus (Thymatron, Somatics, Lake Bluff, Ill.), with pulse width of 1.0 ms. The duration of the pulse train varied from 2.2 to 4.0 seconds. Patients received thiopental anesthesia (1.0–2.5 mg/kg) and succinylcholine (1.0 mg/kg) for muscle relaxation. Physiologic monitoring included pulse oximetry and an electrocardiogram. Seizure duration was determined by using a 2-lead electroencephalography and the cuff technique. ECT was administered at a schedule of 2 treatments per week with moderate-to-high stimulus intensity (202–504 millicoulomb), without measuring seizure threshold by empirical dose titration. Stimulus dosing was based on age, with a minimum of 252 millicoulomb in patients receiving right unilateral ECT. A motor seizure of less than 25 seconds was considered inadequate. The number of ECT treatments was determined by clinical observation, and a minimum of 10 treatments was required before evaluation as a nonresponder. ECT was continued until patients were either asymptomatic or had shown no further improvement over 3 consecutive treatments.

Follow-Up Procedures

Following ECT, patients stayed at the inpatient unit for approximately another 4 to 8 weeks, during which continuation pharmacotherapy was established. After their discharge from the inpatient unit, the majority (N = 28) of the patients were treated either at the day care department or at the outpatient department of our hospital. Follow-up of these patients was prospective. The remaining 12 patients were treated at outpatient departments of referring psychiatric hospitals; their follow-up was retrospective. Because part of our sample was followed-up retrospectively, we had to use rather obvious criteria for relapse. We defined relapse as readmission or the need for addition or change of antidepressant medication (not caused by side effects) or a clear decline in social functioning.

Follow-up information was obtained at least 12 months (range, 12–60 months) after the index ECT course. Prospective follow-up assessments were rated directly (N = 28); retrospective follow-up assessments were obtained from collateral sources, namely the treating psychiatrist or general practitioner (N = 12). Prospective follow-up implies that patients were evaluated monthly. Retrospective follow-up implies that the second author (J.-W.R.) assessed whether a patient had relapsed. In case of relapse, he assessed the time of relapse as accurately as possible. Our hospital is 1 of 2 providing ECT in the southwest part of our country; therefore, when a relapse was suspected, there was a strong tendency for patients to be referred back to our center for evaluation.

Table 1. Demographic and Clinical Characteristics of 40 Depressed Patients Who Responded to ECT

Variable	Total Sample (N = 40)	Depressed With Delusions (N = 25)	Depressed Without Delusions (N = 15)	p Value
Age, mean (SD), y	53.1 (9.8)	56.0 (9.1)	48.1 (9.2)	.005[a]
Female sex, N (%)	27 (67.5)	16 (64.0)	11 (73.3)	NS
Adequate pre-ECT pharmacotherapy, N (%)[b]	31 (77.5)	18 (72.0)	13 (86.6)	NS
Melancholic features, N (%)[c]	36 (90)	24 (96)	12 (80)	NS
Length of index episode, mean (SD), mo	21.7 (18.3)	16.1 (13.9)	31.0 (21.3)	.011[a]
Pre-ECT HAM-D score, mean (SD)	27.2 (5.4)	28.3 (5.9)	25.2 (3.8)	NS
Post-ECT HAM-D score, mean (SD)	8.0 (3.3)	8.0 (2.9)	8.0 (3.6)	NS
Number of ECTs, mean (SD)	13.8 (4.3)	13.3 (4.5)	14.5 (4.1)	NS

[a]Analyzed by Student t test.
[b]Patients were classified as meeting the Antidepressant Treatment History Form criteria when their rating was ≥ 3.
[c]Meeting DSM-III-R criteria for melancholia.
Abbreviations: ECT = electroconvulsive therapy, HAM-D = Hamilton Rating Scale for Depression, NS = not significant.

Statistical Analyses

Statistical analyses were performed using SPSS for Windows, version 9.0 (SPSS Inc., Chicago, Ill.).

For some patients, it turned out to be difficult to assess the exact time of relapse, so we chose not to compute a survival analysis, but to evaluate relapse at 6 and 12 months post-ECT. This could be done fairly accurately because literally all patients that relapsed did so in the first 8 months following ECT termination. Chi-square tests were used to analyze the difference in relapse rate between patients with delusional versus nondelusional depression as well as for medication-resistant versus non–medication-resistant depressed patients. Fisher exact tests (2-tailed) were used for 2-by-2 tables with cell frequencies lower than 5. Student 2-tailed t tests were used to compare group means.

RESULTS

Impact of Delusions on Relapse

The total patient sample for the follow-up study consisted of 40 inpatients, 27 women and 13 men, with a mean age of 53.1 years (range, 29–70 years). Twenty-five had suffered from delusional depression and 15 from depression without delusions. Table 1 shows the demographic and clinical characteristics for the total sample and as a function of either the presence or absence of delusions. The mean age was higher in the delusional group (56.0 vs. 48.1 years; p = .005). Thirty-one patients were classified as having received adequate pre-ECT pharmacotherapy according to the ATHF, while the remaining 9 patients had received inadequate treatment with antidepressant medication prior to ECT. No difference was found concerning the proportion of adequately pretreated patients in the delusional and the nondelusional sample. Patients with delusions more frequently showed melancholic features—24 (96%) of 25 patients versus 12 (80%) of 15 nondelusional patients—however, this difference is not statistically significant (Fisher exact test, p = .14). No significant difference was found in the number of patients achieving full remission (HAM-D ≤ 7) at the end of the ECT course between both samples: 15 (60%) of 25 in the delusional sample versus 7 (47%) of 15 in the sample without delusions (Fisher exact test, p = .51).

Table 2. Remission and Relapse and the Presence of Delusions Prior to ECT

Outcome	Total Sample (N = 39) N	%	Depressed With Delusions (N = 24) N	%	Depressed Without Delusions (N = 15) N	%	p Value
Remission at 6 mo	28	(72)	21	(88)	7	(47)	
Relapse at 6 mo	11	(28)	3	(12)	8	(53)	.01[a]
Remission at 12 mo	23	(59)	19	(79)	4	(27)	
Relapse at 12 mo	16	(41)	5	(21)	11	(73)	.002[a]

[a]Analyzed by Fisher exact test.

Patients without delusions had a significantly longer mean duration of their index depressive episode than did the delusional patients (31.0 vs. 16.1 months; p = .011). The mean number of ECT treatments for patients with and without delusions was 13.3 and 14.5, respectively. Table 2 shows the relapse rates at 6 and 12 months for the total sample and as a function of either the presence or the absence of delusions prior to ECT. Follow-up data were available for 39 of 40 patients who responded to ECT.

One female patient, who belonged to the group with delusions, was lost to follow-up. Eleven (28%) of the 39 remaining patients met criteria for relapse at the end of 6 months. All patients relapsing did so in the first 8 months. Only 3 (12%) of the 24 patients with delusional depression relapsed within 6 months versus 8 (53%) of the 15 patients without delusions. Thus, the relapse rate is significantly lower in the delusional sample (Fisher exact test, p = .01), even when the patient lost to follow-up would be considered as relapsed (p = .03). By the end of 12 months, the general relapse amounted to 16 patients (41%); relapse rates for the groups with and without delusions were 5/24 (21%) and 11/15 (73%), respectively. Again, the relapse rate was significantly lower in patients with delusional depression (Fisher exact test, p = .002).

Table 3. Remission and Relapse as a Function of Prior Adequate Antidepressant Treatment[a]

	Total Sample (N = 39)	Pre-ECT Adequate Antidepressant Trials (N = 31)	Pre-ECT Inadequate Antidepressant Trials (N = 8)	
	N %	N %	N %	p Value
Remission at 6 mo	28 (72)	21 (68)	7 (88)	
Relapse at 6 mo	11 (28)	10 (32)	1 (12)	0.40[b] = NS
Remission at 12 mo	23 (59)	17 (55)	6 (75)	
Relapse at 12 mo	16 (41)	14 (45)	2 (25)	0.43[b] = NS

[a]Patients were classified as adequately pretreated according to the Antidepressant Treatment History Form when their rating was ≥ 3.
[b]Analyzed by Fisher exact test.

Impact of Pre-ECT Pharmacotherapy on Relapse

Table 3 shows the relapse rates at 6 and 12 months post-ECT for patients with and without pre-ECT adequate antidepressant trials according to the ATHF. The ratings of pre-ECT pharmacotherapy are dichotomized, resulting in a relatively large group of adequately pretreated patients, scoring ≥ 3 on the ATHF scale, and a small group without adequate prior pharmacotherapy. No relation between relapse rate at 6 and 12 months post-ECT and ATHF score was found, possibly because the group not meeting ATHF criteria was too small. It was impossible to analyze the relation between the score of the strongest medication trial as a continuous measure and post-ECT relapse, because the great majority of our sample had a score of 3 or 4. The relapse rate of patients with adequate pre-ECT pharmacotherapy amounted to 10/31 (32%) at 6 months and 14/31 (45%) at 12 months, which can be regarded as a rather favorable outcome for a medication-resistant sample.

Post-ECT Pharmacotherapy

Three patients did not receive active medication, 1 patient refused continuation pharmacotherapy, and 2 patients received placebo, while participating in a double-blind randomized study. Both patients taking placebo relapsed; one belonged to the sample with delusions, the other to the nondelusional sample. The patient without medication remained in remission. The majority of the patients on antidepressant therapy were using imipramine or nortriptyline, at a dose sufficient to reach a therapeutic plasma level; only 3 patients were using a selective serotonin reuptake inhibitor. Patients using lithium were kept on a therapeutic plasma level (0.6–1.0 mmol/L) as well. Continuation pharmacotherapy was based on the degree of medication resistance, possible partial response to medication prior to ECT, type of pharmacotherapy that had not been tried before, and patient preference. Thus, it is impossible to draw any conclusions based on our data regarding the efficacy of the various types of continuation pharmacotherapy.

DISCUSSION

In this study, 59% of depressed inpatients who responded to ECT remained well during the following year, while being on various types of continuation pharmacotherapy. The relapse rate in our study sample is somewhat more favorable than rates found in previous studies,[2,5,6,13] particularly when the patients receiving adequate pre-ECT pharmacotherapy are considered. Our data show no relation between ATHF score and relapse rate.

There are several possible explanations why our results were more favorable than expected. Various aspects of the administration of ECT could influence post-ECT relapse. In the present study, ECT was administered without concomitant benzodiazepines. In the study of Shapira et al.,[14] no psychotropic drugs were allowed, but, in the studies of Sackeim et al.,[2,13] patients were allowed to use up to 3 mg of lorazepam daily, which may have reduced ECT response.[15] With regard to post-ECT pharmacotherapy, all patients receiving antidepressant monotherapy or an antidepressant-lithium combination started using the antidepressant during the last 2 weeks of the ECT course, which may have prevented some of the early relapse. The remarkable finding from the present study is the significantly lower relapse rate in the sample with delusions compared with the nondelusional patients, both at 6 and 12 months post-ECT. This finding is contradictory to the results of some of the previous studies.[1,8,9] However, these studies did not include a nondelusional control group. In other studies, no difference in relapse[2] was found in delusional and nondelusional patients. Furthermore, in a recent study, a lower relapse rate was found in psychotically depressed patients.[3]

There are several possible explanations for the differences in relapse rates among studies. Suboptimal administration of ECT could have influenced the results of earlier studies; for instance, the administration of low-dosage unilateral ECT could lead to an incomplete remission and consequently to relapse-proneness. Eleven patients in this study were treated with right unilateral ECT only, without empirical dose titration, so the number of patients receiving more than 5 times the seizure threshold is unknown. Therefore, an unknown proportion may have received an inadequate ECT course. If bilateral ECT had been used in all patients, the number of patients achieving full remission might have been higher, and consequently the number of patients relapsing might have been reduced. Furthermore, the mean number of ECTs

would probably have been considerably lower, as shown by a recent study.[16]

In the present study, we included only delusional depressed patients with mood-congruent delusions. In none of the studies reviewed is the qualification mood-congruence with regard to delusions mentioned. Depressed patients with delusions that are not mood-congruent may show a less complete response to ECT and therefore be more prone to relapse. A relevant confounding factor in the present study that may have influenced the relapse rate to the disadvantage of the nondelusional sample is the finding that this sample had a significantly longer mean duration of the index depressive episode. An alternative explanation for the favorable outcome in patients with delusional depression would be an underreporting of relapse in patients whose follow-up was retrospective. This explanation is considered rather unlikely, as far as the delusional sample is concerned, because, if patients who suffered from psychotic depression experience a relapse or recurrence, it nearly always has psychotic features.[17]

Although in the present study the relapse rate post-ECT is more favorable than those found in previous studies,[2,3,5,13] relapse after successful ECT remains a major problem. Several strategies that could possibly reduce post-ECT relapse warrant further study, such as starting an antidepressant during the final 2 weeks of ECT, which was done in the present study, and adding lithium to the antidepressant as soon as ECT is terminated. The application of continuation ECT may also reduce relapse after successful ECT. This treatment was not used in the present study; in the Netherlands, because continuation ECT is just originating, it is offered only to patients who relapsed after successful ECT while on post-ECT pharmacotherapy. Finally, Sackeim et al.[3] proposed an interesting strategy: they suggested tapering ECT over a few weeks instead of the standard abrupt discontinuation of an ECT course. Since our study is descriptive rather than predictive, our findings regarding the more favorable 1-year outcome in delusional depression need to be confirmed by larger fully prospective studies.

Drug names: droperidol (Inapsine and others), haloperidol (Haldol and others), imipramine (Tofranil and others), lithium (Eskalith, Lithobid, and others), lorazepam (Ativan and others), nortriptyline (Aventyl, Pamelor, and others), succinylcholine (Anectine and others).

REFERENCES

1. Spiker DG, Stein J, Rich CL. Delusional depression and electroconvulsive therapy: one year later. Convuls Ther 1985;1: 167–172
2. Sackeim HA, Prudic J, Devanand DP, et al. The impact of medication resistance and continuation pharmacotherapy on relapse following response to electroconvulsive therapy in major depression. J Clin Psychopharmacol 1990;10:96–104
3. Sackeim HA, Haskett RF, Muslant BH, et al. Continuation pharmacotherapy in the prevention of relapse following electroconvulsive therapy. JAMA 2001;285:1299–1307
4. Bourgon LN, Kellner CH. Relapse of depression after ECT: a review. J ECT 2000;16:19–31
5. Jaarverslag Landelijke Evaluatiecommissie ECT. [Annual Report of the National Committee Evaluation of ECT 1999.] Internal publication, The Hague; 2000
6. Lemstra A, Leentjens AF, van den Boek WW. Only transient results of electroconvulsive treatment in refractory depression; a retrospective study [in Dutch]. Ned Tijdschr Geneesk 1996;140:260–264
7. Verwey B. Electroconvulsive treatment in non-university hospitals [in Dutch]. Ned Tijdschr Geneesk 1991;135:1694–1697
8. Aronson TA, Shukla S, Hoff A. Continuation therapy after ECT for delusional depression: a naturalistic study of prophylactic treatments and relapse. Convuls Ther 1987;3:251–259
9. O'Leary DA, Lee AS. Seven-year prognosis in depression: mortality and readmission risk in the Nottingham ECT cohort. Br J Psychiatry 1996;169:423–429
10. Bech P, Kastrup M, Rafaelsen OJ. Mini-compendium of rating scales for states of anxiety, depression, mania and schizophrenia with corresponding DSM-III syndromes. Acta Psychiatr Scand Suppl 1986;326:23–28
11. Birkenhäger TK, Pluijms EM, Lucius SA. ECT response in delusional versus non-delusional depressed inpatients. J Affect Disord 2003;74: 191–195
12. Prudic J, Haskett RF, Mulsant B, et al. Resistance to antidepressant medications and short-term clinical response to ECT. Am J Psychiatry 1996;153:985–992
13. Sackeim HA, Prudic J, Devanand DP, et al. A prospective, randomized, double-blind comparison of bilateral and right unilateral electroconvulsive therapy at different stimulus intensities. Arch Gen Psychiatry 2000;57:425–434
14. Shapira B, Gorfine M, Lerer B. A prospective study of lithium continuation therapy in depressed patients who have responded to electroconvulsive therapy. Convuls Ther 1995;11:80–85
15. Jha A, Stein G. Decreased efficacy of combined benzodiazepines and unilateral ECT in the treatment of depression. Acta Psychiatr Scand 1996;94:101–104
16. Petrides G, Fink M, Husain MM, et al. ECT remission rates in psychotic versus nonpsychotic depressed patients: a report from CORE. J ECT 2001;17:244–253
17. Schatzberg AF, Rothschild AJ. Psychotic (delusional) major depression: should it be included as a distinct syndrome in DSM-IV? Am J Psychiatry 1992;149:733–745