Efficacy and Tolerability of Olanzapine in Elderly Patients with Psychotic Disorders: A Prospective Study

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Olanzapine is a novel antipsychotic effective in reducing positive and negative symptoms of schizophrenia and with a safe side-effect profile. Premarketing trials, however, included only a few elderly patients. Further data are needed regarding the effects of olanzapine in the elderly and those with comorbid medical illness. In this pilot study, 11 hospitalized patients (age range 60–85 years) who manifested symptoms of psychosis related to schizophrenia and schizoaffective disorders were treated with olanzapine (dose range, 5–20 mg/day). Efficacy and safety were assessed by the Positive and Negative Syndrome Scale (PANSS), Clinical Global Impression Scale (CGI), Extrapyramidal Symptom Rating Scale (ESRS), Mini-Mental State Examination (MMSE), Calgary Depression Scale For Schizophrenia (CDSS), EKG, physical examination, and various laboratory tests. Seven patients responded to treatment and all of them showed improvement in both positive and negative symptoms, with greater reduction in positive symptoms. Treatment was discontinued in 2 patients whose symptoms showed no improvement or worsened. The CGI showed significant improvement in 9 patients, remained the same in 1, and worsened in 1 patient. ESRS showed significant reduction from baseline to final visit. Of the 10 patients who cooperated for MMSE, 9 had improved scores. The CDSS showed significant reduction in scores from baseline to final visit. No significant changes were noted in laboratory tests, prolactin levels, EKG, and physical examination. Concomitant administration of lorazepam, carbamazepine, divalproex sodium, and lithium carbonate caused no adverse consequences. The reduction of positive and negative symptoms, lack of significant extrapyramidal symptoms and other side effects, and lack of any significant drug interaction suggest that olanzapine may be a safe and effective antipsychotic medication in the elderly.

KEY WORDS: olanzapine; elderly; psychotic; efficacy; tolerability.

INTRODUCTION

Elderly patients with schizophrenia and schizoaffective disorders can be especially challenging to treat. With age comes an increased number of comorbid medical problems, which raise the possibility of drug interaction in patients being treated for several conditions simultaneously. Often patients are at risk for cardiovascular problems such as orthostatic hypotension or arrhythmias. Aging also changes the pharmacodynamics and pharmacokinetics, making the elderly more susceptible to side effects of their medications. Finally, older patients are more likely to suf-
fer from neuroleptic induced extrapyramidal symptoms and tardive dyskinesia (1). The risk of acute extrapyramidal symptoms (EPS) and tardive dyskinesia is about 50% in patients 65 years or older (2,3).

The conventional antipsychotics have helped control many of the positive symptoms of schizophrenia. The high dosages required for the drugs to be effective, however, also cause severe side effects such as EPS and tardive dyskinesia. The newer atypical antipsychotics like risperidone and olanzapine have a wider margin between efficacy and toxicity than the earlier neuroleptics, and cause fewer extrapyramidal effects. Olanzapine, an atypical antipsychotic, is reported to be efficacious for both positive and negative symptoms and to have a safe side-effect profile. Agranulocytosis does not appear to be a side effect of the drug and no monitoring is required.

Olanzapine is an antipsychotic belonging to the thio-benzodiazepine class with high affinity for serotonin 5HT2/2c, dopamine D1–5, muscarinic M1–5, histamine H1, and alpha2 adrenergic receptors (4). Olanzapine’s antipsychotic activity is mediated through a combination of dopamine and serotonin type 2 antagonism (4). The mesolimbic selectivity of the drug may explain the effects in relieving schizophrenia symptoms with minimal risk of extrapyramidal side effects. The muscarinic-blocking effects may cause side effects like dryness of mouth and tachycardia. The histamine-blocking effects may cause sedation. The alpha-adrenergic blocking effects may cause hypotension and dizziness.

Clinical trials have shown that olanzapine is safe and effective in the younger population of patients with schizophrenia (5–7). However there is a paucity of published reports on the use of olanzapine in elderly patients and in those with comorbid medical conditions. We report in this paper our clinical experience with olanzapine in a prospective study of 11 elderly patients between the ages of 60 and 85 years who were diagnosed with either schizophrenia or schizoaffective disorders and associated comorbid medical illnesses.

METHODS

The study was performed in the inpatient geropsychiatric unit of St. John’s Episcopal Hospital. The study was approved by the Institutional Review Board of the hospital. Each patient had to provide written informed consent, following an explanation by the investigator of the study aims, procedures, risks, benefits, and alternatives.

Patients

Male and female patients 60 years and older who met the DSM-IV criteria for schizophrenia/schizoaffective disorder were included in the study. The patients had currently to be treated with antipsychotic medication or had to require treatment with antipsychotic medication as documented by a minimum score of 3 on any of the seven positive symptom subscale of the positive and Negative Syndrome Scale (PANSS) (8).

The exclusion criteria included any clinically significant abnormality in hematology, chemistry, urinalysis, or electrocardiogram in the opinion of the investigator, or any clinically significant diseases of the gastrointestinal tract, liver, or kidney interfering with absorption, metabolism, or excretion of olanzapine. However, patients with stable medical conditions were not excluded. Patients who had been treated with antipsychotic drugs had to undergo a washout period of 3 days for oral medication. Patients who had been on long-acting preparations were not allowed in the study.

Clinical Assessments

Efficacy assessments were performed at screening, baseline, weekly, and endpoint. The assessment scales included Positive and Negative Syndrome Scale for Schizophrenia (PANSS), Clinical Global Impression Scale (CGI) (9), Calgary Depression Scale for Schizophrenia (CDSS) (10), and Mini Mental State examination (MMSE) (11).

Safety Assessments

Prior to entry into the study, all patients underwent a full physical examination, chest X-ray, and an electrocardiogram. Plasma samples were obtained at screening, baseline, and endpoint for hematology and serum chemistry. Plasma prolactin levels were obtained at screening, baseline, and endpoint. Extrapyramidal symptoms were assessed with the Extrapyramidal Symptom Rating Scale (ESRS) (12) at baseline, weekly, and endpoint.