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Original Article

Metabolic changes caused by first generation antipsychotic versus second generation antipsychotic in schizophrenic patients

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ABSTRACT

Objectives: To compare between the effects of chlorpromazine and olanzapine on body weight, BMI, waist circumferences, serum glucose concentration, total cholesterol, triglycerides, LDL cholesterol and HDL cholesterol in schizophrenic patients.

Methods: Seventy schizophrenic patients were divided into 2 groups of equal number (Olanzapine and Chlorpromazine). Another group consist of 35 apparently healthy volunteers were also involved in this study as a control group. Calculation of BMI, waist circumference, body weight in, serum glucose concentration, total cholesterol, LDL cholesterol, triglycerides and HDL cholesterol were performed for all patients before and after drug administration, also for all controls.

Results: The results showed that chlorpromazine and olanzapine produce no effects on body weight, BMI, waist circumferences. Olanzapine produce a significant elevation of serum glucose concentration while chlorpromazine produce reduction effect. Both drugs elevate parameters of lipid profile.

Conclusion: It has been concluded that 3 months therapy with olanzapine or chlorpromazine produce no effects on body weight or waist circumferences while elevations of all parameters of lipids were found. Chlorpromazine reduce serum concentration while olanzapine elevate it.

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1. Introduction

Typical antipsychotic drugs have been the cornerstone of the medical management of patients with schizophrenia for a long time. The advent of atypical antipsychotic drugs has brought clear benefits for schizophrenic patients because these compounds have less extrapyramidal side effects and ameliorate negative symptoms.¹ However, a large body of evidence suggests

that the use of these drugs is associated with obesity^{2,3} and diabetes mellitus.⁴ Several studies have looked at the metabolic effects of antipsychotic drugs in nondiabetic schizophrenic patients. The results consistently show that these drugs induce (euglycemic) hyperinsulinemia and impaired glucose tolerance.^{5,6} Treatment with atypical antipsychotic drugs appears to be more harmful for glucose/lipid metabolism than treatment with conventional antipsychotic drugs.^{5,7}

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The first described cases of metabolic side-effects of antipsychotics date back to 1956. That was the time when, four years after introduction of the first antipsychotic chlorpromazine in therapy, data were published on the occurrence of hyperglycemia and glucosuria in previously euglycemic patients who were administered chlorpromazine. There were also concurrent descriptions of cases of impaired glycemic control in diabetics on chlorpromazine therapy. Upon discontinued administration of chlorpromazine, normalization of glycemia was achieved as well as diabetes control at the levels prior to antipsychotic therapy.⁸

Metabolic side-effects have, however, been shown to accompany not only the administration of conventional antipsychotics like chlorpromazine. Actually, similar problems have been reported during introduction of the novel, so-called atypical antipsychotics. Introduction of atypical antipsychotics in therapy has significantly promoted the treatment of patients affected by schizophrenia and other psychotic disorders. Compared to conventional antipsychotics, the major advantage of these drugs is lower frequency of extrapyramidal side-effects and of hyperprolactinemia, and better overall tolerance. Still, some of atypical antipsychotics have been associated with body weight gain, occurrence of diabetes, and increase in cholesterol and triglyceride levels.⁸

Olanzapine, a thienobenzodiazepine derivative, is a second generation (atypical) antipsychotic agent, which has proven efficacy against the positive and negative symptoms of schizophrenia. Compared with conventional antipsychotics, it has greater affinity for serotonin 5-HT_{2A} than for dopamine D₂ receptors. In large, well controlled trials in patients with schizophrenia or related psychoses, olanzapine 5–20 mg/day was significantly superior to haloperidol 5–20 mg/day in overall improvements in psychopathology rating scales and in the treatment of depressive and negative symptoms, and was comparable in effects on positive psychotic symptoms. The 1-year risk of relapse (rehospitalisation) was significantly lower with olanzapine than with haloperidol treatment. Olanzapine is associated with significantly fewer extrapyramidal symptoms than haloperidol and risperidone. In addition, olanzapine is not associated with a risk of agranulocytosis as seen with clozapine or clinically significant hyperprolactinaemia as seen with risperidone or prolongation of the QT interval. The most common adverse effects reported with olanzapine are body weight gain, somnolence, dizziness, anticholinergic effects (constipation and dry mouth) and transient asymptomatic liver enzyme elevations.⁹

Chlorpromazine is one of a group of antipsychotic drugs known as typical agents. It is originally tested as an antihistamine and then proposed as a drug for combating helminth infections, later it was emerged as an effective treatment for psychotic illness in the 1950s. Its uses were associated with many side effects including extrapyramidal effects, anticholinergic effects, hyperprolactinemia, weight gain and sedation.¹⁰

The aim of the present study is to compare between the effects of chlorpromazine (first generation) and olanzapine (second generation) on body weight, waist circumferences, serum glucose concentration and lipid profile in schizophrenic patients.

2. Materials and methods

A total of 70 patients (age 25–53-years old) of both sexes participated in this study. They were divided in two groups of 35 patients each. The patients were randomly allocated to receive any of two different treatments. One group of patients ($n = 35$) received treatment with 5 mg daily oral olanzapine and the second group ($n = 35$) received 100 mg three times daily oral Chlorpromazine. Another 35 healthy individuals, involved in the study as a control group. The study was a randomized controlled comparative study performed over a period of one year from June 2011 to July 2012.

The patients were seen at Psychiatric Unit in IBN-SINA Teaching Hospital in Mosul, Iraq. The study protocol was approved by the Ethics Committees of the College of pharmacy and Mosul Health Administration. Inclusion criteria were a diagnosis of schizophrenia made according to DSM-IV criteria of the American Psychiatric Association (APA). The diagnosis of all the patients was confirmed by consultant psychiatrists at Psychiatric Unit in IBN-SINA Teaching Hospital. The study included those patients who had not received antipsychotic treatment in the last 6 months (long washout period). The exclusion criteria in this study were patients who had received prior antipsychotic medication in the last 6 months. Patients having any type of cardiovascular disorder, whether under treatment or not, and known patients of diabetes (even if having fasting blood sugar controlled below 110 mg/dl by any diabetic medication) all were excluded from the study. Pregnant or lactating patients, patients having family history of diabetes and patients having chronic medical illness were also excluded.

The patients' baseline body weight, waist circumference, BMI, fasting blood sugar and lipid profile were assessed before the treatment was initiated, and after 3 months of the treatment. Total serum TG, HDL, TC and fasting blood glucose levels of the patients and controls were measured by using standard commercial kits. Serum LDL concentration was calculated by using Friedewald equation. Calculation of BMI was done for each patient and control by using Quetelet index (Body weight/Height²). Waist circumference in (cm) was determined with a standard tape measure, as the point midway between the costal margin and iliac crest in the mid-axillary's line, with the subject standing and breathing normally.

Statistical methods: Standard statistical methods were used to determine the mean and standard deviation (SD). Paired student t-test was used to compare patients and control characteristics and the results between before and after drug therapy. P-value of ≤ 0.05 is considered statistically significant.

3. Results

Tables 1 and 2 show the characteristics of the patients and the controls before and after drug administration.

The effects of chlorpromazine on the studied parameters before and after drug administration were present in Table 3. A non-significant differences were found between body weight, BMI, and waist circumferences. A significant reduction of serum glucose concentration was obtained. A

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