GLOBAL JOURNAL OF BIOLOGY, AGRICULTURE & HEALTH SCIENCES
*(**Published By**: Global Institute for Research & Education)*
www.gifre.org

EARLY PREDICTION OF LIPID DERANGEMENT DURING ANTIPSYCHOTIC (OLANZAPINE) TREATMENT

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Abstract

Background: Earlier studies have demonstrated the relationships of lipid levels with psychiatric patients taking atypical antipsychotics, and their results revealed an association between hyperlipidemia and antipsychotic treatment. The present study was undertaken to evaluate the lipid profile alteration after 16 weeks of treatment with Olanzapine and compare with normal subjects.

Material & Methods: This study was conducted at Department of Psychiatry & Department of Biochemistry People's College of Medical Sciences and Research Centre, Bhopal. Thirty newly diagnosed patients, who completed 16 weeks of treatment were included and compared with 40 healthy subjects. In our study we have measured lipid profile which includes serum total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL), low density lipoprotein cholesterol (LDL), very low density lipoprotein cholesterol (VLDL), and cardiovascular risk factors (R1&R2) & Body mass index (BMI).

Results: The concentration of TC, TG,LDL and VLDL and risk factors were increased, whereas HDL was decreased after 16 weeks of Olanzapine treatment ($p<0.05$).

Conclusion: In view of the relationship between antipsychotics (Olanzapine) and lipid derangement, it is clearly evident that lipid parameters and risk factors for coronary heart disease are significantly altered after Olanzapine treatment.

Key Words: *Coronary artery disease, dyslipidemia, atypical antipsychotics, lipid profile.*

Introduction

Psychiatric disorders such as major depressive disorders, generalized anxiety disorders, co-morbid anxiety disorders, schizophrenia, maniacal disorders, dementia and obsessive compulsive neurological disorder are among the leading causes of global morbidity. These are often chronic and need antipsychotic treatment for prolonged periods often extending up to a life time. The bulk of the research on dyslipidemia shows that use of the atypical antipsychotics,(phenothiazine drugs) especially the newer ones, is associated with metabolic side effects such as weight gain, deranged glucose tolerance and lipid profile alterations.[11] There are some studies that show a favorable response of antipsychotic agents in psychotic disorders without causing significant lipid derangements.[5,14]

It has been suggested that persons with psychiatric disorders may have predisposition toward developing metabolic syndrome and dyslipidemia that is exacerbated by their generally sedentary lifestyle, poor dietary habits, limited access to care, poor insight and medication induced adverse effects. Treatment with antipsychotic drugs may further add to this dyslipidemia to worsen the situation and become instrumental in augmenting the incidence of coronary artery diseases. In view of significant variations in the literature on the effects of antipsychotic medication on lipid biochemistry, this study was undertaken as an attempt to arrive at some firm conclusion regarding the relationship of "Atypical Antipsychotic Drugs" and dyslipidemia. The aim of the study was to determine early alterations in the lipid profile after a particular time interval of drug administration in patients treated with olanzapine. Olanzapine (trade name Zyprexa) is an, atypical antipsychotic which is classified as a dibenzodiazepine. The mode of action of olanzapine's may involve antagonism of dopamine and serotonin receptors[4] which is associated with extrapyramidal effects such as sedation, weight gain and apatite stimulation.[1]

Material and Methods

The present study was carried out in Department of Biochemistry People's College of Medical Sciences and Research centre Bhopal in association with Department of Psychiatry Hamidia Hospital Bhopal, and Department of Psychiatry, People's Hospital, Bhopal. The study protocol was approved by the Institutional Ethical Committee. In our study age & sex matched 30 newly diagnosed patients referred to psychiatric clinic for outpatient management, were included in the study group. While forty age- and socio-economically matched apparently healthy subjects served as the control. Because the study had focused on assessment of lipid derangement after treatment, data only from participants

who completed 16 weeks of treatment with prescribed drug (Olanzapine) was included. Subjects in both groups having organic diseases such as hypertension, diabetes, cardiovascular disease, hepatic and thyroid disorders were excluded from the study. Pregnant & menopausal women were also excluded. The blood samples were drawn after an overnight fast and separated serums were stored with proper labeling in deep fridge until analysis was carried out. All lipid parameters were determined on Day 1 (at the start of study when patients were not on antipsychotic medication) and then after 12 weeks and 16 weeks of medication. Serum TC, TG & HDL were measured on Biosystem A25 fully automated analyzer using Biosystem kits. LDL-C and Risk Factors (I&II) were calculated by Friedewald formula. Viz TC divided by HDL (Risk Factor I); LDL divided by HDL (Risk Factor II). Data were analyzed by SPSS-16 software; t-test was done by one way ANOVA. All the values were expressed as mean±SD.

Results

There was no significant difference in age-sex, BMI, family history of diabetes and cigarette smoking between study group and control group. The mean age of subjects in study group was 32.46±12.5 years and 31.2 ±10.5 years for control group. Majority of cases in both groups were of middle aged males. According to table-1, concentration of TC, TG, LDL,VLDL & HDL level were differed significantly between study group and control group ($p<0.05$).psychiatric patients shows significant increase in lipid parameters.

In our study, we have also measured the effect of olanzapine on serum lipid profile after 12 weeks and 16 weeks of treatment in this study group and these results are also shown in table-1. The mean TC, TG, VLDL & LDL level increased significantly after olanzapine treatment. Risk factor I (CHO/HDL) and Risk factor II (LDL/HDL) were also increased after 12 weeks, and 16 weeks of treatment and it was highly significant ($p<0.05$).

TABLE: 1

Showing comparison of lipid profile after treatment with olanzapine in patients and control group

Lipid Parameter	Control group	Before treatment (n=30) Mean±SD	After 12 weeks of treatment (n=30) Mean±SD	After 16 weeks of treatment (n=30) Mean±SD	F-factor	p-value
Total cholesterol	135.45±25.20	176.36 ± 37.69	192.26+39.03	202.10±41.66	24.39	<0.05
Triglycerides	94.96±52.20	143.00+48.30	172.66+51.27	181.50+50.97	28.58	<0.05
HDL-C	41.25±5.65	36.33±5.50	33.66±4.7601	32.56±4.22	21.33	<0.05
LDL-C	75.20±54.89	111.43+30.96	124.06+32.82	133.23+37.64	23.92	<0.05
VLDL-C	18.99±4.71	28.60±9.66	34.53±10.25	36.30±10.19	28.58	<0.05
Risk Factor-I	3.26±0.84	4.87±0.87	5.74±1.03	6.22±1.10	49.36	<0.05
RiskFactor-II	1.83±0.61	3.07±0.74	3.69 ±0.88	4.09±1.05	47.56	<0.05

Discussion

In our study first we have compared the serum lipid profile level of newly diagnosed psychiatric patients with normal subjects. Our findings showed (table-1) significant association between serum lipid levels and psychiatric disorders. It was observed that serum lipid parameters including the CAD Risk factors were significantly ($p<0.05$) higher in newly diagnosed psychiatric patients than in normal subjects. Our results are in agreement with other studies.[6,7,8,13]

Lipid derangement in psychiatric patients is associated with use of traditional or other antipsychotics, although not all drugs are involved in this association. Among atypical antipsychotics, phenothiazine drugs cause highest risk of dyslipidemia. Olanzapine is among the most widely used drug in psychiatric practice. This was originally intended primarily for the treatment of schizophrenia, but over the years its use has spread to other psychotic disorders. In our study it is evident that after 16 weeks of treatment, total cholesterol is increased significantly ($p<0.05$) and our results are consistent with that of other studies [9,12] who found olanzapine is associated with hypercholesterolemia. Table – 1 shows the concentration of mean triglycerides before and after treatment and it is observed that increase in triglyceride in olanzapine treated patients was statistically significant ($p<0.05$). The results are in agreement with other studies.[1,10] The mean HDL level reduced significantly ($p<O.O5$) after olanzapine treatment (Table-1).

The mean LDL and VLDL level increased significantly ($p<0.05$) after 12 weeks and 16 weeks of treatment. Previous works confirmed that olanzapine is one of the most effective and best tolerated of the atypical antipsychotics, but it is also particularly associated with and metabolic problems. Our results also show strong relationship between dyslipidemia and Olanzapine. When we consider the overall lipid profiles as a marker for assessment of cardiovascular risk, in our study the mean total cholesterol, triglycerides, LDL-cholesterol and VLDL-cholesterol was significantly raised after treatment up to 16 weeks with olanzapine. However Serum HDL level is significantly reduced during treatment and these results correlated with these workers [1,3,10] and CATIE (Clinical Antipsychotic trials of intervention Effectiveness) project.

According to Framingham study, persons with Total cholesterol; HDL-cholesterol ratio greater than 5 are at high risk of developing CAD and person with LDL-cholesterol; HDL-cholesterol ratio between 2 and 5 are at intermediate risk of developing CAD. In comparison with this study, our result showed increased risk factors in olanzapine treated patients which suggest an increased risk of developing CAD in this group of psychiatric patients. Hence olanzapine treatment is positively associated with lipid derangement. However our results are not consistence with some earlier studies in available literature [5,14,16] those showed a favorable response of this drug in psychotic disorders without causing significant lipid derangements and do not correlate with our study.

Conclusion

Atypical antipsychotic drugs vary greatly in their pharmacology and in their risk for specific adverse effects such as weight gain and lipid derangement not only add another layer of complexity for physicians managing these patients, but also may have serious prognostic and cost implications with respect to the incidence of treatment-related cardiovascular disease. Our study had certain limitations. The numbers of study subjects were too small and limited time of follow-up. According to "Consensus Monitoring Recommendations" for patients taking atypical antipsychotic, monitoring of lipid profile should be performed at baseline level, after 12 weeks and then after every 5 years of treatment. We could not, however, undertake a long term study because of limited time bound study. In conclusion our study revealed that serum lipid parameters were significantly altered in newly diagnosed patients and olanzapine was found to be associated with increasing dyslipidemia in treatment taking group.

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