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Research article

Differential response to right unilateral ECT in depressed patients: impact of comorbidity and severity of illness [ISRCTN39974945]

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Abstract

Background: Recent electroconvulsive therapy (ECT) efficacy studies of right unilateral (RUL) ECT may not apply to real life clinics with a wide range of patients with major depressive episodes.

Methods: The study included two groups of patients. In addition to a homogeneous group of patients with major depression according to DSM-IV criteria with severity of the major depressive episode > 16 scores on 17-item Hamilton Rating Scale for Depression (HDRS) (Group 1, n = 16), we included a heterogeneous group of patients with less severe major depressive episodes or with a variety of comorbid conditions (Group 2, n = 24). We randomly assigned the patients to an RUL ECT treatment dosed at 5 or 2.5 times seizure threshold with an intent-to-treat design. The outcomes measured blindly were HDRS, number of treatments, and Mini-Mental State Examination (MMSE). The patients were considered to have responded to treatment if the improvement in HDRS score was at least 60% and they had a total score of less than ten.

Results: The Group 2 patients responded poorer (8% vs. 63%), and had more often simultaneous worsening in their MMSE scores than Group 1 patients. The differences in the outcomes between the two different doses of RUL ECT treatment were not statistically significant.

Conclusions: ECT effectiveness seems to be lower in real-life heterogeneous patient groups than in homogeneous patient samples used in experimental efficacy trials.

Background

A routine use of right unilateral (RUL) electroconvulsive therapy (ECT) with an adequately suprathreshold stimulus dose is encouraged by the latest recommendation of the American Psychiatric Association (APA) Task Force Guidelines for ECT [1]. RUL ECT at a moderate dose (100–200%) above seizure threshold (ST) has been often used as the initial standard treatment based on the previous recommendations [2,3]. More recently, high-dose RUL ECT has been shown to be more effective than moderate dose RUL ECT in the treatment of patients with major depression [4,5]. The external validity of these studies, however, is compromised by exclusion of depressive patients who are treated with ECT in real-world ECT practice, i.e. patients with a lower severity of major depression or a variety of co-morbid conditions [4,5], or patients with extremely severe illness [4]. Patients vary considerably in the extent and severity of their cognitive side effects following ECT. Available information about the factors that contribute to the individual differences is limited [1]. Thus, there

is a lack of effectiveness information for a wide range of depressive patients treated with the usual RUL ECT practice.

To clarify ECT effectiveness in a pragmatic heterogeneous patient population, we included in our study, in addition to patients with at least a moderate to severe major depressive episode (Group 1), also depressive patients who would have been excluded from recent efficacy studies (Group 2). The latter group included patients with mild depression and patients with comorbid conditions irrespective of the severity of depression. This study aimed to compare the effect of RUL ECT in the two depression groups, and also the effect of two different doses of RUL ECT (high and moderate doses) on the outcome of treatment in depressive patients separately in Groups 1 and 2.

Methods

Patients

The study patients gave their informed consent to the study. They had been hospitalized at the Lapinlahti Hospital of the Department of Psychiatry of Helsinki University Central Hospital because of a current major depressive episode (DSM-IV)[6]. In addition, they had not received ECT during the preceding 3-months period, and their antidepressant medication was discontinued (the minimum wash-out period was 5 days). For an antidepressant trial to be considered adequate, the threshold for sufficient duration was a minimum of 4 weeks at or above the threshold for the usual dosages of antidepressants [7]. The major depressive episode diagnosis was confirmed by P.H. by a semi-structured clinical interview in which the collection of psychiatric history included a symptom checklist for criteria of major depressive episode.

Sixty-one of the 81 patients referred to us and screened between October 1995 and February 1997 were treated with ECT. Forty of the 61 (66%) patients were recruited for the study. Of the 20 patients who did not have ECT, 11 patients did not have a current major depressive episode, eight patients refused to have ECT, and one patient preferred to continue with antidepressant medication. Of those 21 ECT patients who were rejected, one patient did not give her consent to the study, eight patients received bifrontal (BF) ECT as a part of a preliminary study comparing the effects of BF and RUL ECT, five patients participated in the ongoing magnetoencephalography ECT study, two patients refused to discontinue the antidepressant medication, three patient received outpatient ECT, one patient received bitemporal (BT) ECT for schizophrenia, and one patient BT ECT for catatonia. The mean (SD) age (years) or gender (female/male) was not different between the rejected patients (n = 21) and the study patients (n = 40) (47.7 ± 12.4 vs. 53.0 ± 11.0, t =1.70, df = 59, P = 0.095; 15/6 vs. 25/15, P = 0.58, respectively). Seven of the 21 rejected patients received RUL ECT for depression. Only one of those patients met the above mentioned inclusion criteria but she refused to give her informed consent to the present study.

The severity of the major depressive episode had to be > 16 points on the 17-item Hamilton Depression Rating Scale (HDRS) [8] and there had to be no co-morbidity for inclusion in Group 1. For inclusion in Group 2 the patients had to have a less severe major depressive episode (HDRS ≤ 16), or a history of alcohol abuse during the previous year, a history of schizophrenia, schizoaffective disorder or another psychotic disorder which was not part of the mood disorder, a history of rapid-cycling bipolar illness (i.e., the occurrence of four or more mood episodes during the previous 12 months), a history of neurological illness, or a history of severe medical illness. All psychiatric diagnoses were defined according to DSM-IV. The study protocol was approved by the Ethics Committee of the Department of Psychiatry of Helsinki University Central Hospital according to the principles of the Helsinki declaration.

Group 1 included 16 patients, and Group 2 24 patients. In Group 2, four patients had had a mild major depressive episode, eight patients had a history of alcohol abuse during the previous year, two patients had a history of schizoaffective disorders, four patients had a history of psychotic disorder not otherwise specified, two patients had a history of a neurological illness (one patient had cerebellar ataxia, and the other ischemic cerebrovascular disease) and four patients had a history of a severe medical illness (three patients had hypertensive cardiovascular disease with concomitant risk factors: one had an aortic homograft, one a history of epilepsy, and one a risk for esophageal reflux, and one patient had coronary artery disease with coronary artery bypass grafting).

ECT

The patients were oxygenated (100% O_2), and their cardiovascular function was monitored using a Cardiocap™ II anaesthesia monitor (Datex-Ohmeda, Helsinki, Finland). d'Elia ECT stimulus placement [9], and the same brief-pulse ECT device (THYMATRON-DGx™, Somatics Inc., Lake Bluff, IL, U.S.A) was used for all the patients. The doses (median, range) for medications in i.v. anesthesia were atropine (mg) (0.4, 0.4–0.7), methohexital (mg/kg) (0.88, 0.69–1.26), and succinylcholine (mg/kg) (0.51, 0.39–0.71). There were no statistically significant differences (p > 0.05, Mann-Whitney U test) in the doses of medications between the depression groups, or the ECT groups.

The ST level was measured at the first ECT treatment session using a modified dose titration method [10]. ST was determined by repeating the stimulus (1.0 ms pulse width) at about 30 s intervals with stepwise increased stimulus doses (25.2, 50.4, 75.6, and 100.8 mC). The ST was defined as the ECT stimulus dose, which elicited a generalized convulsive activity lasting visually for at least 25 s. Ictal EEG was monitored with standard THYMATRON electrodes.

ECT was administered 3 times per week by two ECT psychiatrists. In the second and subsequent treatments, the stimulus was dosed either at five times the initial ST level (400% above the ST level, RUL 5) or at 2.5 times the ST level (150% above the ST level, RUL 2.5) according to the random assignment. The treatments were continued with fixed stimuli, making sure that the motor seizure duration exceeded 25 s. If the generalized motor seizure was shorter, the patient was restimulated after about 60 s with a 25% larger charge, and if no seizure occurred, restimulation was given after about 30s.

Randomization

After assignment to Group 1 and Group 2, patients were randomized by computer using a block randomization (six patients per block) to RUL 5, RUL 2.5, and bifrontal (BF) ECT in Group 1, and to RUL 5, and RUL 2.5 in Group 2. Assignment was concealed until administration of the first ECT treatment. The comparison between RUL and BF ECT has been reported separately.

Blinded clinical evaluations

All evaluators (the attending physicians and the raters) and the patients were blinded to the assignment. The number of treatments was determined by the attending physician. The ECT treatment course was finished when a patient 1) had two or less of the nine symptoms for DSM-IV major depressive episode A criteria, or 2) no further improvement occurred after two consecutive treatments based on change of the same criteria. The HDRS ratings were carried out one to three days prior to the first ECT treatment (pre-ECT HDRS), the day after the fourth treatment (HDRS 4) and one to three days after the last randomized ECT (post-ECT HDRS). The reliability ratings of the three HDRS raters were evaluated by videotapes of the depressed patients three times during the study. The HDRS scores at these three occasions for the three raters were as follows: first rating; 21, 18, 20, second rating; 23, 22, 21, and third rating; 20, 22, 20. In the case of a markedly poor clinical improvement after eight treatments (decrease in HDRS score < 30% from baseline), the patient received a course of conventional bitemporal (BT) ECT treatment dosed at 150% above the BT seizure threshold level. Psychiatric nurses assessed global cognitive status by the standardized Mini-Mental State Examination (MMSE) [11] prior to the first ECT (pre-ECT MMSE), the day after the fourth treatment (MMSE 4), and one to three days after the last randomized ECT (post-ECT MMSE).

Medication

The patients were allowed to use either lorazepam (maximally ~3 mg/day) or chlorpromazine (maximally ~300 mg/day) for anxiety and chloral hydrate (maximally ~2 g) at night during the study. The median (mean, range) doses for lorazepam, chlorpromazine, and chloral hydrate were as follows: 0.8, 1.1, 0–3.0; 19.2, 60.3, 0–320.3; 1.0, 1.0, 0–2.1. The median (range) lorazem dose in patients treated with RUL 5 was smaller than in patients treated with RUL 2.5 in Group 2 (0.6, 0–1.7 vs. 1.6, 0–3.0, P = 0.020, Mann-Whitney U test). There were no other statistically significant differences ($p > 0.05$) in the doses of psychotropic medications between the ECT groups or any difference between depression groups.

Table 1: Clinical characteristics of the ITT sample (n = 40)

	Whole Group mean ± SD	Group 1(n = 16) mean ± SD	Group 2 (n = 24) mean ± SD	P
Age (years)	53.0 ± 11.0	57.1 ± 10.4	50.3 ± 10.7	ns
Sex (female/male)	25/15	10/6	15/9	ns
Previous ECT (yes/no)	12/28	6/10	6/18	ns
Unipolar/bipolar depression (yes/no)	34/6	13/3	21/3	ns
Duration of current episode (wk)[a]	54.3 ± 34.5	47.8 ± 34.3	58.6 ± 34.6	ns
Pre-ECT HDRS score	25.3 ± 6.8	28.6 ± 5.4	23.0 ± 6.9	0.0093
Psychotic features (DSM-IV)(yes/no)	5/35	3/13	2/22	ns
Pre-ECT MMSE score	27.2 ± 2.3	26.0 ± 2.6	28.1 ± 1.6	0.0053
Number of antidepressant trials during episode	2.2 ± 1.4	1.9 ± 1.2	2.3 ± 1.5	ns
Prior adequate antidepressant treatment (yes/no)	34/6	14/2	20/4	ns

Fisher's Exact Test is used for nominal variables and independent sample t-test or Mann-Whitney U test (for non-normal distributions) for continuous variables. [a] An upper limit of 104 weeks was used.

Table 2: ECT parameters of the ITT sample

	Whole Group mean ± SD	Group 1 mean ± SD	Group 2 mean ± SD	P
Initial seizure threshold (mC)	52.3 ± 14.4	55.1 ± 13.7	50.4 ± 14.9	ns
RUL 5 / RUL 2.5	20/20	8/8	12/12	ns
Charge (mC)	208.0 ± 88.1	218.5 ± 82.3	200.6 ± 93.0	ns
Duration of seizures, motor (s)	42.8 ± 6.3	41.1 ± 5.3	43.9 ± 6.8	ns
Duration of seizures, EEG (s)	53.3 ± 17.6	54.8 ± 24.9	52.3 ± 10.7	ns

Fisher's Exact Test is used for nominal variables and independent sample t-test or Mann-Whitney U test (for non-normal distributions) for continuous variables. All parameters except those for the initial seizure threshold refer to mean ± SD values after the first treatment. mC, millicoulombs.

Table 3: Clinical outcome of the ITT sample by depression groups

	Whole Group Mean ± SD	Group 1 Mean ± SD	Group 2 Mean ± SD	P
HDRS change (%)	45.6 ± 26.0	64.3 ± 18.7	33.1 ± 22.7	<0.0001[d]
Responders (yes/no)[a]	12/28	10/6	2/22	0.0004
No. of treatments	7.7 ± 3.2	8.3 ± 2.5	7.4 ± 3.5	ns
MMSE change (%)[b]	-1.8 ± -10.1	2.7 ± 11.2	-5.3 ± -7.6	0.0159[e]
Cognitive risk (yes/no)[c]	18/18	6/10	12/8	ns
Cognitive risk and nonresponse (yes/no)	11/25	1/15	10/10	0.0091

Fisher's Exact Test is used for nominal variables and independent sample t-test or Mann-Whitney U test (for non-normal distributions) for continuous variables. [a]Response = HDRS change (%)≥ 60, and post-ECT HDRS score < 10. [b]Positive values on percentage change indicate a better cognitive functioning as compared with baseline. [c]Cognitive risk = MMSE change < 0%. [d]*P* = 0.0036 using ANCOVA with pre-ECT HDRS score and age as covariates. [e]*P* = 0.1803 using ANCOVA with pre-ECT MMSE score and age as covariates.

Primary outcome measures

The HDRS and MMSE scores prior to ECT treatment were used as the baseline values, and the percentage of change by the randomized treatments was calculated after the last treatment. The patients were considered to have responded to treatment if the improvement in HDRS score was at least 60% and they had a total score of less than ten. Our second primary outcome measure was the number of ECT treatments given. We used an estimate for the number of treatments for those patients who had markedly poor response (decrease in HDRS score < 30% from baseline) to eight randomized ECT treatments and were therefore treated with the BT ECT. This estimate was 14 because determined on a clinical basis, the maximal number of the randomized treatments was 13. The patients were considered to have a cognitive risk if they had any worsening in the MMSE total score. The possibility for the concomitant occurrence of cognitive risk and clinical non-response was calculated for all patients.

Statistical methods

Analyses were performed from the intent-to-treat (ITT) sample using the last-observation-carried-forward (LOCF) method. For this analysis, we included both study completers and non-completers who had received at least one ECT treatment after randomization. For five patients, post-ECT HDRS scores were not available. For these patients, the HDRS ratings and number of randomized treatments were as follows: HDRS 4, six; HDRS 4, eight; HDRS 4, twelve; pre-ECT HDRS, one; pre-ECT HDRS, three. Regarding MMSE analysis, pre-ECT MMSE scores were not available for four patients. For three patients post-ECT MMSE scores were not available. The MMSE ratings and number of randomized treatments for these three patients were as follows: MMSE 4, eight; pre-ECT MMSE, three; MMSE 4, seven. As a sensitivity analysis, we also performed an analysis among study completers who had HDRS and MMSE ratings both prior and after the course of the randomized treatment.

Fisher's Exact Test was used to compare the proportions of different characteristics between the groups. For compari-

son of means independent sample t-test was used. For non-normal distributions, the comparisons were done with Mann-Whitney's *U* test. Normality was evaluated with the Shapiro-Wilk-test. The outcome measures were adjusted for the initial group differences by Analysis of covariance (ANCOVA). ANCOVA was not used for the number of treatments because this measure was not normally distributed. All tests were two-tailed, and the statistical significance level was set to $\alpha = 0.05$. Statistical computations were performed with the BMDP New System [BMDP Statistical, Software, Inc, Los Angeles, California, 1994] except for the ANCOVA which was done with the SPSS for Windows 10.0 (SPSS Inc., Chicago, USA).

Results

Attrition

Six out of 40 patients (15%), one in Group 1 (6%) and five in Group 2 (21%) were non-completers. In Group 1, one RUL 2.5 patient had to discontinue the treatment after seven ECT treatments because of ventricular extrasystolia. In Group 2, one RUL 5 patient had to discontinue the course of the treatment after three treatments because of regurgitation of gastric contents, one RUL 2.5 patient after the first treatment because of a hypomanic switch, two RUL 5 patients after three treatments because of high elevations of blood-pressure, and one RUL 2.5 patient after three treatments due to alcohol abuse. The decision to discontinue ECT treatment was made by the patient in one case, by the anesthetist in four cases, and by the attending physician in one case.

Baseline characteristics

The Group 1 patients tended to be older ($t = 1.99$, df = 38, $P = 0.0539$), had higher baseline HDRS scores ($t = 2.74$, df = 38, $P = 0.0093$), and lower baseline MMSE scores ($P = 0.0053$, Mann-Whitney *U* test) than Group 2 patients (Table 1). The mean (SD) age (years) of the RUL 5 patients was higher than that of the RUL 2.5 patients in Group 2 (55.3 ± 10.6 vs. 45.2 ± 8.5, $t = 2.59$, df = 22, $P = 0.017$). There were no other statistically significant differences between the depression groups or between the RUL ECT groups.

Outcome of the treatment

Group 1 vs. Group 2

The number of responders vs. nonresponders was higher in Group 1 than in Group 2 both in the ITT analysis (10/6 vs. 2/22, $P = 0.0004$, Table 3) and among study completers (10/5 vs. 2/14, $P = 0.0032$).

The improvement in HDRS score was higher in Group 1 than in Group 2 both in the ITT analysis and among study completers (64.3% vs. 33.1%, $t = 4.56$, df = 38, $P = 0.0001$; 64.6% vs. 35.9%, $t = 3.71$, df = 29, $P = 0.0009$, respectively). Using ANCOVA with pre-ECT HDRS scores as a covariate, the difference was statistically significantly different in the ITT sample ($P = 0.0016$), and among study completers ($P = 0.0076$), and remained statistically significantly different when both the pre-ECT HDRS scores and age were used as covariates both in the ITT sample ($P = 0.0036$, Table 3), and among study completers ($P = 0.0152$).

Three patients received a course of BT treatment due to a markedly poor response to randomized RUL ECT treatment. The number of BT patients was not statistically significantly different between Group 1 and Group 2 (1/15 vs. 2/22, $P = 1.0$).

The number of treatments was not different between Group 1 and Group 2 in the ITT sample (Table 3) or among study completers (median, mean, range: 8.0, 8.3, 4–14 vs. 8.0, 8.8, 4–14, $P = 0.5844$).

The mean MMSE scores improved in the Group 1 patients in contrast to impairment in the Group 2 patients both in the ITT sample and among the study-completers (2.7% vs. -5.3%, $t = -2.53$, df = 34, $P = 0.0159$; 2.6% vs. -6.9%, $t = -2.52$, df = 27, $P = 0.0178$, respectively). Using ANCOVA with pre-ECT MMSE scores as a covariate, the difference did not remain statistically different in the ITT sample ($P = 0.2518$), and among study completers ($P = 0.2333$). The difference was non-significant also with pre-ECT MMSE scores and age as covariates in the ITT sample ($P = 0.1803$, Table 3), and among study completers ($P = 0.0961$).

The likelihood of the occurrence of a simultaneous cognitive risk and non-response was significantly higher for Group 2 than for Group 1 in the ITT sample (10/10 vs. 1/15, $P = 0.0091$, Table 3) and among the study completers (8/6 vs. 1/14, $P = 0.0052$).

The ten patients in Group 2 who had simultaneous cognitive risk and non-response were included in Group 2 because of their mild major depressive episode (n = 4), because of their history of previous non-affective psychosis (n = 2), because of alcohol abuse (n = 2), and because of severe medical illness (n = 2). Nine of them had had adequate antidepressant treatments during the current major depressive episode.

RUL 5 vs. RUL 2.5

In the ITT sample, there were no statistically significant differences in primary outcome measures between the RUL ECT treatments in Group 1 or Group 2. The median (mean, range) number of treatments of RUL 5 patients tended to be smaller than that of RUL 2.5 patients in Group 1 (7.0, 7.3, 4–12 vs. 8.0, 9.3, 7–14, $P = 0.0503$). Among study completers, the difference was statistically significant in Group 1 (7.0, 7.3, 4–12 vs. 8.0, 9.6, 7–14, *P*

= 0.0321), but not in Group 2 (8.0, 8.1, 4–12 vs. 8.0, 9.5, 6–14, $P = 0.5886$).

Treatment characteristics

There was no difference in ECT parameters between the depression groups (Table 2). The median (mean, range) RUL 5 dose (mC) was higher than the RUL 2.5 dose both in Group 1 and Group 2 (252.0, 277.7, 252.0–378.0 vs. 126.0, 159.3, 75.6–252.0, P = 0.0014; 252.0, 268.0, 126.0–378.0 vs. 126.0, 127.1, 75.6–201.6, P = 0.0001, Mann-Whitney U test, respectively). No other differences were found between the RUL ECT groups.

Discussion

This study shows that patients with low severity of a major depressive episode or with a variety of somatic or psychiatric comorbidities have a significantly lower response rate to RUL ECT (8%) than patients with a pure, moderate to severe major depressive episode (63%). The abysmal response rate in Group 2 is based upon quite strict response criteria, i.e., a decrease of at least 60% in HDRS scores from baseline and a post-ECT score less than ten. For comparison, the mean percentage improvement in HDRS was 33% in Group 2 as compared with 64% in Group 1. This difference is also both clinically and statistically significant.

Why did the patients in our two depression groups have such different antidepressant responses to the RUL ECT? A long duration of a current depressive episode, and failure to respond to one or more adequate medication trials have been shown to predict a diminished rate of ECT response [12]. In our study, there were no differences between these variables in the depression groups (Table 1). Furthermore, when patients take benzodiazepines during a course of unilateral ECT, the maximum therapeutic response may be compromised [13]. The mean dose of lorazepam (1.1 mg/d) of our patients was at the same level as in the previous efficacy studies (1.0 mg/d, and 1.2 mg/d) [5,14]. In our study, the mean dose of lorazepam was not different between the depression groups. Findings regarding the effects of age on short-term efficacy of ECT have been somewhat inconsistent. Some studies have reported that advancing age can be used to predict good response to ECT [15,16] while other studies have not found this relationship [17]. Thus, the higher mean age of our Group 1 patients (Table 1) may have had some beneficial effect on their treatment outcome as compared to Group 2 patients, but on the other hand, the lower mean age in Group 2 may reflect a greater burden of co-morbidity leading to earlier referral for ECT. The patients in Group 2 had less severe depression than those in Group 1. None of our patients who were included in the analysis in Group 2 because of a mild major depression responded to the ECT treatment. This finding is in agreement with that of Hamilton and White [18] and questions, in general, the usefulness of RUL ECT in patients with a major depression of low severity. Many of our patients in Group 2 had secondary major depression, i.e. a depression occurring in a person who has a preexisting non-affective psychiatric disorder (which may or may not still be present), or a serious or life-threatening medical illness, which precedes and parallels the symptoms of depression [19,20]. It has been shown that patients with secondary depression are less likely to recover from the index depressive episode [21] and are more likely to receive inadequate treatment [22] than patients with primary major depression. Moreover, patients with secondary depression have been found to have a poorer response to ECT treatment than patients with a primary depressive disorder [15,22–24]. Zorumski et al. [24] found that patients with alcohol dependence and secondary depression had a favorable response to ECT. However, concurrent alcohol dependence diminishes the likelihood that depression will respond to treatment [25]. The subgroups in our study were too small for any statistical analyses but one may conclude that the lack of ECT efficacy in Group 2 was due to the prevalence of secondary depression in this group especially as the effect of ECT was lower in Group 2 than in Group 1 also after the adjustment for initial differences in severity of depression and age between the two groups.

The lack of statistically significant differences in primary outcome measures between RUL 5 and RUL 2.5 may indicate that those two RUL ECT doses are equally good. On the other hand, it may be due to insufficient statistical power especially in Group 1 whereas in Group 2, it may also be due to the very low response rate. The difference in the median number of treatments between RUL 5 and RUL 2.5 (seven vs. eight) was statistically different among study completers but non-significant in the ITT sample in Group 1. No reliability ratings concerning determinations of number of treatments were done in contrast to the HDRS ratings. Furthermore, despite the lower mean lorazepam dose in RUL 5 patients as compared to RUL 2.5 patients in Group 2, the difference between number of treatments was statistically nonsignificant. Thus, the relation between speed of response and dose of RUL ECT stimulus can not be answered by this study. The number of cardiovascular complications (one in Group 1, and two in Group 2) was so low that conclusions regarding tolerability between our RUL treatments cannot be drawn. However, in the study of Mayur et al. [26] none of the cardiac-healthy patients (n = 95) treated with seizure threshold level RUL ECT (mean dose 68 mC) had any clinically observable cardiac complications. On the other hand, patients with cardiac disease have been shown to have a significantly higher rate of cardiac complications during ECT than a comparison group without cardiac disease [27].

Therefore, there is a need to further study cardiovascular side-effects induced by suprathreshold RUL ECT.

Depression affects a range of cognitive functions [28]. In our study, the global cognitive status before ECT treatment was poorer in Group 1 than in Group 2. Pre-ECT global cognitive impairment has been found to be a strong predictor of the magnitude of retrograde amnesia for autobiographical information [29]. After RUL ECT in our study, the possibility for simultaneous worsening in global cognitive status and nonresponse was significantly higher (Table 3) for Group 2 patients (50%) than Group 1 patients (6%). The difference of pre-ECT global cognitive status, and the difference of the occurrence of simultaneous cognitive risk and nonresponse between depression Group 1 and Group 2 needs clearly future studies using more sophisticated neuropsychological tests. The MMSE is a superficial method for ascertaining ECT's cognitive side effects. Therefore, until there are more studies on depressive patients with co-morbidity, the risk/benefit ratio has to be assessed individually in different subgroups of patients with major depression.

Conclusions

The good response to RUL ECT of the patient group with major depression without co-morbidity was not found in a heterogeneous co-morbid patient group. Most of the patients in this group had secondary major depression. In addition, patients with a low severity of major depression have a high risk/benefit ratio. The differences in the outcomes between the two different doses of RUL ECT were not statistically significant in the ITT sample. More research is needed to clarify the response to ECT treatment in different subgroups of patients with major depressive episodes.

Competing interests

None declared

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