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Effectiveness of risperidone long-acting injection in first-episode schizophrenia: In naturalistic setting

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ABSTRACT

Patients with first-episode schizophrenia frequently relapse during the first years of the illness. This may be associated with clinical deterioration. It is important to prevent relapses in first-episode schizophrenia. We examine whether risperidone long-acting injection (RLAI) could effectively act to prevent relapse in first-episode schizophrenia. We conducted a prospective, naturalistic, controlled, and open-label study over 2 years in 50 patients with first-episode schizophrenia. 22 patients with schizophrenia were assigned to the RLAI group and 28 patients with schizophrenia to the oral risperidone group as control. We compared medication adherence, time to non-adherence, and relapse rate between the RLAI and control groups. There were no significant difference in sociodemographic findings and initial psychometric measures between two groups. The RLAI group showed significantly lower relapse rate and higher medication adherence than the control group. The result demonstrated by Kaplan-Meier survival analysis that time to non-adherence is associated with the difference in the groups. Cox proportional survival analysis revealed that time from baseline to relapse was associated with time to non-adherence. This result showed that RLAI could be effective in maintaining medication adherence and preventing relapse. However, studies with a larger sample size will be needed to examine whether these results are applicable to schizophrenic population.

1. Introduction

Schizophrenia is a chronic disorder usually characterized by relapses alternating with periods of full or partial remission. Although antipsychotic medication is effective in reducing relapse rates, 30% to 40% of patients relapse within the year following hospitalization discharge even if they are receiving maintenance medication (Davis, 1975; Hogarty et al., 1979). According to neurodegenerative theory, relapse or recurrence in schizophrenic patients makes their brain structures more neurotoxic. This results in ventricular enlargement, cortical atrophy in brain, longer duration of illness, less effectiveness of the medication, deficient cognitive function, and prominent negative symptoms (Lieberman, 1999).

There has been an effort to identify and intervene early in first-episode schizophrenia to improve the long-term outcome, as most clinical and psychosocial deterioration in schizophrenia occurs within the first 5 years of the onset of the illness (Lieberman et al., 2001). Birchwood et al. (1998) called the early period after onset of schizophrenia the 'critical period' to impact on the long-term outcome. Early intervention is emphasized.

Relapse or recurrence is strongly associated with partial adherence or non-adherence even in first-episode schizophrenia (Coldham et al., 2002; Edwards et al., 2002; Kasper, 1999). Kane (2006) suggested that none of interventions to improve adherence had been completely reliable, but several strategies like long-acting injectable antipsychotics, and 2nd generation oral antipsychotics could improve the medication adherence in schizophrenic patients.

Many advantages of 2nd generation injectable antipsychotics exist because it combines the advantages of both the newer type of medication and the long-acting formulation (Kane, 2003). Reviewers (Kane, 2003; Keith et al., 2004) concluded that long-acting injectable risperidone was efficacious, safe and well-tolerated and every patients should be evaluated for suitability for treatment with long-acting atypical antipsychotics. Long-acting antipsychotics can reduce relapse rate through the increased medication adherence in patients with schizophrenia (Kane, 2006). Therefore, among the many antipsychotic drugs, long-acting injectable atypical antipsychotics can be ideal and suitable drugs for improving the adherence and preventing the relapse or recurrence in patients with first-episode schizophrenia.

However, there has been no evidence or study about the efficacy and tolerability of long-acting injectable antipsychotics in first-episode schizophrenia. Here we examine whether long-acting atypical

Abbreviations: APA, American Psychiatric Association; CGI, Clinical Global Impression; DSM-IV, Diagnostic and Statistical manual of mental disorders; ESRS, Extrapyramidal Symptom Rating Scale; GAF, Global Assessment of Functioning; PANSS, Positive and Negative Symptom Score; RLAI, Risperidone long-acting injection.

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antipsychotics was more effective for maintaining medication adherence and reducing relapse rates than oral risperidone in patients with first-episode schizophrenia.

2. Methods

2.1. Study design and subjects

We conducted naturalistic, controlled, and open-label trial and recruited patients with schizophrenia and enrolled 55 consecutively in this prospective study. Initially 25 patients with schizophrenia were assigned to the risperidone long-acting injection (RLAI) group, 30 patients were treated with oral risperidone as the control group. Of the long-acting injectable atypical antipsychotic drugs, risperidone long-acting injectable (Risperdal Consta®) was chosen as the antipsychotic drug. It was the only long-acting injectable atypical antipsychotic drug available in Korea at the time of the study. We conducted the study at the Department of Psychiatry, Bundang CHA General Hospital, South Korea, between December 2004 and July 2007. The study was conducted in accordance with the Declaration of Helsinki and the principle of Good Clinical Practice. The Bundang CHA Institutional Review Board (Ethics Committee) approved the research. The research outline was explained to potential participants, and only patients and their families who signed an informed consent document were chosen to participate in this study. The participants also had to 1) be between 17 and 60 years of age; 2) be diagnosed with first-episode schizophrenia or schizoaffective disorder based on the Structured Clinical Interview for DSM-IV(SCID), and the clinical interview with patients and their family members about their present illness show reveal no past history of psychiatric treatment, and the starting point of functional impairment (prodrome); 3) have an IQ above 80; and 4) receive treatment of long-acting injectable risperidone or oral risperidone as outpatients. In addition, the subjects had to have been stable for at least 4 weeks in an outpatient setting immediately before the baseline date (Fig. 1). Exclusion criteria were 1) evidence of organic mental disorder or mental retardation and 2) severe drug or alcohol dependence that required inpatient treatment and/or detoxification. Two patients were excluded in this study because of Low IQ (<80). After the termination of this study, three patients were also excluded because they had not visited the hospital regularly within 3 months of the baseline. At the final analysis, 22 schizophrenias remained in RLAI group, 28 schizophrenias remained in the oral risperidone group.

All patients in the RLAI group had been on oral risperidone before starting the RLAI. Unlike others, patients included in the RLAI group were expected to have poor compliance, as well as poor perception of their schizophrenia judging from that the fact they thought that they were mentally well or did not need medication (Drake et al., 2007). The oral risperidone dose in patients in the oral group was flexible below 6 mg. The mean oral risperidone dose in patients in the oral group was 2.79 mg (Mean ± SD = 2.79 ± 0.92). Every visit was scheduled within a month in the oral group. Both groups were permitted individual supportive psychotherapy for less than 15 min. In the RLAI group, patients were instructed to visit the hospital biweekly. The RLAI dose was flexible within 50 mg in the RLAI group. The RLAI dose was 28.98 mg in the RLAI group (Mean ± SD = 28.98 ± 6.00). Concomitant psychotropic medications in this study included benztropine, alprazolam, and propranolol.

2.2. Assessments

All patients were evaluated for drug adherence, relapse or recurrence on every visit to the outpatient clinic. Positive and Negative Symptom Score (PANSS), Global Assessment of Functioning (GAF) and Clinical Global Impression(CGI) of patients were assessed by subject-blinded board certified psychiatrists every 6 months (TK Choi, SY Suh).

The primary outcome measures were as follows.

1) Medication adherence, non-adherence. In the RLAI group, medication adherence was defined as the number of actual visits for injection divided by the number of days patients were scheduled to visit during the study period. In the oral group, medication adherence was defined as the number of actual visits to the outpatient clinic divided by the number of days when patients were scheduled to visit during the study period. In both groups, medication non-adherence was defined as a 1 week drug-free state after the day appointed for patients to receive RLAI or the study discontinuation, if the reason for study discontinuation was refusal to take any antipsychotic (Perkins et al., 2006).

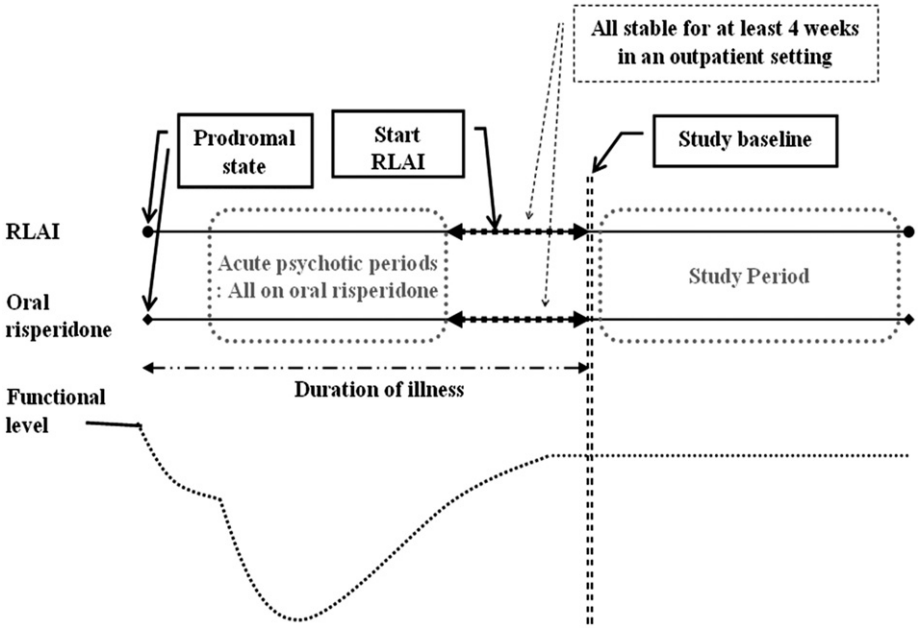

Fig. 1. Study design.