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# Effect of Risperidone and Olanzapine on blood glucose levels and lipid profile among individuals with schizophrenia

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## Abstract

**Background:** Treatment of schizophrenia requires use of antipsychotics for considerable time. Studies established that patients have risk of metabolic side effects.

**Objectives:** To study fasting blood glucose levels and lipid profile in schizophrenic patients and to see that same was present in study population.

**Methods:** This study was conducted at psychiatry outpatient department, Nobel Medical College and Teaching Hospital Kanchanbari Biratnagar from October 2018 till august 2019 after due approval from college ethics committee. A total of 50 consenting drug naive schizophrenia patients 17- 60 years of age, with no comorbidity, were divided alternatively into two groups. group 1 was treated with olanzapine, group 2 with risperidone for eight weeks. With flexible dosage for ease of the therapy and individual patient requirement. Fasting blood glucose and lipid profile was measured at day baseline, four, eight weeks.

**Results:** There was rise of fasting blood glucose in both groups but more in olanzapine group with no statistically significant intergroup difference (The p-value after eight weeks was 0.504). In lipid profile, mean total cholesterol levels were higher in the group 1, ($p = 0.005$ after eight weeks). Triglycerides, on intergroup comparison significant difference ($p = 0.002$) was noted. Higher values in group 1 were recorded. However, very low-density lipoprotein was elevated ($p = 0.003$) in group1 only.

**Conclusion:** olanzapine and risperidone cause non-significant rise in fasting blood sugar. Olanzapine caused statistically significant rise of total cholesterol, triglycerides, very low-density lipoprotein as compared to risperidone.

**Key words:** Fasting blood glucose; Lipid profile; Olanzapine; Risperidone.

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## INTRODUCTION

Current treatment protocols for the treatment of Schizophrenia prefers the use of second-generation antipsychotics like olanzapine, risperidone, quetiapine, ziprasidone, aripiprazole. There is evidence to say they have many metabolic effects like weight gain, deranged lipid profile and fasting blood glucose.[1] Some patients end up by suffering from diabetes or cardiovascular diseases.

The use of first-generation antipsychotics decreased because of the side effects which include extra pyramidal syndrome. The newer antipsychotics have side effects that clinicians should know.[2] The clinician requires to be well versed in it. There is a need in these patients to regularly monitor the blood parameters. These side effects could also lead to non-compliance of the therapy[2].

According to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines the waist circumference, serum lipid and blood sugar

levels are important parameters of the development of metabolic syndrome.[3]

This study was aimed to assess the effect of commonly used antipsychotics like Olanzapine and Risperidone in Nepali population on the Fasting Blood Glucose and Lipid profile of drug naive patients with schizophrenia. Also, the aim was to find if these medications caused similar changes in the Nepali patients.

## METHODOLOGY

This was a prospective, open label study of the Fasting Blood Glucose levels and Lipid profile in the first 50 patients from first week of October, diagnosed as suffering from Schizophrenia. The patients were drug naïve and attended the Psychiatry Outpatients Department at Nobel Medical college Teaching hospital from October 2018 to August 2019.

The patient who fulfilled the diagnostic criteria for based on international classification of diseases of mental health tenth edition (ICD 10) system,[4] had no history of use of antipsychotic medication, were 17 to 60 years of age and not suffering from any cardiac or metabolic illness at the time of study were included in the study. Patients who were a known case of Schizophrenia, having a history of use of Antipsychotics, known case of cardiac illness or diabetes and not ready to participate in the study were excluded from the study.

Written informed consent was obtained from each subject before the initiation of the study. Only such people who agreed to participate in the study were included.

The subjects fulfilling the above conditions were alternatively allotted into group 1 (olanzapine group) or group 2(risperidone group). The study period was kept of Eight weeks to record the initial trends of the parameters under study in the population. The patients who were included in the study, were if required admitted otherwise sent home with the therapy after taking the initial samples for fasting blood Sugar and lipid Profile. Their Waist circumference and blood pressure was also recorded. They were administered brief psychiatry rating scale. They were called on a regular follow up and the blood samples were collected after completion of four weeks and eight weeks of the study. Doses as per requirement were titrated by the clinician. The data was recorded on baseline, week four, and week eight.

The data so collected was tabulated and analysed using descriptive analytical tools. Statistical analysis was done using SPSS statistics for windows version 16 (SPSS Inc., Chicago, Ill., USA). At baseline, the unpaired t-test was used to analyze data collected. At the baseline, week 4 and week eight mean and standard error of mean was calculated. Paired t-test was applied for intragroup analysis whereas independent t-test was applied for intergroup analysis. The p-values <0.05 were considered significant and <0.001 were highly significant. This study was conducted after due permission of the Institutional Review Committee wide their letter (Ref. 659/2018) dated 18 June 2018.

## RESULTS

The study included 50 patients, 25 in each group. The socio-demographic and recorded data of the patients like brief psychiatry rating scale score, blood pressures of the patients in both the study groups in tabulated in Table 1. The mean age was 25.16 ± 2.93 years in group 1 whereas the mean age is 26.54 ± 3.63years in group 2. Majority of the patients were males in both the groups 20:5 in group 1 and 18:7 in group 2. Majority of the patients were from the urban background and were having non vegetarian diet. The Brief Psychiatry Rating scale score was 43.02 ± 0.36 in group 1 and group 2 had 42.2 ± 0.38.

The Table (2) and Table (3) shows the data collected during the study on all parameters. The mean fasting blood sugar was 85.29 ± 2.33 mg/dl in group 1 whereas 86.21 ± 1.34 mg/dl in group 2 at day 0 whereas after 8 weeks the figure was 90.02 ± 3.11, 88.01 ± 2.62 mg/dl in group 1 and group 2 respectively. There was a total increase of 4.73 ± 0.78 mg/dl in group 1 whereas in group 2, it was 1.86 ± 1.28 mg/dl. There was no statistical significance intergroup difference (The p-value after eight weeks was 0.504).

The serum Total cholesterol levels were 152.43 ± 2.11 in group 2 whereas 175.76 ± 1.73 in group 1 at baseline, whereas after eight weeks it was 157.01 ± 3.29, 187.93 ± 2.17 mg/dl in group 2 and group 1 respectively. There was an increase of 4.59 ± 2.82 mg/dl in risperidone group and 12.17 ± 0.44 increase in the olanzapine group. The mean total cholesterol levels were found to be significantly higher in the group 1, (p = 0.005 end of eight weeks).

The triglycerides were 103.64 ± 3.25 mg/dl, 109.34 ± 1.22 mg/dl in the beginning of the study in the group 1 and 2 respectively, but they ended at 134.72 ± 3.62mg/dl, 121.56 ± 1.43 mg/dl after 8 weeks of the study in group 1 and 2 respectively. There was an increase of 31.08 ± mg/dl in group 1 whereas the group 2 had an increase of 12.22 ± 0.21 mg/dl. On intergroup comparison of values

after 8 weeks we noted a significant difference (p = 0.002). Higher values were noted in the group 1 patients.

The high-density lipoprotein was 49.01 ± 2.46 mg/dl, 53.92 ± 2.34 mg/dl in the beginning of the study in the group 1 and 2 respectively, but they ended at 51.04 ± 2.14 mg/dl, 55.62 ± 2.16 mg/dl after 8 weeks of the study in group 1 and 2 respectively. There was a decrease of 2.04 ± 0.05 mg/dl in group 1 whereas group 2 had a decrease of 1.96 ± 0.81mg/dl. When the values were compared within group 1 and 2, no significant differences were noted (p = 0.891 after eight weeks).

The low-density lipoprotein levels were 106.44 ± 7.22 mg/dl,105.56 ± 2-01 mg/dl in the beginning of the study in the group 1 and 2 respectively, but they ended at 114.99 ± 2.51 mg/dl, 117.51 ± 2.01 mg/dl after eight weeks of the study in group 1 and 2 respectively. There was an increase of 8.55 ± 4.71mg/dl in group 1 whereas the group 2 had an increase of 11.95 ± 0.09 mg/dl. Although the low-density lipoprotein level was numerically higher in risperidone treated patients, this difference was not statistically significant p = 0.332 at eight weeks).

The mean change in very low-density lipoprotein values over eight weeks was 20.12 ± 1.73 mg/dl and 21.59 ± 1.28mg/dl in the olanzapine and risperidone groups, respectively. Although there was no statistical difference between the groups at four weeks (p = 0.027), the Very low-density lipoprotein levels were significantly higher (p = 0.003) in the olanzapine-treated patients than those treated with risperidone at the end of eight weeks.

**Table 1: Patients' profile**

| Variables | Group 1 (olanzapine) N = 25 | Group 2 (risperidone) N = 25 |
|---|---|---|
| Age (years) | 25.16 ± 2.93 | 26.54 ± 3.63 |
| Sex ratio (Male: female) | 20:5 | 18:7 |
| Urban: Rural | 16:9 | 17:8 |
| Vegetarian: Non-vegetarian | 24:1 | 25:0 |
| Brief psychiatric rating scale (BPRS) score | 43.02 ± 0.36 | 42.2 ± 0.38 |
| Blood pressure Systolic/diastolic mm of Hg | 115.3 ± 0.36/75.3 ± 0.5 | 119.4 ± 0.5/76.8 ± 0.32 |
| Waist circumference | 78.02 ± 1.02 | 77.21 ± 1.52 |

**Table 2: Depicting the blood levels of parameters under study in group 1 (olanzapine)**

| Parameters | Day 0 Mean ± SEM | Week 4 Mean ± SEM | Week 8 Mean ± SEM | p-value |
|---|---|---|---|---|
| Fasting blood glucose (mg/dl) | 85.29 ± 2.33 | 88.11 ± 3.53 | 90.02 ± 3.11 | <0.05 |
| Total cholesterol (mg/dl) | 175.76 ± 1.73 | 181.06 ± 2.11 | 187.93 ± 2.17 | <0.001 |
| Triglycerides (mg/dl) | 103.64 ± 3.25 | 119.52 ± 2.52 | 134.72 ± 3.62 | <0.001 |
| High density lipoproteins (mg/dl) | 51.04 ± 2.14 | 49.71 ± 3.41 | 49.01 ± 2.46 | <0.05 |
| Low density lipoproteins (mg/dl) | 106.14 ± 7.22 | 111.89 ± 4.12 | 114.99 ± 2.51 | <0.05 |
| Very low-density lipoproteins (mg/dl) | 20.12 ± 1.73 | 25.75 ± 2.45 | 28.03 ± 4.2 | <0.001 |

**Table 3: Depicting the blood levels of parameters under study in group 2 (risperidone)**

| Parameters | Day 0 Mean ± SEM | Week 4 Mean ± SEM | Week 8 Mean ± S | p-value |
|---|---|---|---|---|
| Fasting blood glucose (mg/dl) | 86.21 ± 1.34 | 87.91 ± 3.42 | 88.07 ± 2.62 | <0.001 |
| Total cholesterol (mg/dl) | 152.43 ± 2.11 | 154.05 ± 2.46 | 157.01 ± 3.29 | <0.001 |
| Triglycerides (mg/dl) | 109.34 ± 1.22 | 116.67 ± 1.8 | 121.56 ± 1.43 | <0.001 |
| High density lipoproteins (mg/dl) | 55.61 ± 2.16 | 53.92 ± 2.34 | 52.33 ± 1.22 | <0.05 |
| Low density lipoproteins (mg/dl) | 105.55 ± 2.01 | 110.06 ± 2.71 | 117.51 ± 2.1 | - |
| Very low-density lipoproteins (mg/dl) | 21.59 ± 1.28 | 24.19 ± 5.19 | 26.95 ± 2.6 | <0.001 |

## DISCUSSION

It has been postulated that antipsychotic drugs cause hyperglycemia inside body tissues by blocking the transporter protein,[5] Similarly, in the skeletal muscles the uptake of glucose was stopped by 5HT2A receptor blocking[6] supplemented by dysfunction of pancreas, caused by the blockade of muscarinic type 3, 5- HT1A receptors. Insulin resistance was associated with an atherogenic plasma lipid profile.[7] Antipsychotic drugs may cause accumulation of lipids by changes in the action of insulin on adipocytes.[8] With The combination of altered Very low-density lipoprotein synthesis and impaired removal together can increase plasma low density lipoprotein and triglycerides, and lately very low-density lipoprotein. Also, it is known that defective lipoprotein lipase activity causes decrease in high density lipoprotein.[9]

The exact reason that causes the newer generation antipsychotics to cause alteration in lipid profile and elevated fasting blood glucose is not clearly demarcated, but it can be probably due to drug and receptors interaction.

Mc Evoy et al. in a study in the year 2007, found in his study that after 12 weeks there was a decrease in high density lipoprotein levels but there was a simultaneous rise in the total cholesterol and triglycerides levels in both olanzapine and risperidone-treated patients. The change was higher in the olanzapine group patients.[10] The current study findings are similar.

In a similar study conducted by Lindenmayer et al. in 2003, they reported that olanzapine treated patients had higher levels than risperidone treated schizophrenia patient, whereas both the groups had increase in the fasting sugar levels. They also observed a substantial increase in the serum total cholesterol levels. The study was for a period of fourteen weeks of olanzapine and risperidone treatment. Their study found out the statistical significance was in the group of patients taking Olanzapine,[11] which was not different from our study as our study had not found any statistical significance in rise of blood glucose between both groups.

A study conducted by Sikich et al. in 2004 after eight weeks of treatment reported a non-significant increase in values of fasting blood sugar in both olanzapine and risperidone-treated patients and there was decrease in the high-density lipoprotein levels in olanzapine-treated patients after eight weeks and increase in the high density lipoprotein levels in risperidone treated patients. Low density lipoprotein and triglycerides levels were also increased in both groups but were statistically not significant.[12] Another study by Sikich et al. in 2008 which was similar to their previous study but on a different set of subjects stated that the patients treated with olanzapine had lower fasting sugar levels than risperidone. Whereas the blood lipid profile showed that triglycerides were increased similarly in both the groups after study period of eight weeks, there was a marginal increase in total cholesterol, high density lipoprotein, low density lipoprotein levels of olanzapine group patients and a decrease in the risperidone group.[13] A study conducted by Henderson et al. demonstrated no statistically significant differences in total cholesterol levels during treatment with olanzapine and risperidone.[14]

In a meta-analysis done by Zhang et al. in 2017, he found out that olanzapine having statistically significant increase in blood glucose levels than risperidone or placebo treatment. Their study also found that risperidone had marginal effect on the fasting sugar levels.[15]

In a meta-analysis by Li et al. in 2020, twenty-one studies and 1790 schizophrenia patients who received olanzapine therapy were included in the analysis. An olanzapine-induced increase was observed in plasma total cholesterol, triglyceride, and low-density lipoprotein levels ($p < 0.05$). The review came to the conclusion that olanzapine therapy increases the lipid profile in the parameters of triglycerides, total cholesterol, and low-density lipoprotein levels, by four weeks.[16]

The study has some limitations like short (eight weeks) duration of the study, absence of control group, small group size. This happens to be an initial study on the Nepalese population on this subject, this study will serve as a starting point for further studies in our population.

## CONCLUSION

In conclusion, this study compared the effects of olanzapine and risperidone on multiple parameters of fasting blood sugar and lipid profile. The study drugs have changed these parameters, but difference was greater in olanzapine than risperidone group. In the intergroup comparison statistically, significant difference was seen in three levels namely total cholesterol, triglycerides, very low-density lipoprotein.

**Conflict of interest:** None
**Source(s) of support:** None

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