Schizophrenia Research 137 (2012) 97–103

Contents lists available at SciVerse ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Electroconvulsive therapy improves antipsychotic and somnographic responses in adolescents with first-episode psychosis — A case–control study

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ARTICLE INFO

Article history:
Received 17 September 2011
Received in revised form 10 January 2012
Accepted 26 January 2012
Available online 17 February 2012

Keywords:
Electroconvulsive therapy (ECT)
Adolescents
First-episode psychosis
Polysomnography (PSG)

ABSTRACT

Objective: Previous studies have demonstrated the effectiveness of electroconvulsive therapy (ECT) in pharmacotherapy-resistant neuropsychiatric conditions. This study aimed to evaluate the efficacy and safety of ECT in adolescents with first-episode psychosis.

Method: This case–control study was conducted in inpatients aged 13–20 years with first-episode psychosis. Every three similar age and same gender patients consecutively recruited were randomly allocated to control and ECT group at a ratio of 1:2, while they had antipsychotic treatment. ECT treatment was performed for 3 sessions per week with a maximum of 14 sessions. The endpoint was discharge from hospital. Clinical outcomes were measured using hospital stay days, the Positive and Negative Syndrome Scale (PANSS) and response rate. Polysomnography (PSG) was conducted at baseline and at week 2. Safety and tolerability were also evaluated.

Results: Between March 2004 and November 2009, 112 eligible patients were allocated to control ($n=38$) and ECT ($n=74$) group. Additional ECT treatment significantly reduced hospital stay compared to controls (23.2 ± 8.2 days versus 27.3 ± 9.3 days, mean $\pm$ SD, $P=0.018$). Survival analysis revealed that the ECT-treated group had a significantly higher cumulative response rate than controls (74.3% versus 50%, relative risk (RR) $=1.961$, $P=0.001$). Additional ECT also produced significantly greater improvement in sleep efficiency, rapid eye movement (REM) latency and density than control condition. The PSG improvement significantly correlated with reduction in scores on overall PANSS, positive symptoms, and general psychopathology. No patients discontinued ECT treatment regimen during hospital stay. The incidence of most adverse events was not different in the two groups, but ECT-treated group had more complaints of transient headache and dizziness than controls.

Conclusions: ECT is an effective and safe intervention used in adolescents with first-episode psychosis. Its antipsychotic effects are associated with improved PSG variables. ECT can be considered as an early psychosis intervention.

1. Introduction

With the dramatic socioeconomic and demographic transformation of modern life, the prevalence of various mental illnesses has sharply risen in the adolescent population (Srinath et al., 2010). Psychotic disorders are a relatively common psychiatric condition occurred in adolescents, with an estimated prevalence of 0.5% (Remschmidt and Theisen, 2005). Although new generation antipsychotic agents are the mainstay of the treatment of adolescent psychosis, a majority of patients present with moderate to severe impairment at onset, do not obtain full remission from pharmacotherapy, and eventually develop relapse and to follow a chronic course (Fraguas et al., 2011; Masi and Liboni, 2011). Moreover, young patients are more susceptible to the adverse effects of antipsychotics compared to adults (Fraguas et al., 2011). These shortcomings have led to a growing demand for development of alternative strategies to improve antipsychotic response in early psychosis.

Electroconvulsive therapy (ECT) is a well-accepted brain stimulation therapy that has been confirmed to be effective in treating adults with pharmacotherapy-resistant neuropsychiatric conditions (Chakrabarti et al., 2010), including schizophrenia (Tharyan and Adams, 2005). The use of ECT in adolescents was first reported in 1942 (Heuyer and Bour, 1942). Although ECT may be underutilized in adolescents due to ethical concerns and unrealistic fears, a large number of case reports indicate that ECT is an effective and safe procedure in the treatment of adolescents with intractable mood

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doi:10.1016/j.schres.2012.01.037

disorders, catatonia, and schizophrenia (Consoli et al., 2010; Shoirah and Hamoda, 2011). In 2004, the American Academy of Child and Adolescent Psychiatry (AACAP) published practice parameters for the use of ECT in adolescents, defining its indications in terms of diagnosis, severity and refractoriness of symptoms (Ghaziuddin et al., 2004). Despite this, little is known about the clinical efficacy and tolerability of ECT as an early intervention in first-episode young patients.

As a useful electrophysiological measure, polysomnography (PSG) has been widely applied in the investigation of various neuropsychiatric disorders and therapeutic response (Monti and Monti, 2004; Krystal et al., 2008). It has been shown that abnormal PSG manifestation is associated with the psychopathology of schizophrenia and antipsychotic effects are associated with the improvement of abnormal PSG variables (Monti and Monti, 2004).

We therefore have reason to hypothesize that additional ECT could produce more rapid and greater improvement than antipsychotics alone on clinical symptoms and PSG profiles in adolescents with first-episode psychosis. To test this hypothesis, a case–control trial was designed to compare the efficacy, tolerability, and changes in PSG profiles in the patients treated with antipsychotics combined with and without ECT intervention. Polysomnographic correlates of clinical variables were also examined.

2. Methods

2.1. Setting and subjects

This case–control study was conducted in Department of Psychiatry at Xijing Hospital of Fourth Military University in Xi'an of China between March 2004 and November 2009. The study protocol was approved by the Medical Ethical Committee of Xijing Hospital of the Fourth Military Medical University. A detailed and full explanation of the study goal, ECT procedures, and potential side effects was presented to each patient and his/her parents/guardians by psychiatrists. All participants and their guardians gave voluntary, written, informed consent for their acceptance of the study.

The inclusion criteria were: (1) 13–20 years; (2) newly hospitalized for current first-episode psychosis with duration of illness of less than 1 year; (3) Psychotic symptoms comprising delusions, hallucinations, and/or thought disorder scoring 4 or higher on the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) and confirmed using the Structured Clinical Interview for DSM-IV (First et al., 1997); and (4) no previous antipsychotic treatment or less than 1 month antipsychotic treatment. Subjects were excluded if they had: (1) significant cardiovascular, respiratory, epilepsy, or other neurological conditions; (2) a diagnosis of brain tumors or intracranial space-occupying lesions within the previous 12 months; (4) a history of alcohol or substance abuse within the previous 12 months; or (5) received ECT or other brain stimulation therapies within the previous 6 months.

2.2. Group allocation

In order to avoid unequal age and gender distribution potentially caused in full randomization, a combination of match and randomization was applied in group allocation. Every three similar age and same gender patients who were consecutively recruited were randomly assigned by a designated psychiatrist (H.H.W.) to control and ECT group at a ratio of 1:2, using pre-produced random numbers with a block size of 3. For example, the first, fourth, and eighth patients recruited were first three 18-year females and then allocated to ECT, control, and ECT group, respectively, based on the first block of 3 random numbers.

2.3. ECT and antipsychotic treatment

In ECT intervention, patients were required to fast for at least 8 h prior to the procedure. One dose of 0.5 mg atropine was given to inhibit salivation and respiratory tract secretions during ECT. Patients were anesthetized with propofol (1–2 mg/kg). The muscles were relaxed with succinylcholine (1–2 mg/kg), a neuromuscular blockade. Stimulus electrodes were placed on the right temple and the vertex of the scalp. Such placement could minimize amnesia caused by ECT (Nobler and Sackeim, 2008). Stimulus intensity (percentage of energy) was initiated at 5% equivalent to 25 mV with a fixed constant current of 0.9 A, and gradually increased to achieve a seizure discharge lasting at least 20 s on electroencephalogram (EEG), using Thymatron IV machine (Somatics Inc, USA). ECT treatment was conducted three times per week with a maximum of 14 sessions in the course of the study.

After hospitalized, patients of both groups received antipsychotic treatment. Those who had been medicated with antipsychotics for no more than one month at hospitalization continued their medication in designated dosing regimens. Those with no previous antipsychotic treatment when hospitalized received orally administered risperidone, which was initiated at 1 mg/day and escalated to an optimal dose based on individual patients' response, with a maximum dose of 6 mg/day. Combination with other antipsychotic and psychotropic agents was allowed at psychiatrists' discretion based on clinical need. Patients whose medication compliance was less than 80% with the designated schedules were excluded from the analyses.

2.4. Polysomnographic (PSG) examination

Nearly half of patients in both groups were randomly selected for PSG examination. The examination was conducted at baseline and at week 2 when most patients were expected to achieve clinically meaningful outcomes. Overnight PSG was recorded with a PSG device (Model 3000B, Beijing Solar Company, China), consisting of 8-channel electroencephalogram, electrooculogram, submental electromyogram, electrocardiogram, nasal and oral airflow, thoracic and abdominal movements, and oxyhemoglobin saturation. A video camera installed above the bed recorded the patient's position and movement during sleep. The PSG variables, including total sleep time, sleep efficiency, percentage of each sleep stage, rapid eye movement (REM) latency, and REM density, were obtained.

2.5. Clinical assessments

The endpoint of the study was discharge of patients from hospital. The criteria for the discharge were near or complete remission of psychotic symptoms and the restoration of judgment and self-insight in his/her illness, as evidenced by a score of 3 or less on PANSS for delusions (P1), conceptual disorganization (P2), hallucinatory behavior (P3), and lack of judgment and insight (G12) (Schennach-Wolff et al., 2011). Hospital stay days were counted as a clinical outcome variable. The severity of psychotic symptoms was evaluated using changes from baseline in scores on PANSS overall scale and subscales for positive and negative symptoms, and general psychopathology at baseline and once weekly thereafter during hospital stay. The clinical response, defined as a $\geq$30% reduction in score on PANSS overall scale from baseline, was calculated from weekly assessment. The cumulative proportion of patients who had achieved the clinical response was compared over time in the two groups using survival analysis (see below). Safety and tolerability were assessed using the Treatment Emergent Symptom Scale (TESS) (Guy, 1976).

To ensure consistency and reliability of clinical assessments over time, training workshops were conducted in a regular manner to examine and re-examine interrater reliability coefficients (κ value).