

ORIGINAL ARTICLE

Naturalistic study on long term use of Quetiapine as monotherapy in Bipolar mania and mixed episodes

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ABSTRACT

Introduction: The therapeutic approach of bipolar disorders is commonly based on polipharmacotherapy. Lithium and atypical antipsychotics (AA) have been used as standard treatment for therapy and prevention of paroxysmal episodes but a full coverage of responsiveness has not been succeeded. Quetiapine, known as AA, was recently approved in the US for use in bipolar depression, in addition to its previously approved indications of mania associated with bipolar I disorder and schizophrenia.

Aim: To assess the effectiveness and safety of quetiapine as monotherapy in the treatment of manic or mixed episodes in resistant patients to previous mood stabilizers or/and antipsychotic medications.

Methods: Twenty-two young patients with a DSM IV diagnosis of Bipolar I and Bipolar II disorder in current manic or mixed episode were enrolled in the study. They were switched to quetiapine alone from multidrug scheme not adequately controlling the symptoms. Clinical evaluation was done at baseline, 8 and 32 weeks with the Young Mania Rating Scale (Y-MRS), the Clinical Global Impression Scale (CGI) and the Krawiecka Manchester Rating Scale (KMRS).

Results: Significant improvement in KMRS, YMRS, CGI scores was seen ($p < 0,001$). No adjunctive therapy was necessary to control psycho-behavioral symptoms.

Conclusion: This study found that treatment-resistant patients with manic or mixed episode could be safely and effectively switched to quetiapine.

Key words: *Bipolar disorders, antipsychotic agents, quetiapine, safety, manic state.*

INTRODUCTION

The treatment of bipolar disorders often requires a complex medication regimen. Lithium is the cornerstone of maintenance therapy but long-term naturalistic studies show up to 50% of patients are inadequately responsive.^{1,2} Clinicians have long recognized

that most of patients benefit from a combination of medications, rather than monotherapy, during different phases of the disorder including anticonvulsants, antidepressants and antipsychotic agents. Despite the careful use of polipharmacotherapy, a suboptimal response and the risk of additional drug-related problems can result.

Atypical antipsychotics (AA) have been shown to be effective either as combination therapy or as monotherapy for the treatment of bipolar mania. These agents have showed efficacy in maintenance therapy because they exhibited both antimanic and antidepressant effects.^{4,7} Although speculatively, the biochemical profiles of AA could explain these properties: dopamine blockade would lead to antimanic effect while serotonin-2 (5-HT₂) receptor blockade (as with certain antidepressants like nefazodone and mirtazapine) could produce some antidepressant effects.⁸

Quetiapine fumarate is an effective novel antipsychotic agent with mixed serotonergic and dopaminergic activity and a well-tolerated side-effect profile. A number of randomized controlled clinical trials have been conducted in the last years with the aims to assess the efficacy of the Quetiapine in acute phases.^{3,5} However, the effects of maintenance treatment with quetiapine for at least 3 months are less well investigated. Two open-label studies suggest that long-term treatment with quetiapine therapy reduced the recurrence rate for manic/mixed and depressive episodes and improved symptoms in patients with bipolar disorder.^{3,4}

Quetiapine was recently approved in the US for use in bipolar depression, in addition to its previously approved indications of mania associated with bipolar I disorder and schizophrenia. Thus, quetiapine is the only AA officially indicated in both manic and depressive phases of bipolar disorder as monotherapy. The precise mechanism of action of quetiapine in bipolar depression is unknown. It is proposed that antidepressant activity of quetiapine may be linked to its higher affinity for serotonergic than dopaminergic receptors.

On the basis of these observations we undertook this naturalistic open-label, 32-week prospective study to assess the effectiveness and safety of quetiapine in the treatment of manic and mixed episodes patients not responsive to previous mood stabilizers or/and antipsychotic agents.

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