Effects of Twice- *Versus* Thrice-weekly Electroconvulsive Therapy in Schizophrenia†

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Abstract

Electroconvulsive therapy (ECT) has been used to treat a variety of psychiatric disorders since 1938. In clinical practice, a schedule of administration varies greatly and definitive guidelines are not available. The disparity of treatment schedules may influence the rate of response and the duration of morbidity and hospital stay, as well as cognitive adverse effects. The authors conducted a retrospective, comparative study of twice-weekly versus thrice-weekly ECT schedules in ECT-responder schizophrenic patients. Forty-three patients received acute treatment with bilateral ECT and flupenthixol (12-24 mg/d). Outcome measures were the Brief Psychiatric Rating Scale, Global Assessment of Functioning, and the Mini-Mental-State Exam.

The thrice-weekly ECT patient group (N = 21) had shorter duration of morbidity and more rapid response than the twice-weekly ECT patient group (N = 22). Twice-weekly ECT treatment is as equally effective as thrice-weekly schedule regarding the degree of improvement. There were no significant differences in the degree of improvement and the cognitive impairment at the end of the study.

Key word : ECT, Schizophrenia, Comparative Study, Twice-weekly ECT Treatment, Thrice-weekly ECT Treatment

Although electroconvulsive therapy (ECT) has been used to treat a variety of psychiatric disorders for almost 60 years[1], an optimum schedule of administration has yet to be defined[2,3]. As mentioned by The American Psychiatric Association (APA) Task Force on ECT (1990) and The Royal College of Psychiatrists' special committee on ECT (1995), clinical practice with regard to a schedule of

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administration of acute treatment varies widely and definitive guidelines are not available. Approximately 82 per cent of the American psychiatrists preferred a thrice-weekly schedule[4], whereas 80 per cent of the British psychiatrists employed twice-weekly ECT treatment[5]. In Thailand, almost all psychiatrists use a thrice-weekly schedule[6].

Although studies on electrode placement, stimulus waveform, and stimulus intensity dosing demonstrate significant effects on the therapeutic and cognitive effect of ECT[7-14], the disparity of ECT treatment schedules may have a role in clinical practice. ECT schedule may influence rate of response and duration of morbidity and hospital stay [15]. The spacing of treatment and number of ECT sessions may also increase cognitive effect, which is an important adverse effect of ECT administration[16-18]. Unfortunately, previous studies on comparison of ECT treatment schedules were done only in depressive patients[19-23].

Stromgren et al[19,20] compared depressive patients who were treated with unilateral ECT twice (N = 52) or four times (N = 52) weekly. The latter group had a tendency to have better response during the first six treatments. There was no difference in cognitive impairment. McAllister et al[21] conducted a prospective, single-blind, comparative study, using unilateral ECT in patients with major depression. Both the twice- (N = 10) and thrice- (N = 10) weekly ECT groups had no difference in clinical outcome measures at the second and fourth weeks of treatments. There was a significantly greater impairment of visual memory in the thrice-weekly group. Kellner et al[22] compared thrice-weekly (N = 7), bilateral ECT with once-weekly (N = 8) treatment in elderly patients. Although depression improved significantly in both groups, a significant advantage was found in the thrice-weekly schedule both in outcome and in rate of response. Lerer et al[23] randomly assigned patients with major depressive disorder to a double-blind comparison of twice- (plus one simulated ECT, N = 23) or thrice-weekly (N = 24) bilateral ECT during the four-week period of study. There was no difference in clinical outcome of both patient groups either 1 week or 1 month after the end of the ECT series. However, the rate of response to thrice-weekly ECT was significantly faster, and cognitive effects were more prominent with this patient group.

There has been no ECT study comparing the effect of different treatment schedules done in schizophrenic patients. The authors conducted a retrospective, comparative study of twice- versus thrice-weekly treatment schedule in schizophrenic patients to examine whether the results could be comparable to the studies done in depressive patients.

METHOD

All patients were part of our project on ECT research in treatment-resistant schizophrenia[24-26]. Forty three from a total of 99 ECT-responder patients, matched for age, sex, and illness duration; were drawn to compare the effect of different treatment schedules. Twenty two schizophrenic patients received a twice-weekly ECT treatment in Srithunya Hospital, whereas, 21 had thrice-weekly treatment in Vajira Hospital. Acute treatments assigned to both centers were conducted by the first author. Flupenthixol (12-24 mg/day) was prescribed to each patient just before the first ECT treatments were started. The neuroleptics prescribed prior to entering the study were immediately discontinued and there was no wash-out period. The ECT devices were MECTA SR1 and Thymatron DGx. Diazepam (up to 20 mg/day) was prescribed to control agitation on a PRN basis. Thiopental (2-4 mg/kg) was used as the lowest dosage to induce anesthesia. Ketamine (1 mg/kg) was used as a replacement in patients in whom seizure duration was shorter than 30 seconds at the maximal charge settings of the ECT device. Succinylcholine (0.5-1 mg/kg) served as the muscle relaxant. The traditional bilateral electrode placement was used throughout. In each treatment one adequate seizure was required. An adequate seizure was defined as a tonic-clonic convulsion occurring bilaterally for at least 30 seconds, plus electroencephalogram (EEG) evidence of a cerebral seizure. The electrical dosing schedule suggested by Duke University for the Mecta SR1 and Thymatron DGx was used[27] in both centers.

The criterion for clinical response corresponded to a BPRS score of 25 or less, as described elsewhere[28]. The patients who manifested this level of clinical improvement, went on to a 3-week stabilization period[29,30]. The stabilization period comprised the following treatment schedule : 3 regular ECT treatments (2 ECT/week in one group, and 3 ECT/week in another), then once a week for 2 consecutive weeks (during which BPRS scores of $\leq$ 25 had to be consistently achieved). If BPRS scores rose above 25 at any time during this period,

and the total number of ECT treatments was less than 20, patients returned to regular ECT treatments and repeated the above schedule again. ECT responders were patients who completed the 3-week stabilization period, during which, the BPRS score assessed before each treatment was always $\leq$ 25.

Measures used to assess study outcome were : 1) BPRS assessed before each treatment, during the acute and stabilization periods, and end of the study (1 week after the last treatment); 2) Global Assessment of Functioning (GAF) assessed before each acute treatment, and at the end of the study; 3) the Mini-Mental-State Exam [MMSE, Thai version,[31]] assessed at the same time as the BPRS. Three psychiatric nurses served as raters, they were neither otherwise involved in any part of the treatment nor aware of the existence of this study. Each patient was rated by the same nurse. These raters underwent training for 12-24 months. An inter-rater reliability test between these 3 raters yielded a good correlation (r = 0.93).

The results are expressed as means $\pm$ SD. For discontinuous data, chi-square tests were used to test for significant differences between groups. When the sample size was small, the Fisher's two-tailed exact test was used. Pair-wise differences between groups on continuous variables were evaluated with *t*-tests.

The speed of response of the two treatment schedules was determined by the Kaplan-Meier cumulative survival function[32]. The generally accepted statistic for this comparison is the logrank test [Mantel-Haenszel test[33]].

RESULTS

Twenty one schizophrenic patients received thrice-weekly ECT treatment, and 22 underwent twice-weekly ECT treatment. Table 1 presents demographic and clinical features as a function of treatment condition. Independent *t*-tests and chi-square tests revealed no differences between both groups.

Table 2 shows the clinical data. There was no difference in any of the variables between the two treatment groups, except for the duration of acute ECT treatment. The thrice-weekly ECT group had significantly shorter duration of treatment (35.4 $\pm$ 10.2 days, range : 24-61 days), compared to the twice-weekly ECT group (53.8 $\pm$ 17.3 days, range : 30-84; F = 6.94, df = 41,34, p = 0.01). The parametric regression analysis of the treatment time data yielded the main effect of treatment condition, χ^2 = 6.6, p = 0.04. In the nonparametric analysis, a significant effect of treatment condition was also obtained, logrank χ^2 = 7.2, p = 0.02. The thrice-weekly ECT group had a more rapid clinical res-

Table 1. Demographics and clinical characteristics.

Variable	Thrice-weekly group (N = 21) mean $\pm$ SD (range)	Twice-weekly group (N = 22) mean $\pm$ SD (range)
Age (yr)	29.4 $\pm$ 6.3 (20-40)	31.4 $\pm$ 7.4 (21-48)
Sex	11 female, 10 male	10 female, 12 male
Education (yr)	9.8 $\pm$ 3.4 (4-16)	9.5 $\pm$ 3.2 (5-16)
Subtype*	15P (71.4%), 4D, 2C	17P (77.3%), 3D, 2U
Onset of illness (yr)	21.3 $\pm$ 4.5 (16-32)	20.8 $\pm$ 5.5 (15-35)
Duration of illness (yr)	8.2 $\pm$ 4.5 (3-19)	10.5 $\pm$ 4.1 (3-18)
Duration of current episode (yr)	1.2 $\pm$ 1.4 (1mo-5yr)	1.4 $\pm$ 1.2 (2mo-4yr)
Prior psychiatric admissions	4.5 $\pm$ 3.7 (0-15)	5.4 $\pm$ 4.1 (2-15)
Prior failure of adequate NT trials	2.9 $\pm$ 1.1 (2-6)	3.0 $\pm$ 1.2 (2-5)
Ave.duration of each NT trial (mo)	10 $\pm$ 8.3 (2.5mo-3yr)	12.4 $\pm$ 9.6 (3mo-3.5yr)
Mean CPZ equivalent dose (mg)	1,123 $\pm$ 240 (825-1,800)	1,260 $\pm$ 283 (800-1,950)
Prior failure of flupenthixol	43 %	31.8 %
BPRS at entry	49.9 $\pm$ 10.8 (37-67)	51.2 $\pm$ 9.2 (37-66)
MMSE at entry	25.9 $\pm$ 2.8 (20-30)	25.3 $\pm$ 3.2 (20-30)
GAF at entry	32.4 $\pm$ 5.2 (22-45)	30.4 $\pm$ 5.6 (22-45)

* subtype : P - paranoid, D - disorganized, C - catatonia, U - undifferentiated
Other abbreviations : NT - neuroleptic, CPZ - chlorpromazine

Table 2. Treatment results.

Variable	Thrice-weekly group (N = 21) mean ± SD (range)	Twice-weekly group (N = 22) mean ± SD (range)
Status	17 inpatients, 4 outpatients	20 inpatients, 2 outpatients
BPRS at the end of study (1 week after the last ECT treatment)	16.8 ± 7.2 (6-27)	19.3 ± 6.7 (3-33)
% of reductions of BPRS scores	63.9 ± 18 (27-90 %)	61.8 ± 14.2 (34-91.9%)
MMSE at the end of study	28.5 ± 2.1 (23-30)	27.8 ± 3.1 (23-30)
% of increments of MMSE scores	10.9 ± 13 (50-6.7% decrease)	11 ± 13.1 (40-13% decrease)
GAF at the end of study	50.6 ± 11.2 (30-65)	50.4 ± 8.5 (36-62)
Dosage of flupenthixol (mg)	18.5 ± 5.1 (9-24)	21 ± 4.4 (12-24)
Number of ECT treatments	13.6 ± 5.2 (7-25)	15 ± 5.1 (8-25)
Duration of ECT treatments (days)*	35.4 ± 10.2 (24-61)	53.8 ± 17.3 (30-84)
Seizure duration (per ECT session)		
- motor (sec)	38.2 ± 12.1 (21-67)	41.8 ± 9.4 (28-62)
- EEG (sec)	40.4 ± 9.8 (28-64)	54.5 ± 14.3 (33-70)
Ave. stimulus charge (mC, per ECT session)	220.6 ± 139.5 (48-526)	221.7 ± 90 (92-441)
Anesthetics & muscle relaxants (per ECT session)		
- Thiopental (mg)	138.1 ± 34.9 (75-250)	161.1 ± 25.2 (119-202)
- Ketamine (mg)	47.1 ± 4.9 (40-50)	52.5 ± 8.6 (50-68.2)
- Succinylcholine (mg)	27.7 ± 8.1 (12.5-37.5)	24.4 ± 6.4 (12.5-47.5)

* p = 0.01

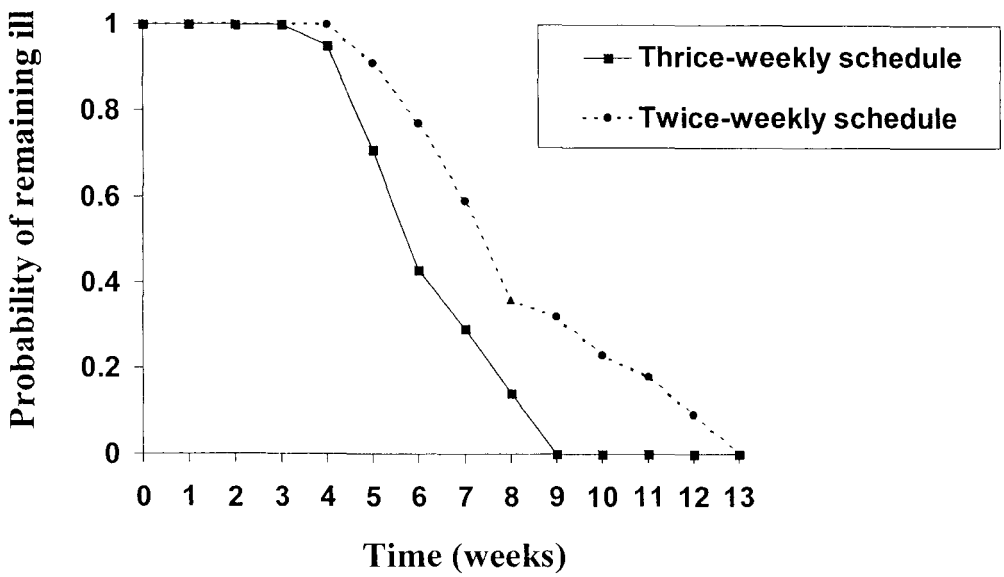

Fig. 1. The survival curve of the two treatment schedules.

ponse. Fig. 1 presents the Kaplan-Meier cumulative survival plot for the two treatment schedules. It is evident that by the fourth week, the survival function for thrice-weekly ECT group begins to diverge from the twice-weekly ECT group.

DISCUSSION

This is the first ECT study in the English language literature conducted in schizophrenic patients, comparing the effect of different treatment schedules. The purpose of this study was to examine

which of the two commonly used schedules of ECT administration is optimum for clinical practice. The results show that both the twice-weekly and thrice-weekly ECT patient groups improved, and there were no differences in clinical outcome at the end of the treatment course. This is parallel with the results reported in depressive patients(21,23,34).

Although treatment outcome was almost the same, rate of response was more rapid in the thrice-weekly ECT group. Therefore, increasing the frequency of ECT administration may accelerate the antipsychotic effect of the treatment. This finding is also similar to previous studies done in depressive patients(19,20,22,23).

Since schizophrenic patients respond to ECT treatment much less favorably than depressive patients, comparisons of speed of recovery in the different treatment schedules must be restricted to the patients who actually respond(35-37). All the patients in this study were ECT responders whom were evaluated by the same criteria(24-26,28-30).

Effects on cognitive functions are an important factor in considering which of the two schedules is optimum for clinical practice. Evaluation should be done for both acute and chronic effects of ECT treatment. Although there is no consensus on recommendations for a suitable cognitive test(29, 38,39), some cognitive batterries have occasionally been used in this regard(40-44). MMSE is too crude to assess the cognitive impairment. It was used in our studies because it is the only cognitive test translated into the Thai language, and, MMSE is more comfortable to use in a study which contains a large number of patients.

Since this study is a part of the acute treatment phase of our ongoing ECT studies of schizophrenic patients, the scientific merit is limited by the retrospective nature of the study. There should be a controlled, random-assignment, double-blind comparison of twice- and thrice-weekly schedules of ECT administration; with the use of comprehensive cognitive batteries in assessment of the adverse effect.

In summary, the twice- and thrice-weekly ECT treatments were equally effective in acute treatment of the schizophrenic patients. The thrice-weekly schedule had a more rapid rate of response.

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การเปรียบเทียบผลของการรักษาด้วยไฟฟ้าสัปดาห์ละ 2 ครั้งและ 3 ครั้งในโรคจิตเภท†

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การรักษาด้วยไฟฟ้าถูกนำมาใช้ในการรักษาโรคจิตเวชหลายชนิด ในทางปฏิบัติมีการใช้การรักษาในความถี่ที่แตกต่างกันได้มากและไม่มีผู้ใดให้แนวทางการให้การรักษาที่ชัดเจน ความแตกต่างนี้อาจมีผลต่อระยะเวลาของการตอบสนอง ระยะเวลาของการป่วย และผลข้างเคียงต่อการทำงานของสมอง คณะผู้วิจัยทำการศึกษาแบบย้อนหลังเพื่อเปรียบเทียบผลของการรักษาด้วยไฟฟ้าสัปดาห์ละ 2 ครั้ง (22 คน) กับสัปดาห์ละ 3 ครั้ง (21 คน)ในผู้ป่วยโรคจิตเภทที่มีการตอบสนองดีต่อการรักษาด้วยไฟฟ้า ผลการรักษาประเมินจาก Brief Psychiatric Rating Scale, Global Assessment of Functioning, และ Mini-Mental-State Exam

การรักษาด้วยไฟฟ้าสัปดาห์ละ 3 ครั้ง ได้ผลการรักษารวดเร็วกว่าสัปดาห์ละ 2 ครั้ง การรักษาด้วยไฟฟ้าทั้ง 2 แบบ ได้ผลการรักษาดีเท่ากันและไม่มีความแตกต่างในผลข้างเคียงของการรักษา

คำสำคัญ : การรักษาด้วยไฟฟ้า, โรคจิตเภท, การรักษาสัปดาห์ละ 2 ครั้ง และ 3 ครั้ง, การศึกษาเปรียบเทียบ

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