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Short communication

Adjunctive risperidone, olanzapine and quetiapine for the treatment of hospitalized patients with bipolar I disorder: A retrospective study

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Abstract

This study evaluated the overall effectiveness and tolerability of atypical antipsychotics (risperidone vs. olanzapine vs. quetiapine) used in the treatment of bipolar inpatients. After screening 463 patients, the medical records of 158 inpatients with bipolar I disorder, who were given olanzapine, risperidone or quetiapine as adjuncts to mood stabilizers for at least 1 month and not administered with any other antipsychotics, were examined. Details of the tolerability and effectiveness were reviewed according to the treatment records during their hospital stay. The results showed equivalent effectiveness based on the Clinical Global Impression (CGI) and Global Assessment Functioning (GAF) score between the three atypical antipsychotics. The frequency of the extrapyramidal symptom-related side effects were higher in the risperidone-treated group than in the olanzapine and quetiapine-treated group. This suggests that risperidone, olanzapine and quetiapine have a comparable effectiveness in inpatients with bipolar I disorder in a naturalistic setting. However, there were some differences in tolerability between these results as reported from previous Western studies.

Keywords: Bipolar I disorder; Inpatients; Naturalistic study; Olanzapine; Quetiapine; Risperidone

1. Introduction

There are not many therapeutic options for bipolar disorder in real clinical practice. This is despite the availability of mood stabilizers as well as some adjunctives albeit with some limitations (Lieberman and Goodwin, 2004). Typical antipsychotics are commonly given to patients with bipolar disorder in clinical practice (Lieberman and Goodwin, 2004). However, there are some side effects associated with typical antipsychotics such as extrapyramidal symptoms (EPS) and tardive dyskinesia (TD). Elderly patients are particularly sensitive to these side effects due to the pharmacodynamic and pharmacokinetic changes that occur with age (Kane, 1999; Bowden, 2004). It is not unusual for bipolar patients to take 3–4 medications, including several antipsychotics, which might have problems associated with long-term compliance and harmful drug interactions (Zarate, 2000). Atypical antipsychotics such as risperidone, olanzapine and quetiapine have been introduced for the treatment of bipolar disorder. These drugs have been suggested to be effective and tolerable in patients with bipolar disorder with a wide range of applications and variable options (Hirschfeld et al., 2004; Tohen et al., 2000, 2002; Vieta et al., 2004; Sachs et al., 2002, 2004; Bowden et al., 2005; Yatham et al., 2004).

Double blind and placebo-controlled studies are essential for determining the efficacy of any new drug before it can be

Abbreviations: ANOVA, anaysis of variance; CGI, clinical global impression; EPS, extrapyramidal symptom; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, fourth edition; GAF, global assessment of functioning; HAMD, Hamilton Depression Rating Scale; OCG, olazapine combination group; QCG, quetiapine combination group; RCG, risperidone combination group; TD, tardive dyskinesia; YMRS, Young Mania Rating Scale.

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Table 1
Demographic data of the inpatients with bipolar I disorder, who had received adjunctive treatment with risperidone, olanzapine or quetiapine along with mood stabilizers

		RCG (n=61)	OCG (n=51)	QCG (n=46)
Sex	Male	37	30	20
	Female	24	21	26
Duration of admission, days		41.4±10.2	45.9±12.5	43.6±11.2
Number of past admission		2.3±1.2	2.4±1.3	2.0±1.4
Onset age, years		28.9±6.8	29.6±4.7	28.6±4.9
CGI score on admission		5.6±0.9	5.8±0.5	5.7±1.1
GAF score on admission		36.5±3.8	35.4±4.6	35.2±3.3
Current diagnosis	Manic	39	38	29
	Depressive	12	4	10
	Mixed	10	9	7

Values are expressed as the mean±SD or number of subjects. Abbreviations: RCG, risperidone combination group; OCG, olanzapine combination group; QCG, quetiapine combination group; CGI, clinical global impression; GAF, global assessment of functioning.

placed on the market and for providing safety data for clinicians. However, these controlled trials are limited by the selection bias, and other important data in real clinical situations might be overlooked. On the other hand, naturalistic studies provide readily accessible data on the daily clinical application as well as providing information on the off-label/overall use for special populations excluded from the controlled trials. Most important is that a direct comparison of specific drugs is possible in real clinical practice (Chengappa et al., 1999; Miller et al., 2001).

This study examined the effectiveness and tolerability of risperidone, olanzapine and quetipaine as an adjunctive treatment with mood stabilizers in inpatients with bipolar I disorder in a naturalistic setting.

2. Methods

2.1. Subjects

The eligibility criteria for this study are as follows: inpatients diagnosed with bipolar I disorder according to the DSM-IV criteria (American Psychiatric Association, 1994); treated with either olanzapine, risperidone or quetiapine for more than 1 month; and given no other antipsychotics or mood stabilizers. Patients with organic mental disorders, serious medical illness, and major psychiatric comorbidities such as substance abuse were excluded. All psychotropics including risperidone, olanzapine or quetiapine were started and adjusted according to the treating clinician's experience and preference during the patients' admission period. This study examined the medical records of 463 patients with bipolar I disorder, aged between 18 and 65 years, who were consecutively admitted to the Department of Psychiatry at St. Mary's Hospital, College of Medicine, The Catholic University of Korea, between January 1997 and July 2004.

2.2. Procedures

The medical records of the 463 recruited patients were reviewed and evaluated by two board-certified psychiatrists (W. M.B, J.H.C.). According to the selection and exclusion criteria, 158 patients were enrolled in this study. The age, gender, diagnosis, number of past admissions, duration of hospitalization, type of mood stabilizers used, and the initial, maximum and average daily doses of risperidone, olanzapine and quetiapine were evaluated. In order to evaluate the naturalistic effectiveness of the medications, the Clinical Global Impression-severity (CGI, Guy, 1976) and Global Assessment of Functioning (GAF, American Psychiatric Association, 1994) scores on the medical records were re-assessed by one of the authors (C.U.P.) who was not involved in treating the patients based on the medical records. The tolerability of each medication was determined by examining the complete blood count, blood chemistry, urinalysis, the equivalent dose of benztropine for the administered antiparkinsonian drug as an indirect measure of EPS, the frequency of the observed EPS, the equivalent dose of lorazepam, the weight at the time of admission and after 4 weeks of admission. The institutional review board of ethics approved this study.

2.3. Statistical analysis

The data was analyzed using Windows SPSS 10.0 (SPSS Inc., Chicago, USA). Repeated measure of analysis of variance (ANOVA), Wilcoxon signed rank test, χ^2-test (Monte Carlo method was used with small cell counts), and descriptive statistics according to characteristics of the variables and comparisons made. A $p<0.05$ was considered significant.

3. Results

There were 87 males and 71 females. The mean age of the patients in the risperidone combination (RCG), olanzapine

Table 2
Pharmacological data of the inpatients with bipolar I disorder, who had received adjunctive treatment with risperidone, olanzapine or quetiapine along with mood stabilizers

	RCG (n=61)	OCG (n=51)	QCP (n=46)
Dosage (mg/day)			
Starting dose	2.3±0.8	6.6±2.8	212.3±98.7
Mean dose during study	3.3±1.5	11.1±3.7	421.3±179.5
Maximum dose	4.3±1.1	16.7±3.3	624.5±245.9
Benztropine equivalent dose *	1.2±0.6	0.8±0.8	0.7±0.6
Lorazepam equivalent dose	1.1±0.8	0.8±0.5	1.1±0.9
Combination of mood stabilizer			
Lithium	28	20	16
Valproate	27	25	27
Carbamazepine	2	0	0
Lithium+Valproate	3	2	0
Lithium+carbamazepine	1	4	3

Values are expressed as the mean±SD or number of subjects. Abbreviation: RCG, risperidone combination group; OCG, olanzapine combination group; QCG, quetiapine combination group.
*F=8.593, p=0.0003.