Improvement of Psychiatric Symptoms after Electroconvulsive Therapy in Young Adults with Intractable First-Episode Schizophrenia and Schizophreniform Disorder

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SUZUKI, K., AWATA, S., TAKANO, T., EBINA, Y., TAKAMATSU, K., KAIJWARA, T., ITO, K., SHINDO, T., FUNAKOSHI, S. and MATUSOOKA, H. Improvement of Psychiatric Symptoms after Electroconvulsive Therapy in Young Adults with Intractable First-Episode Schizophrenia and Schizophreniform Disorder. Tohoku J. Exp. Med. 2006, 210 (3), 213-220 —— Schizophrenia is a serious psychiatric disorder that develops mainly in young adults. Electroconvulsive therapy (ECT) is known to be effective and safe in patients with schizophrenia with acute psychotic exacerbation. Because of the shortage of systematic studies, we conducted a prospective naturalistic study to examine the short-term effects of acute ECT and its safety in young adults with medically intractable first-episode schizophrenia. Subjects were seven consecutive patients, 15-35 years of age, with first-episode schizophrenia or schizophreniform disorder (Diagnostic and Statistical Manual of Mental Disorders, 4th edition; DSM-IV), who had failed to respond to neuroleptics. The seven patients were treated with a first course of ECT, and their clinical symptoms were evaluated on the basis of the Brief Psychiatric Rating Scale (BPRS) (18 items, rated 0-6) and Global Assessment of Functioning (GAF) Scale. The GAF Scale is presented in DSM-IV as a means of assessing global functioning of a psychiatric patient. Scores range from 1-100; the higher GAF score indicates the higher global functioning. Adverse effects resulting from acute ECT were also evaluated. The total BPRS score 1 week after the final session improved significantly compared to the total pre-ECT BPRS score. The GAF score also improved significantly compared to the pre-ECT GAF score. There were no adverse effects during the acute ECT course, except for mild delirium. We conclude that ECT may be an effective and safe treatment option for young adults with intractable first-episode schizophrenia.

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Schizophrenia is a serious psychiatric disorder that develops mainly in young adults. The outcome is poor in about 10-20% of first-episode cases despite neuroleptic treatment (Sheitman et al. 1997; Vazquez-Barquero et al. 1999; Barnes et al. 2000; Lieberman et al. 2003). The management of these poor-outcome cases is important in clinical practice. Because some symptoms of schizophrenia, for example, hallucination, delusion, loose association, and abulia, can compromise the patient’s quality of life for a long time, the need for an efficacious treatment strategy for such patients is urgent.

Electroconvulsive therapy (ECT) is widely used and known to be effective and safe in patients with schizophrenia with acute psychotic exacerbation who have a limited response to neuroleptics (Kruger and Sackeim 1995; Chanpattana et al. 1999; Weiner 2001; Tharyan and Adams 2005). Thus, some authors have speculated that ECT would be a useful treatment option for patients with first-episode schizophrenia (Kellner 1995; Fink and Sackeim 1996; Abrams 2002). However, to our knowledge, with the exception of one seminal study (Ucok and Cakr 2006), there have been no systematic studies on the short-term efficacy and safety of acute ECT in the treatment of young adults with medically intractable first-episode schizophrenia. We conducted a prospective naturalistic study to examine the short-term effects of acute ECT in young adults with medically intractable first-episode schizophrenia.

**METHODS**

**Background**

Subjects of this study were young adults identified among 58 psychiatric patients referred to Tohoku University Hospital between January 1, 2000, and March 31, 2006, for first-time acute ECT. Diagnoses were mood disorder (n = 31, 53.4%), schizophrenia (n = 26, 44.8%), and somatoform disorder (n = 1, 1.7%). Our study subjects were taken from 26 patients with schizophrenia and comprised seven consecutive patients less than 35 years for age who were suffering their first episode of schizophrenia. Before the acute ECT course, all seven were evaluated with MRI of the brain, which revealed no abnormality in any subjects. The ethics committee at Tohoku University Graduate School of Medicine approved this study.

**SUBJECTS AND METHODS**

**Subjects**

The seven subjects were five males and two females with a mean ± s.d. age of 23.6 ± 6.8 years (range, 15-34 years). All met the following inclusion criteria: 1) use of acute ECT approved independently by two research psychiatrists on the ECT team; 2) fulfillment of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) criteria for schizophrenia or schizophreniform disorder (American Psychiatric Association 1994); 3) disease intractability, as described below, and marked psychopathologic symptoms (as evidenced by a Brief Psychiatric Rating Scale [BPRS] score > 35 [18 items, rated 0-6]) (Overall and Gorham 1962); 4) age between 15 and 35 years at the start of acute ECT; 5) written informed consent provided by the patient or guardian; 6) ECT for patients less than 18 years of age approved by the entire ECT team and one consultant experienced in treating psychiatric disorders of children and adolescents. Intractability was defined as disease resistant to medication or medication intolerance or a severe resultant medical or psychiatric condition (e.g., inanition due to refusal eat or high risk of suicide). Resistance to medication was defined as failure to achieve substantial relief of symptoms (as evidenced by a BPRS score > 35) despite the use of at least one class of neuroleptics for a period of at least 4 weeks at a dose equivalent to more than 600 mg chlorpromazine. Patients with a clinical history that included dementia or substance abuse were not included in the study.

**Acute ECT**

Only modified ECT was used. Atropine sulfate (0.5 mg) was administered intramuscularly, and thiopental (2-4 mg/kg) or propofol (1-1.5 mg/kg) was used as an anesthetic agent and succinylcholine (1-1.5 mg/kg) as a muscle relaxant. The ECT device used in the phase 1 study was a CS-I sine-wave apparatus (Sakai Medical Corp., Tokyo) or a Thymatron System IV brief-pulse square-wave apparatus (Somatics, LLC, Lake Bluff, USA). Electrodes were placed in the traditional bilateral fronto-temporal manner. Only one adequate seizure was required for each session, and this was defined as a cerebral seizure monitored electroencephalographically and exceeding 20 seconds. Stimulation with the CS-1 apparatus was done with an alternating current of 100 volts at
50 Hz for 5 seconds. If a missed or inadequate seizure occurred, the patient was restimulated at the same electrical dose after a 20- to 30-second pause. The maximum number of stimulation for each treatment session was three. When stimulation was done with the Thymatron System IV apparatus, the electrical dosing schedule followed stimulus dose titration (Kellner 1997). If a missed or inadequate seizure occurred, the patient was restimulated (after a 20- to 30-second pause [for a missed seizure] or a 60-second pause [for an inadequate seizure]) at a stimulus intensity increment of 100% to obtain an adequate seizure. The maximum number of stimulations for the first treatment session was four and that for the later treatment sessions was three. ECT was administered two or three times per week, and the total number of ECT sessions in an acute ECT course was limited to 20. In general, neuroleptics were used to augment the effect of ECT during the acute ECT course. The attending physician and the ECT team selected the class and dosage of the medication on a case-by-case basis.

**Clinical evaluation**

Outcome in each case was determined by comparing the BPRS score obtained just before the ECT course, the score obtained at the end of the ECT course, and the score obtained 1 week after the final ECT session and by comparing the Global Assessment of Functioning (GAF) score determined just before the ECT course with that obtained 1 week after the final ECT session (American Psychiatric Association 1994). Two experienced research psychiatrists on the ECT team served as raters for these evaluations. Average scores were used. The BPRS consists of 18 items (each item rated 0-6) measuring the severity of a patient’s psychiatric symptoms; the higher total BPRS score indicates the greater severity of the psychiatric symptoms. The GAF Scale is presented in the DSM-IV as a means of assessing global functioning. Scores range from 1-100; the higher GAF score indicates the higher global functioning. The Chanpattana et al. criterion, that patients were considered clinical responders if they had a BPRS score ≤ 25 for 1 week after the final ECT session, was adopted for our study (Chanpattana et al. 1999).

Patients were also evaluated on the basis of Guy’s five factors, which groups the 18 BPRS items into five subscales: thought disturbance (conceptual disorganization, grandiosity, hallucinatory behavior, unusual thought content), activation (tension, mannerisms and posturing, excitement), anxiety-depression (somatic concern, anxiety, guilt feelings, depressive mood), hostility-suspiciousness (hostility, suspiciousness, uncooperativeness), and anergia (emotional withdrawal, motor retardation, blunted affect, disorientation) (Guy 1976).

Adverse cognitive effects resulting from acute ECT were evaluated on the basis of the Mini Mental State Examination (MMSE), which that was administered before and 2 weeks after the acute ECT course. Adverse physical effects from acute ECT were noted in the patient’s record by the attending physician. To identify any epileptic abnormality induced by ECT, electroencephalographic examination was performed before and 2 weeks after the acute ECT course. Characteristics of the study patients before ECT are shown in Tables 1, 2, and 3. Values are shown as mean ± s.d. Differences in test

| Table 1. Clinical characteristics* of the study patients before the first acute ECT course (n = 7). |
|-------------------------------------|-------------------|
| Sex ratio (male/female)             | 5/2               |
| Age (years)                        | 23.6 ± 6.8 (15-34) |
| Age at onset of illness (years)    | 21.9 ± 7.1 (15-33) |
| Duration of the untreated psychotic episode prior to the first administration of neuroleptics (months) | 4.3 ± 3.6 (1-12) |
| Duration of the psychotic episode prior to the first acute ECT (months) | 18.1 ± 17.9 (4-48) |
| Neuroleptic dosage before the first acute ECT | Dose (CPZ-equivalence, mg) | 1,032.9 ± 434.8 (400-1,750) |
| Medication resistance              | 5/7 (71.4%)       |
| Dose in medication-resistant cases (CPZ-equivalence, mg) | 1,126.0 ± 407.0 (630-1,750) |
| Family history of schizophrenia (first-degree relative) | 0/7 (0%) |

* Mean ± s.d. (range) values are shown unless otherwise indicated.
CPZ, chlorpromazine.
### TABLE 2. Clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
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<tbody>
<tr>
<td><strong>Age (years)/Sex</strong></td>
<td>26/Male</td>
<td>30/Female</td>
<td>34/Male</td>
</tr>
<tr>
<td><strong>Age at onset of illness (years)</strong></td>
<td>25</td>
<td>29</td>
<td>33</td>
</tr>
<tr>
<td><strong>Duration of the psychotic episode prior to the first neuroleptic medication (months)</strong></td>
<td>3</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td><strong>Duration of the psychotic episode prior to the first acute ECT course (months)</strong></td>
<td>4</td>
<td>5</td>
<td>16</td>
</tr>
<tr>
<td><strong>DSM-IV diagnosis at the first acute ECT course</strong></td>
<td>Schizophreniform disorder</td>
<td>Schizophreniform disorder</td>
<td>Schizophrenia, paranoid type</td>
</tr>
<tr>
<td><strong>Neuroleptics before the first acute ECT course</strong></td>
<td>Haloperidol 10.5 mg and levomepromazine 105 mg</td>
<td>Olanzapine 20 mg and levomepromazine 200 mg, haloperidol 4.5 mg, risperidone 2 mg</td>
<td>Olanzapine 20 mg and levomepromazine 150 mg, risperidone 12 mg and levomepromazine 200 mg</td>
</tr>
<tr>
<td><strong>Main psychiatric symptoms</strong></td>
<td>Severe auditory hallucinations, delusions of persecution, control, and grandeur</td>
<td>Severe auditory hallucinations, delusions of persecution, suicide attempt, refusal to eat</td>
<td>Severe auditory hallucinations, delusions of reference and persecution, agitation, suicidal thoughts</td>
</tr>
<tr>
<td><strong>EEG findings just before the first acute ECT course</strong></td>
<td>Slight diffuse slowing</td>
<td>Within normal limits</td>
<td>Within normal limits</td>
</tr>
<tr>
<td><strong>MMSE score just before the first acute ECT course</strong></td>
<td>26</td>
<td>Could not take MMSE</td>
<td>30</td>
</tr>
<tr>
<td><strong>Reason for acute ECT</strong></td>
<td>Medication resistance</td>
<td>High risk of suicide</td>
<td>Medication resistance</td>
</tr>
<tr>
<td><strong>Total number of ECT sessions</strong></td>
<td>12</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td><strong>Neuroleptics combined with the acute ECT course</strong></td>
<td>Haloperidol 10.5 mg, levomepromazine 50 mg</td>
<td>Levomepromazine 100 mg, Olanzapine 20 mg</td>
<td>None</td>
</tr>
<tr>
<td><strong>Residual symptoms after the first acute ECT course</strong></td>
<td>Slight aspontaneity</td>
<td>Auditory hallucinations, delusions of persecution</td>
<td>Anxiety</td>
</tr>
<tr>
<td><strong>EEG findings 2 weeks after the first acute ECT course</strong></td>
<td>Moderate slowing, small sharp spikes</td>
<td>No data</td>
<td>Slight slowing</td>
</tr>
<tr>
<td><strong>MMSE score 2 weeks after first acute ECT course</strong></td>
<td>26</td>
<td>22.5</td>
<td>30</td>
</tr>
</tbody>
</table>

EEG, electroencephalography; MMSE, mini mental state examination.
of each patient in the study.

<table>
<thead>
<tr>
<th>Patient</th>
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<tr>
<td>4</td>
<td>4</td>
<td>1</td>
<td>2</td>
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Schizophrenia, disorganized type

Olanzapine 20 mg
Perospirone 32 mg, olanzapine 15 mg, quetiapine 450 mg
Haloperidol 20 mg and levomepromazine 300 mg and propericiazine 90 mg
Risperidone 6 mg and sultopride 600 mg and levomepromazine 150 mg, olanzapine 10 mg, olanzapine 15 mg, bromoperidol 3 mg and sultopride 300 mg and risperidone 3 mg levomepromazine 100 mg

Blocking, mutism, stereotypy, delusional ideas, aspontaneity, blunted affect
Severe auditory hallucinations, delusions of reference and persecution, stereotypy, catatopsis, staring, akinesia, blunted affect, negativisms
Auditory hallucinations, delusions of reference, and persecution, aspontaneity
Auditory hallucinations, delusions of persecution, aspontaneity, blunted affect

Within normal limits
Within normal limits
No data
Slight slowing

Could not take MMSE
Could not take MMSE
Could not take MMSE
20

Medication resistance
Catatonic substupor
Medication resistance
Medication resistance

12
20
10
10

None
Risperidone 5 mg
Haloperidol 10 mg, levomepromazine 50 mg
Quetiapine 200 mg, levomepromazine 50 mg

Slight blocking, aspontaneity, blunted affect
Moderate auditory hallucinations, delusions of persecution, aspontaneity, blunted affect
Slight blunted affect, aspontaneity
Slight blunted affect

Slight slowing
Moderate slowing
No data
Slight slowing

Could not take MMSE
Refused to take MMSE
No data
30

EEG, electroencephalography; MMSE, mini mental state examination.
scores obtained before therapy and those obtained 1 week after the ECT course were analyzed statistically with the Wilcoxon signed-rank test. Comparisons were of total BPRS scores, Guy’s five factors, and GAF scores. A p value of < 0.05 was accepted as statistically significant. The analyses were performed with STATISICA version 5.5 for Windows.

RESULTS

All seven patients completed the study. The mean number of ECT sessions was 11.3 ± 4.3 (range, 7-20 sessions). Three patients (patients 1, 2, and 6) were treated with the CS-1 apparatus and four (patients 3, 4, 5, and 7) with the Thymatron System IV brief-pulse square-wave apparatus. The mean duration of electroencephalographic cerebral seizures was 67.4 ± 37.0 seconds (range, 20-204 seconds). The mean initial and maximal stimulus charges used in the four patients treated with the Thymatron System IV apparatus were 68.9 ± 37.5 milliCoulomb (mC) (range, 25.1-100.4 mC) and 175.7 ± 93.1 mC (range, 75.3-301.2 mC), respectively.

The total BPRS score at the end of the ECT course and that 1 week after the final session improved significantly in comparison to the total pre-ECT BPRS score (10.7 ± 6.6 at the end of the ECT course and 10.1 ± 7.9 1 week after the final session versus 44.4 ± 5.3 just before ECT, respectively; Z = 2.37, p = 0.018; Z = 2.37, p = 0.018). The GAF score also improved significantly (from 18.6 ± 9.0 just before ECT to 54.3 ± 23.7 1 week after ECT; Z = 2.37, p = 0.018). All seven patients were considered ECT responders (Fig. 1); thus, the ECT response rate was 100%. Three of the seven patients responded completely (total BPRS score < 5). All five factors (thought disturbance, activation, anxiety-depression, hostility-suspiciousness, and anergia) improved significantly (p = 0.018, p = 0.018, p = 0.018, p = 0.018, and p = 0.028, respectively) (Table 3).

The MMSE score did not decrease after the acute ECT course in any of the five examined patients (Table 2). After several ECT sessions, two (patients 2 and 3) of the seven patients (28.6%) exhibited mild to moderate delirium that disappeared within 1 hour. Slight to moderate slowing was recorded on the electroencephalograms (EEGs) of the five patients after the acute ECT course (Table 2). No patient exhibited epileptic discharge on the EEG after the acute ECT course (Table 2). No patient experienced any other adverse cognitive or physical effect during the course of acute ECT.

DISCUSSION

We studied the short-term effects and safety of acute ECT in young adults with first-episode schizophrenia or schizophreniform disorder. Both psychiatric symptoms and global functioning of
these patients improved significantly with administration of acute ECT combined with neuroleptics. All seven patients responded to the acute ECT course. There were no marked adverse cognitive, physical, or electroencephalographic effects due to ECT. Thus, acute ECT may be effective and safe for young patients with medically intractable first-episode schizophrenia.

Recently, Ucok and Cakr (2006) reported a good short-term effect of ECT vs neuroleptics in 13 patients with first-episode schizophrenia. Our study subjects differed from theirs in three ways. First, duration of the psychotic episode prior to the first acute ECT in our patients appeared to be longer than that reported by Ucok and Cakr (2006). Second, there were fewer patients with catatonic type schizophrenia in our study. Third, there were more patients with medication-resistant schizophrenia in our study. All three of these factors are predictors of a poor response to acute ECT (Dodwell and Goldberg 1989; Chanpattana and Chakraband 2001; Weiner 2001; Abrams 2002; Suzuki et al. 2003). However, the favorable result of our study accorded well with that of the Ucok and Cakr study. One full trial of ECT appears to be warranted for patients with first-episode schizophrenia even if factors predictive of a poor response to acute ECT are present.

Our finding that ECT may be effective for first-episode schizophrenia suggests that ECT should be considered a treatment option for first-episode schizophrenia. The rationale is as follows: First, ECT is more effective for acute schizophrenia than for chronic schizophrenia (Dodwell and Goldberg 1989; Krueger and Sackeim 1995; Chanpattana and Chakrabhand 2001; Abrams 2002). It may be helpful to administer ECT before the illness becomes chronic. Second, young adults are in particular need of a rapid and definitive resolution of schizophrenia. Young adulthood is a critical time for development of a balanced personality. Persistent, severe psychiatric symptoms stunt development, leading to an inability to maintain good social relationships and to stigmatization. Third, the clinical picture in first-episode psychosis is often elusive (Fennig et al. 1994). It is sometimes difficult to distinguish schizophrenia from affective disorder. When affective disorder is mistaken for schizophrenia, administration of potent neuroleptics can

Fig. 1. Total brief psychiatric rating scale (BPRS) scores before and after the first acute ECT course (n = 7).
cause severe side effects. However, ECT is efficacious and safe in patients with either disorder (Weiner 2001; Abrams 2002). Further studies in large numbers of patients are needed to establish the efficacy and safety of ECT for first-episode schizophrenia. In addition, further studies pertaining to long-term outcome of the use of ECT for first-episode schizophrenia are needed.

Our study was limited by our partial use of the sine-wave ECT apparatus, the small number of subjects, and the fact that it was naturalistic. However, it was a prospective study of the efficacy and safety of ECT in young adults with medically intractable first-episode schizophrenia. We conclude that ECT may be an effective and safe treatment option for such patients. Further systematic studies on a large scale are warranted.

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References


