



The Prevalence of Metabolic Syndrome of Patients on Treatment with Haloperidol and Risperidone or Olanzapine

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: The background of the work stems from the observation due to the prevalence of antipsychotic drugs in causing metabolic disorder. The metabolic disorder is one of the major concern of antipsychotic drugs for schizophrenic patients. The present study is mainly aimed to establish the role of haloperidol and risperidone or olanzapine in causing metabolic syndrome of schizophrenic patients.

Methods: Sixty-four schizophrenic patients were divided into two groups. First and second group received haloperidol and risperidone or olanzapine respectively for three months. Body mass index,

random blood sugar and lipid profile were investigated before and after the treatment.

Results: Both groups of schizophrenic patients have shown a significant increase in the BMI, random blood sugar and lipid profile indicating a propensity to cause metabolic disorder.

Conclusion: From the present study it is concluded that there is a high prevalence of metabolic disorder those who received antipsychotic drugs like haloperidol and risperidone or olanzapine.

Keywords: Metabolic syndrome; haloperidol; risperidone; olanzapine.

1. INTRODUCTION

Presently atypical antipsychotic drugs are used for the management of schizophrenia due to the advantage of causing less amount of extrapyramidal symptoms [1]. However, the main disadvantage of atypical antipsychotics are elevated blood pressure, weight gain, hyperglycaemia and hyperlipidaemia which are the hallmark of metabolic syndrome [2]. The outcome of extrapyramidal symptoms produced by the conventional antipsychotic drugs is considered to be much safer than the atypical antipsychotics due to their propensity in causing metabolic disorders [3,4]. Chronic mental illness like schizophrenia itself has been implicated with the higher frequency of metabolic disorder. In addition, administration of atypical antipsychotics might aggravate the metabolic dysfunctions thereby causing increase in morbidity and mortality [5,6] It has been reported that schizophrenic patients have lesser lifespan of 61 years as compared to the normal population with the lifespan of 76 years. Schizophrenic patients life expectancy is decreased by 20%, with 60% enhanced mortality because of the disease [7] and also due to the possibility of antipsychotic drug treatment [8]. Increased waist circumference, lipid profile and blood sugar level are accountable for metabolic dysfunction. This parameters can lead to diabetes thereby causing micro and macro vascular complications. It has been found that there is a positive correlation between coronary artery disease and increased plasma triglyceride level (TG), increased low-density lipoprotein (LDL), decreased level of highdensity lipoprotein HDL) and plasma cholesterol. Besides diabetes also can contribute to increased lipid profile which also can lead to atherosclerosis and hypertension [9,10,11].

Therefore the present study is aimed to investigate whether administration of drugs like haloperidol with risperidone or olanzapine can contribute to the changes in the body weight, blood glucose level and lipid profile which are the triggering factor for metabolic disorder.

2. MATERIALS AND METHODS

An observational study was conducted in different hospitals in western India to evaluate the effect of combined drug on various parameters like body weight, blood glucose and lipid profile for assessing the metabolic syndrome. A total of 273 subjects were screened based on the age, sex and diagnostic criteria (ICD-10 classification) [12] for schizophrenia and schizo-affective disorder. Patients already suffering from diabetes mellitus, hypertension, hyperlipidaemia and obesity with other antipsychotic drug were excluded from the study. The study has been conducted for fifteen months.

After conducting inclusion and exclusion criteria 70 patients were selected for the drug regimen of haloperidol and risperidone or olanzapine. However, 6 participants were not included in the study due to non-availability of the data in the record. Remaining 64 patients were divided into two groups (Group-I and group-II) both groups of 32 patients each. Group I received haloperidol (5mg) and risperidone (2mg) and group II received haloperidol and olanzapine (5mg).

Participants selected from both gender and aged between 18 to 50 years. Informed consent were taken. The samples in each group were assessed for baseline parameters like BMI (body weight, height, and waist circumference), random blood sugar and lipid profile. The same parameters were repeated 3 months after the aforementioned drug treatment. Blood sugar was estimated by using the glucometer and serum lipid profile also was investigated by standard method. The National Cholesterol Education Program Adult Treatment Panel III criteria were used to evaluate the parameters of metabolic disorder. According to NCEP ATP III criteria following values are normal : HDL < 40mg/dl, male < 50 mg/dl female, serum TG > 150 mg/dl, and abdominal girth >35 women and >40 men [13].

Statistical analysis was carried out by using Prism software, Kolmogorov-smirnov test was used to check the normality of the data and found to be normally distributed. Thus, paired t-test to compare the difference with in the group and Chi-square test used to find out the association between the demographic variables of the schizophrenic patients such as age, sex and diet. The level of $p < 0.05$ was considered as significant.

3. RESULTS

The BMI of (Height, weight and waist circumference) of schizophrenic patients treated with haloperidol and risperidone or olanzapine was shown to be significantly higher than their pre-treatment value. (Fig:1 & 2) suggesting the role of antipsychotics in metabolic disorder.

Treatment with haloperidol and risperidone or olanzapine have shown a marked differences in the random blood sugar level among schizophrenic patient before and after treatment. (Fig:3& 4) These result also suggests a positive correlation towards metabolic syndrome when the schizophrenic patients are treated with antipsychotics.

There was a significant increase in the level of TG, LDL, TC and decreased level of HDL in patients treated with haloperidol and risperidone or olanzapine as compared to their pre-treatment value among schizophrenic patients. (Fig:5 & 6) The result obtained from the lipid profile has shown a strong association between antipsychotic treatment and metabolic syndrome.

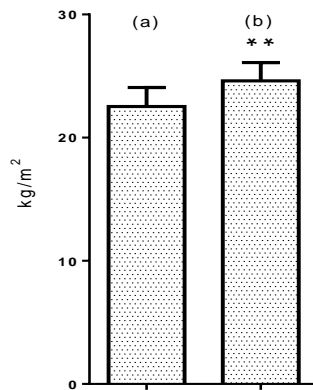


Fig. 1. BMI of Schizophrenic patients before (a) and after (b) treatment with haloperidol + risperidone. Each value represent mean \pm SEM (n=32 subjects per group) It shows significant difference in BMI before and after treatment of haloperidol + risperidone. **P<0.001 as compared to pre-treated group

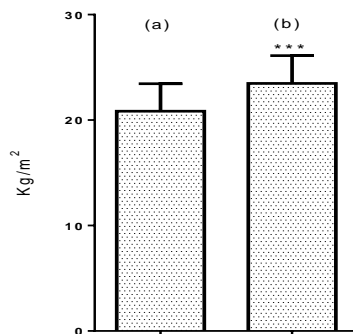


Fig. 2. BMI of Schizophrenic patients before (a) and after (b) treatment with haloperidol + olanzapine. Each value represent mean \pm SEM (n=32 subjects per group) **P<0.0001 as compared to pre-treated group. It shows significant difference in BMI before and after treatment of haloperidol + olanzapine

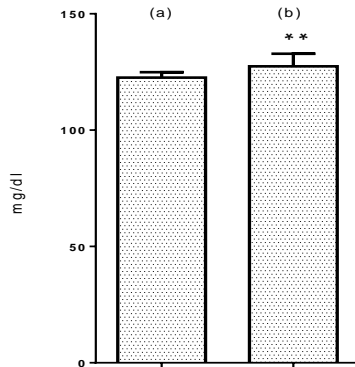


Fig. 3. Random blood sugar level of Schizophrenic patients before (a) and after (b) treatment with haloperidol + risperidone. Each value represent mean \pm SEM (n=32 subjects per group) ****P<0.001** as compared to pre-treated group. It shows significant difference in blood sugar level before and after treatment of haloperidol + risperidone

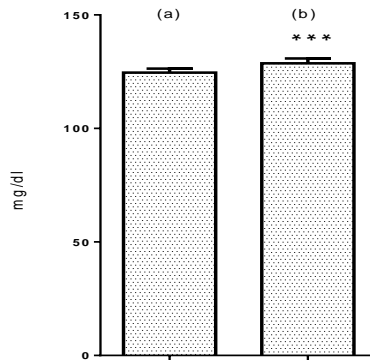


Fig. 4. Random blood sugar level of Schizophrenic patients before (a) and after (b) treatment with haloperidol + olanzapine. Each value represent mean \pm SEM (n=32 subjects per group) ****P<0.0001** as compared to pre-treated group. It shows significant difference in blood sugar level before and after treatment of haloperidol + olanzapine

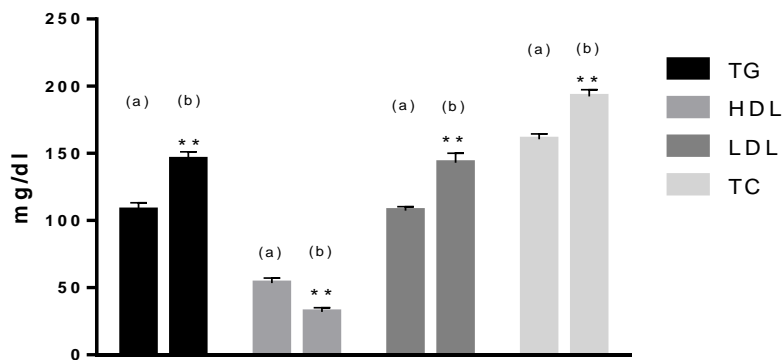


Fig. 5. Lipid profile (TG, HDL, LDL, TC) of Schizophrenic patients before (a) and after (b) treatment with haloperidol + risperidone. Each value represent mean \pm SEM (n=32 subjects per group) ****P<0.001** as compared to pre-treated group

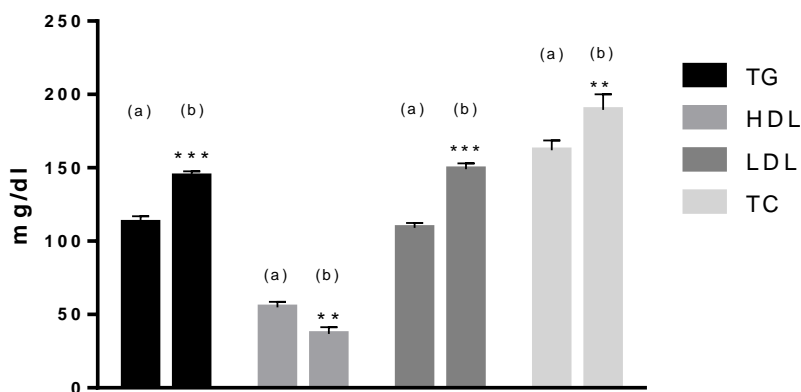


Fig. 6. Lipid profile (TG, HDL, LDL and TC) of Schizophrenic patients before (a) and after (b) treatment with haloperidol + olanzapine. Each value represent mean \pm SEM (n=32 subjects per group) **P<0.001, *P<0.0001 as compared to pre-treated group**

The present study also explored the association between metabolic syndrome with selected demographic variables of patients with schizophrenia. However, It has been found that there was a significant association in age (X^2 -14.524) and gender (X^2 6.781) while there is no significant association found between diet and metabolic syndrome (X^2 .1211. The level of $p < 0.05$ was considered as significant.

4. DISCUSSION

The present study has shown a correlation between the prevalence of antipsychotic drugs with metabolic disorder. It has been found that schizophrenic patients treated with haloperidol and risperidone or olanzapine caused a significant increase in the BMI, random blood glucose and lipid profile such as TG, HDL, LDL and TC.

In the present study it has been observed that (48.3%) of the schizophrenic patient who are treated haloperidol and risperidone are having high BMI suggesting a prevalence of metabolic syndrome. Similarly there was a significant increase in the percentage of BMI (56.8%) in patients who received haloperidol and olanzapine. The present study is in line with the previous work which also showed a similar increase in the waist circumference, blood glucose level and lipid profile after treating with antipsychotic drugs [10,14,15,16]. From the present data it is shown that there is an increase in the random blood sugar level of (34.8%) patients who were under the treatment of haloperidol and risperidone. However the patients who were treated with haloperidol and

olanzapine showed a high percentage (40.05%) of blood sugar level, suggesting a propensity to develop diabetes. It has been reported that the patients who were receiving various antipsychotics shown Improvements in symptom but drugs also have adverse effect in weight ($r=0.36$, $p=0.0021$), BMI ($r=0.84$, $p<0.0001$), total-cholesterol ($r=0.31$, $p=0.047$), and LDL cholesterol ($r=0.42$, $p=0.013$), and decreases in HDL cholesterol ($r=-0.35$, $p=0.035$) [17].

There was a significant change in the overall percentage (33.5%) of lipid profile such as TG, HDL, LDL and TC over three months of treatment with the haloperidol and risperidone. The percentage (39.8%) of patients who were treated with haloperidol and olanzapine showed a significant increase in the lipid level suggesting a greater risk of developing metabolic disorder. The mechanism of antipsychotic drugs induced diabetes due to the following reason: (1) direct effect of antipsychotic drugs in causing insulin resistance, (2) insulin resistance due to obesity, and (3) β - cell dysfunction and apoptosis [18].

There is a strong evidence that both conventional and atypical antipsychotic drugs could lead to metabolic disorders. On the basis of a recent meta-analysis, the antipsychotics which are liable to cause metabolic syndrome are amisulpride, quetiapine, clozapine, olanzapine, risperidone, and aripiprazole [19,20]. It has been suggested that the antipsychotic drugs disturb metabolic regulation by interfering both CNS and peripheral system. It has been shown that antipsychotics activate hunger and inhibit satiety centre and also interfere food reward. All these effects could lead to weight gain due to increased energy

intake and decreased energy expenditure with additional alteration with peripheral metabolism [21,22]. The mechanism of weight gain might be due to impairment of glucose and lipid metabolism thereby causing antipsychotic induced metabolic disorder. A meta-analytic study shown that adjunctive metformin is more effective in case of antipsychotic induced dyslipidaemia [23].

In addition it has been found that antipsychotic drugs have a direct effect on liver causing lipogenesis and glucose output. There is also an increase in adipogenesis, lipogenesis and the release of inflammatory cytokines from adipose tissue and also decrease glucose uptake in the skeletal muscles [24,25,26,27]. There are reports that antipsychotic drugs increase the level of prolactin and ghrelin, hormones associated with metabolic dysfunctions. It is also been shown that antipsychotic drugs might alter beneficial hormones like glucagon-like peptide-1 along with the adipokines, leptin and adiponectin leading to metabolic disorder [22].

From the above mentioned mechanism it is well established that antipsychotic drugs could lead to metabolic dysfunction in schizophrenia patient thereby causing increased morbidity and mortality.

5. CONCLUSION

The present study concludes that treatment with antipsychotic drugs like haloperidol and risperidone or olanzapine alters the glucose and lipid metabolism which can ultimately lead to metabolic disorder. To circumvent this condition it is necessary to assess schizophrenic patients glucose and lipid profile periodically by the nurses and physician and also a strategy should be adopted to counteract the metabolic dysfunction produced by antipsychotic drugs.

CONSENT

Informed consent were taken from patients.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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