Maintenance ECT in Schizophrenia : A Pilot Study†

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Abstract

Maintenance electroconvulsive therapy (M-ECT) has been used to control schizophrenic patients for more than 50 years. In spite of this, there has been no prospective study made of this treatment. Most of the available information comprises naturalistic studies or case reports. As a result many unanswered questions concerning M-ECT remain, including its therapeutic efficacy. This pilot study was done prospectively on 11 schizophrenic patients suffering acute exacerbations, in order to determine the merits of M-ECT. After acute treatment, using only ECT, in 16 patients, 11 were able to pass the 3-week-stabilization-period. They were identified as ECT responders and enrolled into the M-ECT study. M-ECT was started one week after the last treatment in the stabilization period using a tapering regimen, fixed interval schedule, beginning with weekly intervals for 1 month (4 treatments), then biweekly intervals for 2 months (4 treatments) and with monthly intervals thereafter. No neuroleptic drugs were used. Benzodiazepines were the only medications prescribed to control agitation on a prn basis. The duration of the study was one year. Bilateral ECT was used throughout the study. Global Assessment of Functioning (GAF), Brief Psychiatric Rating Scale (BPRS) and the Thai Mental State Exam (TMSE) were used to measure the outcome. A total of 8 patients completed the study or stayed until relapse and 3 dropped out. At the 6-month-evaluation there were no relapses. After this, however, 5 patients suferred relapses. Only 3 could complete the one year study. There were no serious side effects. This study indicates that M-ECT may have a role in the maintenance of some schizophrenic patients. Further studies are needed to determine the optimum frequency and the role of concurrent neuroleptic use.

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Seeking a more effective treatment for schizophrenia has always been a focus of interest and a great challenge for many psychiatrists. Both chemically induced convulsive therapy, in 1934 by Meduna, and electrically induced convulsive therapy (ECT), by Cerletti and Bini in 1938, were chosen respectively as their first treatments for schizophrenic patients[1]. Since then, ECT has gained popularity in treating schizophrenia and various other kinds of psychiatric illnesses. Neuroleptic drugs rapidly replaced ECT since their introduction in the 1950s. During the 1970s, when limitations on their efficacy in treating schizophrenia and some adverse effects from prolonged use were recognized, the interest in ECT as a treatment for therapy resistant patients returned[2].

The use of maintenance ECT (M-ECT) as a treatment for schizophrenic patients was reported by Moore and Kalinowsky in 1943[3]. This treatment was the most important tool for controlling these patients during that time. Despite its widespread use by many psychiatric practitioners, there has never been a prospective study made of this treatment. Most of the available information comprises naturalistic studies or case reports. As a result many unanswered questions concerning M-ECT remain, including its therapeutic efficacy in treating schizophrenic patients. All M-ECT studies used poor research methodology; all used wide varieties of treatment frequencies and techniques with many variations in medical use; or were done in heterogeneous diagnostic groups. The treatment outcome was only considered by the relapse rate or by numbers and duration of hospitalizations[3,4]. The American Psychiatric Association (APA) Task Force on ECT[5] proposed guidelines for patient selection to C-ECT & M-ECT programs. They recommended that this treatment should be given exclusively to patients with a history of recurrent illness that is acutely responsive to ECT, and have demonstrated a refractoriness or intolerance to pharmacotherapy alone, or who preferred C-ECT & M-ECT. Also the patients must be willing and able to receive this treatment.

Although all the literature points to the apparent benefits of this intervention, there has never been a prospective study to document the therapeutic efficacy of M-ECT in schizophrenia. This pilot study was conducted prospectively to determine the merits of M-ECT in treating schizophrenia in order to find better techniques for use in future M-ECT research.

METHOD

During an 11-month period from July 1st, 1994 to May 31st, 1995; 30 patients were treated with ECT in the psychiatric unit of Vajira Hospital. Of these, sixteen patients met the DSM-III-R criteria[6] of schizophrenia as assessed by the ward staff. Several kinds of neuroleptics were prescribed orally to12 patients, which were discontinued just before the start of the ECT treatments. Four patients did not take any neuroleptics during this episode. All underwent acute treatment (phase I of the study) with ECT alone. The inclusion criteria were :- 1) schizophrenic patients with acute psychotic exacerbation, 2) no prior ECT treatment, 3) age 16-45 years, and, 4) no serious medical conditions as assessed by history, physical examination or by some appropriate laboratory tests e.g. CBC, blood chemistry, electrolytes, chest X-ray and electrocardiographs. Consent was obtained from the patients and/or their guardians. The exclusion criterion was known hypersensitivity to drugs used in modified ECT (thiopental and succinyl choline). Clinical responses were evaluated by ward staff who were not part of this study. The first signs of clinical improvement corresponded to scores on the Brief Psychiatric Rating Scale (BPRS), rating 0-6[7], about 25 as described elsewhere[8]. The patients who showed clinical improvement (and also BPRS $\leq$ 25), went on to pass a 3-week stabilization period during which these effects had to be sustained. The stabilization period comprised the following treatment schedule :- 3 regular ECT (3 treatment/week) in the first week, then once a week for the second and third weeks (during which BPRS scores of $\leq$ 25 must always be achieved). If their BPRS scores rose above 25 any time during this period, and the total number of ECT treatments was less than 20, these patients had to go back to receive regular ECT treatments and repeat the above schedule again. The patients whose BPRS scores were still more than 25, and had already received 20 ECT treatments, were considered ECT nonresponders. The same considerations were also applied to the patients who had never shown significant improvement (and BPRS always more than 25) until their twentieth ECT treatment. The ECT responders were the patients who were able to pass the 3-week stabilization period, during which, the BPRS scores assessed before each treatment were always $\leq$ 25. The BPRS scores of the last treatments in this period were called base-

line BPRS. The same psychiatric nurse was used as a rater throughout phase I and phase II (M-ECT) of the study.

M-ECT was started one week after the last treatment of the stabilization period, on an outpatient basis using a tapering regimen, with a fixed interval schedule. Beginning with weekly intervals for 1 month (4 treatments), then biweekly intervals for 2 months (4 treatments), and finally with monthly intervals for 9 months (9 treatments). The flexibility allowed for the ECT treatment schedule was : within three days for weekly and biweekly schedules, and a maximum of 1 week for the monthly schedule. The patients who came to receive ECT treatment later than this, were considered drop-outs. The duration of the study was 1 year. The ECT device was MECTA-SR 1. No neuroleptics were used in this study. Diazepam was the only medication prescribed to control agitation on a prn basis. Bilateral ECT was used throughout this study starting with acute treatments. Thiopental was used as an anesthetic agent and succinyl choline as a muscle relaxant. In each treatment only one adequate seizure was required. For the purpose of this study, an adequate seizure is a tonic-clonic convulsion occurring bilaterally for at least 30 seconds plus an electroencephalogram (EEG) showing evidence of cerebral seizures. Measurements used for the study outcome were :- 1) Global Assessment of Functioning (GAF) assessed before acute treatment, at baseline, 6 months, and 1 week after the end of study; 2) Brief Psychiatric Rating Scale (BPRS) assessed before acute treatment, weekly during the acute treatments, every treatment during the stabilization period, every M-ECT treatment, and 1 week after the end of study; and 3) the Thai Mental State Exam[9] which is a variation of the Mini-Mental-State Exam, and commonly used in aging and neurological patients, was assessed at the same time as BPRS. The last two measurements were assessed just before each treatment. A relapse was defined as BPRS score 25 plus an increase of at least 50 per cent from the maximum baseline BPRS (the score was also 25). Therefore, the minimum BPRS score considered for relapse was 37, that persisted in two consecutive ratings, three days apart.

Table 1. Demographics and clinical characteristics of phase I study.

Variable	Responders* [N= 8, mean±SD (range)]	Nonresponders (N= 5)	Drop-outs (N= 3)
Age (yr)	25.9 ± 8.1 (22-41)	31.4 ± 3.8 (25-35)	23.3 ± 2.3 (22-26)
Sex	6F, 2M	2F, 3M	1F, 2M
Subtype **	7P, 1D	2D, 3U	2P, 1C
Onset of illness (yr)	23.9 ± 7.9 (15-33)	19.6 ± 4.1 (16-22)	21 (all)
Duration of illness (yr)	5.0 ± 2.7 (1-11)	11.8 ± 4.4 (5-16)	2.3 ± 2.3 (1-5)
Duration of current episode (yr)	0.96 ± 0.8 (0.08-2)	8.0 ± 4.3 (3-14)	0.28 ±0.2 (0.17-0.5)
Prior psychiatric admissions	2.9 ± 3.2 (1-10)	7.0 ± 5.9 (2-14)	3.0 ± 3.5 (1-7)
Prior neuroleptic (NT) trials	3.7 ± 1.3 (1-6)	4.2 ± 3.3 (2-6)	2.0 ± 1.7 (1-4)
Prior failure of adequate NT trials	patient 1 - 4 NTs	patient 1 - 3 NTs	patient 2 - 1 NT
(≥ 800 mg CPZ equiv. dose of	patient 3 - 3	patient 2 - 3	patient 3 - 3
at least 6 weeks)	patient 4 - 4	patient 3 - 6	
	patient 5 - 4	patient 4 - 2	
	patient 8 - 2	patient 5 - 3	
BPRS on admission	46.4 ± 7.1 (37-56)	50.2 ± 3.6 (46-56)	52.0 ± 10.6 (44-64)
TMSE on admission	28.6 ± 2 (25-30)	26.6 ± 3.9 (21-30)	28.3 ± 2.9 (25-30)
GAF on admission	29.6 ± 5.9 (22-38)	30.2 ± 4.8 (25-35)	32.7 ± 4.2 (28-36)
Number of acute ECT treatments	14.9 ± 6.4 (8-23)	21 ± 1.7 (20-24)	10.7 ± 3.4 (9-14)
Seizure duration, motor (s)	40.6 ± 11.4 (27-67)	36.2 ± 8.1 (26-51)	55.7 ± 4.8 (56-61)
Stimulus charge (mC)	110.6 ± 34 (67.2-150)	311.1 ± 108.8 (162-409.6)	140.0 ± 56 (84-196)

* 'ECT responder' is determined by the criteria used in this study

** Subtype : P = paranoid, D = disorganized, U = undifferentiated, C = catatonic

Table 2. Clinical data of phase II study

Variable	Responders* [N=8, mean ± SD (range)]	Drop-outs (N = 3)
BPRS - at entry (baseline)	12.3 ± 4.9 (4-21)	11.7 ± 3.1 (9-15)
- at weekly treatment	8.3 ± 4.8 (3-17)	_
- at biweekly treatment	7.9 ± 5.9 (2-23)	_
- at monthly treatment	7.7 ± 4.5 (2-16)	_
- at 6 months	12.5 ± 11.3 (2-25)	_
- at 1 year	11.0 ± 5.6 (5-16, N=3)	_
TMSE - at entry (baseline)	26.8 ± 5.2 (17-30)	28.7 ± 1.2 (28-30)
- at weekly treatment	29.3 ± 1.3 (25-30)	_
- at biweekly treatment	29.4 ± 1.0 (26-30)	_
- thereafter	30 all	_
GAF - at entry (baseline)	43.9 ± 5.5 (36-52)	47.0 ± 6.2 (42-54)
- at 6 months	52.0 ± 9.5 (42-62)	_
- at 1 year	67.0 ± 11.1 (57-79, N=3)	_
Seizure duration, motor (s)	37.0 ± 7.9 (27-48)	80.3 ± 32.3 (46-110)
Stimulus charge (mC)	230.8 ± 150.5 (105-576)	115.6 ± 94.7 (46-196)

* 'ECT responder' is determined by the criteria used in this study.

RESULTS

Sixteen patients underwent acute ECT treatment. Five patients had BPRS scores of more than 25 in their last ECT treatments, and were considered ECT nonresponders. Eleven patients were able to pass the stabilization period, they were then identified as ECT responders and enrolled into the M-ECT study. Three patients dropped out during the first few months, and giving as their reasons fear of ECT (in 2 patients) and denial of illness (1 patient). These three patients were followed-up to observe for relapse; which ultimately occurred at 3, 5, and 11 months, thereafter. Only 8 patients remained in the study.

Table 1 and 2 show the demographics and clinical characteristics of all 16 patients, which are divided into 3 groups :- ECT responders, nonresponders, and drop-outs. There was a tendency to have some differences between the ECT responders & drop-outs and the nonresponders. The nonresponder group was older (31.4 ± 3.8 yrs, range: 25-35 yrs), had longer duration of illness (11.8 ± 4.4 yrs, range: 5-16 yrs), longer duration of the current episode (8 ± 4.3 yrs, range: 3-14 yrs), more previous psychiatric admissions (7 ± 5.9, range: 2-14), received more ECT treatments (21 ± 1.7, range: 20-24), and more stimulus charge used (311.1 ± 108.8 mC, range: 162-409.6 mC); compared to the responder and drop-out groups (25.9 ± 8.1 & 23.3 ± 2.3 yrs, range: 22-41 & 22-26 yrs; 5 ± 2.7 & 2.3 ± 2.3 yrs, range: 1-11 & 1-5 yrs; 0.96 ± 0.8 & 0.28 ± 0.2 yrs, range: 0.08-2 & 0.17-0.5 yrs; 2.9 ± 3.2 & 3 ± 3.5, range: 1-10 & 1-7; 14.9 ± 6.4 & 10.7 ± 3.4, range: 8-23 & 9-14; and 110.6 ± 34 & 140 ± 56 mC, range: 67.2-150 & 84-196 mC, respectively). The average onset of illness, prior neuroleptic trials, prior failure of adequate neuroleptic trials, motor seizure durations, BPRS on admission, TMSE on admission, and GAF on admission, did not differ from these 3 groups.

At the 6-month evaluation there were no relapses. The average BPRS scores were 12.5 ± 11.3 (range: 2-25) and all patients had TMSE scores of 30 (perfect score). After this 5 patients had relapses; 2 at the eighth month, 2 more at the ninth month and the remaining one at the twelfth month. Changes in BPRS scores throughout the study are shown in Fig. 1 and 2. Only 3 patients were still remaining in the study after 1 year with GAF scores of 79, 65, and 57. There were no significant cognitive side effects as assessed by TMSE.

DISCUSSION

To summarize, ECT was helpful for 11/16 patients and M-ECT for 3/11. This is the first systematic study of M-ECT in schizophrenia and it supports its therapeutic efficacy in some patients. M-ECT is generally chosen for patients

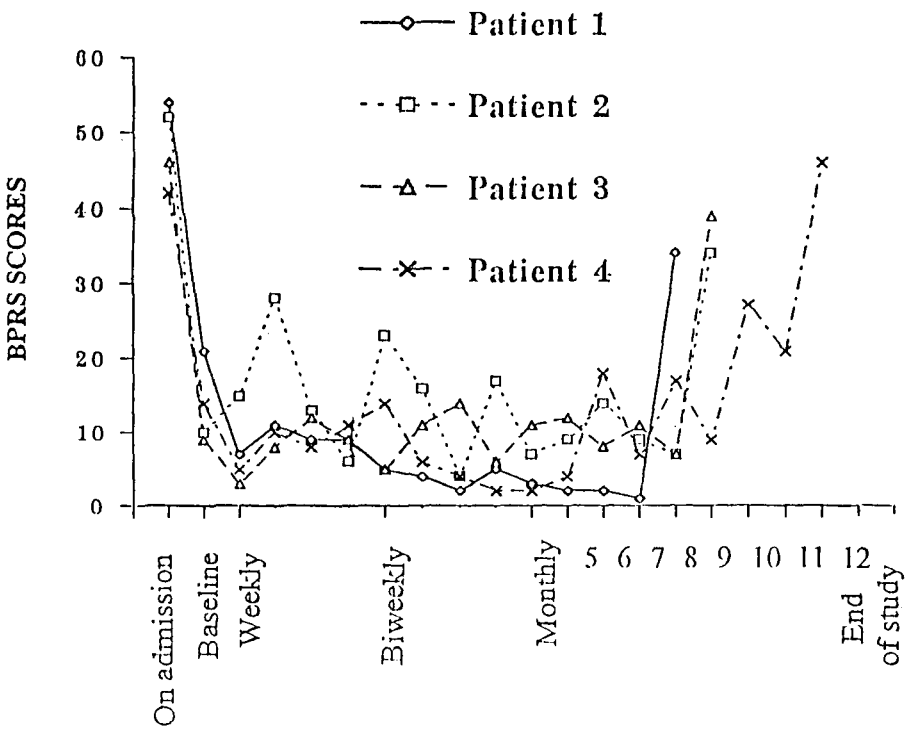

Fig. 1. Changes in Brief Psychiatric Rating Scale (BPRS).

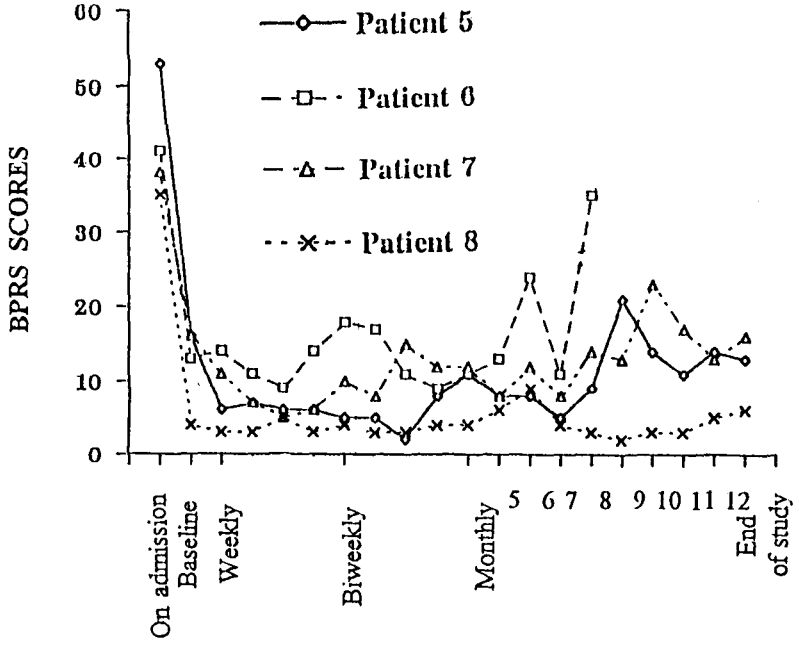

Fig. 2. Changes in Brief Psychiatric Rating Scale (BPRS).

whose course is characterized by multiple hospitalizations and failure to respond adequately to other treatment[5]. The great variability in the utilization of M-ECT may be due to the lack of consensus on indications and doubts about its efficacy[10].

The role of ECT treatment in schizophrenia is controversial and this may account for the paucity of research into both acute and longterm ECT uses. With regard to therapeutic efficacy, the research design should ideally be a double-blind study that compares real M-ECT to sham M-ECT without neuroleptic usage. However, ethical considerations preclude this. The author used an open-trial study of the ECT treatment without neuroleptic drugs as an alternative. This is despite better results being obtained in combined treatment with ECT and neuroleptics[2,11,12].

The 3-week stabilization period was operationally designed to ascertain whether the ECT responders did respond to ECT treatment and whether the effect could be sustained, during this period, in order to obtain an homogeneous group of patients suitable for the M-ECT study. This stabilization period may also serve as another method to justify the number of acute ECT treatments. This is always an important concern when considering the termination of ECT courses[13]. None of the patients in this study had received ECT before and this, could thus eliminate any bias regarding the study outcome. However, the name 'stabilization period' may not be proper, as some patients continued to improve during this period.

Illness duration is an important factor concerning the therapeutic efficacy of ECT treatment. A review of the literature indicates a poor ECT response in patients who have been ill for more than two years[2,11,14]. The average duration of illness, for the responders was 5 $\pm$ 2.7 yrs (range: 1-11), and 2.3 $\pm$ 2.3 yrs (range: 1-5) for the drop-outs. When compared to 11.8 $\pm$ 4.4 yrs (range: 5-16) of the nonresponder group, this confirms the above conclusion. And, it also means that not all chronic schizophrenics have a poor ECT response.

The duration of the current episode also influences the treatment outcome, the shorter the former, the better is the latter[2,12]. In this study, the responder and drop-out groups had a shorter duration in the current episode (0.96 $\pm$ 0.8 yrs, range: 0.08-2; and 0.28 $\pm$ 0.2 yrs, range: 0.17-0.5, respectively) than the nonresponder group (8 $\pm$ 4.3 yrs, range: 3-14).

The total number of acute ECT treatments for each patient is of paramount importance. Every schizophrenic patient should try at least 20 ECT treatments before being considered unresponsive to ECT[2,14]. Some ECT studies which have mentioned very low response rates in chronic schizophrenics have usually tried a lesser number of treatments.

As to the frequency schedule of M-ECT, it is based on clinical judgement and has been used with wide variations. The American Psychiatric Association Task Force on Electroconvulsive therapy (1990) described the most prevalent M-ECT practice in the United States : treatments are started on a weekly basis, with the interval between treatment gradually being extended to a month, depending on the patient's response[5]. Kramer, in his survey of M-ECT[15], found that a monthly interval is most common. The author of this study used a fixed schedule of monthly intervals and this may be responsible for the poorer outcome in this study. Biweekly intervals may have better results[16,17].

Memory impairment is an interesting topic. Every patient in this study subjectively complained of memory loss, at least partially. The cognitive measurement used in this study (TMSE) is too crude and may not be able to detect these subtle defects. Currently there is no consensus on recommendations for a suitable cognitive test, or when the most appropriate time to perform such a test during the ECT course is[18,19]. Future research should be directed towards addressing this problem.

In summary, M-ECT may have a role in the maintenance of some schizophrenic patients. Further studies are needed to determine the optimum frequency and the role of concurrent neuroleptic use. The limitations of this study were the lack of a control group (that could be pharmacotherapy, placebo, or no treatment), and the small numbers. Therefore, this study could not allow firm assessment on the efficacy of M-ECT nor identification of some specific gap of knowledge in the previous studies.

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การรักษาด้วยไฟฟ้าชนิดต่อเนื่องในผู้ป่วยจิตเภท†

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ถึงแม้ว่าการรักษาด้วยไฟฟ้าชนิดต่อเนื่อง (M-ECT) ได้ใช้ในการควบคุมผู้ป่วยจิตเภทมานานกว่า 50 ปี แต่ก็ยังไม่มีเคยมีการศึกษาวิจัยอย่างเป็นระบบ รายงานทั้งหมดที่มีเป็นเพียงรายงานการใช้การรักษาวิธีนี้ในผู้ป่วย จึงยังไม่มีผู้ใดทราบรายละเอียดและประสิทธิภาพของ M-ECT มากนัก รายงานนี้เป็นการศึกษานำร่องชนิด prospective ในผู้ป่วยจิตเภท 16 ราย ซึ่งมีการกำเริบขึ้นของโรคจิตเพื่อศึกษาถึงประสิทธิภาพของ M-ECT หลังการรักษาด้วยไฟฟ้า (ECT) ในระยะแรกโดยไม่ใช้ยารักษาโรคจิต มีผู้ป่วยผ่านตามเกณฑ์ของการคัดเลือก 11 ราย ตลอดช่วงของการรักษา 1 ปีมีเพียงยาไดอะเซแพมที่ใช้ควบคุมอาการหงุดหงิด ผลการรักษาประเมินจาก Global Assessment of Functioning (GAF), Brief Psychiatric Rating Scale (BPRS) และ Thai Mental State Exam (TMSE) มีผู้ป่วยออกจากการศึกษา 3 ราย ในช่วง 6 เดือนแรกอาการของโรคถูกควบคุมได้ดี แต่หลังจากนั้นผู้ป่วย 5 รายมีอาการกำเริบ เหลือผู้ป่วยที่อยู่ในการศึกษาครบ 1 ปี 3 ราย ไม่พบอาการข้างเคียงที่เป็นอันตราย สรุปผลการศึกษาได้ว่า M-ECT อาจมีประสิทธิภาพในการควบคุมการกำเริบของโรคจิตเภท

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