A Retrospective Study on Antipsychotic Induced Metabolic Diseases

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ABSTRACT

Background: Schizophrenia is a psychiatric disorder which requires long term treatment with antipsychotics. The occurrences of metabolic side effects are fearsome with the use of antipsychotics.

Aim: To evaluate the metabolic effects such as diabetes, dyslipidemia, weight gain caused by 4 atypical antipsychotics (Olanzapine, Clozapine, Risperidone and Quetiapine).

Methods: This was a retrospective study conducted during the period of April 15, 2015- April 15, 2016 with a sample size of 274 patients in a neuro-psychiatric hospital in North India.

Results: Out of 274 patients collected 53% of patients were females and 47% were males. 44% of patients come under the age group 46-60. Olanzapine (32%) was prescribed more followed by clozapine (30%) and risperidone (27%). Quetiapine (11%) was prescribed least. The occurrence of weight gain is more with olanzapine (96%) and clozapine (96%). The chances of getting diabetes is also more for olanzapine (98%) and clozapine (98%). Olanzapine shows a rise in the cholesterol level in 99% patients.

Conclusion: All atypical antipsychotics induce metabolic disorders. It is important to monitor the metabolic parameters and cardiovascular risks in antipsychotic patients.

Key words: Antipsychotics, Metabolic effects, Diabetes, Weight gain, Dyslipidemia.

INTRODUCTION

The metabolic syndrome is a combination of risk factors associated with cardiovascular diseases. Based on the diagnostic criteria of the Adult Treatment Program [ATP III] of the National Cholesterol Education Program [NCEP], when any three or more of the following conditions like hypertension (systolic or diastolic blood pressure ≥90th percentile for age and gender), visceral adiposity defined by a waist circumference >102cm in men and >88cm in women, triglyceride level >150mg/dl, HDL <40mg/dl for men and <50mg/dl for women, LDL level >100mg/dl and FBS ≥110mg/dl exist in the patients are said to be have metabolic syndrome [1]. The metabolic syndromes can be caused by various factors such as diet, genetics, stress, aging, sedentary behavior or low physical activity, disrupted sleep, mood disorders, psychotropic medication use and excessive alcohol use. Mainly frequent use of antipsychotics results in life threatening metabolic disorders.

The emergence of atypical or second generation antipsychotics in 1990s has become the main choice of therapy for treating schizophrenia [2]. The primary aim of
antipsychotics in schizophrenia is the inhibition of its disturbances both in subjective ways and also in the behavioral status of an individual patient and to reinstate the patient to a normal condition by improving the quality of life and to decrease the length of stay in hospitals.

Success in treatment of the positive symptoms of schizophrenia were achieved by first generation antipsychotics but their main drawback was they had a lack of response to the negative symptoms and showed higher risks for extrapyramidal symptoms [3]. Arising of the first atypical drug, clozapine with activity against both the positive and negative symptoms, in 1958 became a breakthrough in the treatment of schizophrenia [4, 5]. Still then, other side effects thrived into the world of second generation antipsychotics with other metabolic disorders like Hypertension, Diabetes Mellitus, Dyslipidemia, weight gain, hyperprolactinaemia, etc [3]. These medical complications increase the risk of heart disease.

A comprehensive research synthesis conducted by David B. Allison et al shows that antipsychotic agents have the greatest potential induce weight gain and are at increased risk of obesity associated conditions including type II DM and cardiovascular diseases [6]. Increased adiposity in treated patients were due to insulin sensitivity and abnormalities in lipid and glucose levels [7] and it is considered as the conspicuous signal of metabolic syndrome.

Second generation antipsychotics may induce hyperlipidemia and diabetes in long term treated patients which act as an independent risk factors for the development of cardiovascular diseases. Clinical Antipsychotics trials of intervention effectiveness (CATIE) study have found that Olanzapine resulted in greater weight gain and increased glucose and lipid metabolism [8].

Second generation antipsychotics are coupled with many co morbid metabolic disturbances which may lead to cardiovascular diseases and associated mortality in schizophrenic patients. The aim of our study is to evaluate the metabolic effects of 4 different second generation antipsychotics.

MATERIALS AND METHODS
This was a retrospective study conducted during the period of April 15, 2015 to April 15, 2016 in a Neuro-Psychiatric hospital of North India. Total sample size was 274 patients. The study included the patients with following criteria: a) age over 18 years b) schizophrenic patients c) patients administering any one of the 4 second generation antipsychotics like Olanzapine, Clozapine, Risperidone and Quetiapine d) under long term treatment e) patients with metabolic diseases developed after the initiation of the treatment. The presence of metabolic disorder can be defined when any of the following criteria are met: a) BMI > 30 b) HDL< 40mg/dL in men and < 50mg/dl in women c) triglycerides >150mg/dl d) LDL >100mg/dl e) fasting blood glucose >110mg/dl. Exclusion criteria includes a) pregnant women b) with a past history of diabetes, obesity, hyperlipidemia even before the initiation of the treatment c) patients with concomitant use of medications like birth control pills, anti-depressants, SSRIs, Aspirin, diuretic like thiazides, Antihistamines, corticosteroids d) drug abused patients e) incomplete medical records.

Demographics, medical history, laboratory values, treatment and diagnostic data were abstracted from the medical records of the schizophrenic patients under long term treatment. Data were entered to well formulate data collection form and later collected data was entered and analyzed in MS excel.

RESULTS
Our study includes 274 patients in which 53% were females and 47% were males (Fig. 1). The Fig.2 illustrates the age distribution of our subjects, categorized into four groups. Most of the patients come under the age group of 46 to 60 years with a mean age of 49.8 years.

We evaluate four atypical antipsychotics such as olanzapine, clozapine, risperidone and quetiapine. In that 32% of patients were prescribed with olanzapine followed by clozapine (30%) and risperidone (27%). Only 11% were prescribed with quetiapine (Fig.3).
On examination of data, it was found that there was a considerable weight gain in patients receiving atypical antipsychotics. In that olanzapine and clozapine shows a higher incidence of weight gain (96%). Fig.4 shows drug induced weight gain of these four atypical antipsychotics.

The biochemical parameters such as lipid and glycemic parameters were evaluated in our study. On analyzing we found that olanzapine and clozapine received patients had a higher possibility of developing diabetes mellitus. Blood glucose values considerably increased in 98% of olanzapine and clozapine patients. Risperidone and quetiapine patients also show an increase in blood glucose level, 51% and 66% respectively (Fig.5).

The lipid parameters such as HDL, LDL and Triglycerides were considered and patients receiving olanzapine (99%) show significant alteration in this parameters followed by clozapine (98%). Around half of the patients receiving risperidone (53%) and quetiapine (52%) also show alteration in the lipid parameters (Fig.6).

In general estimation, olanzapine and clozapine has maximum potential to cause metabolic syndrome followed by risperidone and quetiapine.
Fig. 3: Percentage of Drug Distribution

Fig. 4: Antipsychotics Induced Weight gain
DISCUSSION

Schizophrenia is a psychiatric disorder which needs long term treatment with antipsychotics. Even though these drugs are effective in treating the illness, the occurrence of metabolic diseases is fearsome. Our study is to assess the relation between four antipsychotics (Olanzapine, Clozapine, Risperidone and Quetiapine) in the development of metabolic diseases. We evaluated the occurrence of...
metabolic diseases like Diabetes mellitus, Dyslipidemia and Obesity. The burden of illness increases as the metabolic diseases leads to cardiovascular risks. The study conducted by Correll et al shows a high prevalence of cardiovascular risks due to metabolic syndromes in psychiatric patients [9].

The study sample has more females compared to males and most of the patients were in the age group of 46-60 years. The previous studies also showed that female patients are more prone to adverse effects of antipsychotics [10, 11].

Current study shows that all the 4 antipsychotics causes rise in body weight. Among them olanzapine and clozapine had more weight gain effects. The lowest risk of obesity is for quetiapine. Differential affinities for serotonin 5-HT2C and H1 receptors were suggested as the cause of increased weight gain for clozapine and olanzapine [12]. The induction of leptin is also suggested as a factor of weight gain [13]. Genetic factors and lifestyle could be other reasons for weight gain in patients. Musil R et al, suggests that polymorphism in resistin gene contributes to weight gain in psychiatric patients [14].

Present study reveals that all 4 antipsychotics causes diabetes and the leading drugs are olanzapine and clozapine. Compared to other 3 drugs, risperidone has the lowest risk of getting diabetes. This finding is also supported by Caro J J et al, in his study [15]. The reason for causing increased glucose levels are decreased sensitivity, increased insulin resistance and decreased insulin secretion. A study suggests that the antipsychotic drugs might block glucose transporter protein in cells [16]. Another study says that impaired parasympathetic regulation of β-cell activity leads to metabolic risk [17].

In this study, all the 4 drugs causes’ abnormal lipid profile but olanzapine and clozapine are foremost in occurring dyslipidemia. Studies also support that both the above said drugs has higher rate of dyslipidemia while Quetiapine and risperidone has lower chances [8, 18].

The study has few limitations that limit the ability to generalize the study findings. It was a retrospective study and there is chance of missing the data that were not recorded in the medical records. This limitation may underestimate the findings of the study.

CONCLUSION
All atypical antipsychotics induce metabolic disorders, in that olanzapine and clozapine have more effects. It is important to monitor the metabolic parameters and cardiovascular risks in antipsychotic patients. It is necessary to educate the patients about the diet and life style modification to reduce the side effects.

REFERENCES


