# METABOLIC SIDE EFFECTS OF HALOPERIDOL AND RISPERIDONE- A SIX MONTHS FOLLOWUP STUDY

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**ABSTRACT**

**BACKGROUND**

To compare and analyse the metabolic side effects of Risperidone and Haloperidol in newly diagnosed drug-naive schizophrenic disorder patients attending Govt. Stanley Medical College Hospital during initial 6 months of therapy.

**MATERIALS AND METHODS**

Newly diagnosed drug-naïve Schizophrenic Patients (n = 60) aged between 18 - 45 years are recruited and randomly allocated into Group A (Risperidone 4 - 6 mg daily) and Group B (Haloperidol 5 - 10 mg daily) after getting informed consent from the patient's family members. Patients are followed up monthly for the occurrence of metabolic abnormalities like weight gain, rise in blood pressure, elevated fasting, post-prandial blood sugar level, dyslipidaemia for a period of 6 months.

**RESULTS**

Risperidone group showed the mean body weight increase from 64.40 to 69.27, SBP/DBP increase from 123.80/79 to 129.90/83.13; FBS/PPBS increase from 100.20/129.30 to 135.40/185.00; TC increase from 177.23 to 206.23; LDL from 124.30 to 158.30; HDL 48.83 to 50.07; TG 133.47 to 197.83: Haloperidol group showed the mean body weight increase from 64.07 to 68.48, SBP/DBP increase from 123.80/79.00 to 124.27/81.67; FBS/PPBS increase from 100.20/129.30 to 119.87/167.10; TC increase from 177.23 to 197.40; LDL from 119.77 to 139.00; HDL remained 48.83; TG 133.47 to 171.40.

**CONCLUSION**

This study showed that patients in both the groups had weight gain, rise in blood sugar, LDL cholesterol and Triglycerides level, but the rise was significant in patients on Risperidone when compared to those on Haloperidol during the 6-month followup.

**KEYWORDS**

Metabolic Side Effects, Drug Naïve Patients, Risperidone, Haloperidol.

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## BACKGROUND

Metabolic syndrome is a cluster of at least three of the five following medical conditions: obesity, elevated blood pressure, hyperglycaemia, high serum triglycerides and low HDL levels. It is associated with the risk of developing cardiovascular disease and type II diabetes in 20% of the general population.[1]

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Some of the studies attributed metabolic syndrome in mentally ill patients to their sedentary lifestyle, lack of exercise and physical work, poor nutrition, chronic stress, smoking as well as abnormalities of hypothalamic pituitary adrenal axis.[2] However, recent studies are trying to evaluate the role of drug treatment on causation of metabolic syndrome in psychiatric patients.

Conventional antipsychotics block the D2 receptors in the mesolimbic dopamine pathway in brain, thereby reducing the positive symptoms of schizophrenia like delusions and hallucinations. But as they are non-specific, they tend to block D2 receptors in all pathways resulting in profound side effects like extrapyramidal symptoms.[3] To overcome these drawbacks and to improve drug adherence, atypical antipsychotics were introduced.

Atypical antipsychotics are effective against both positive and negative symptoms. These drugs are also associated with lower risk of extrapyramidal side effects, as they act by dual serotonin and dopamine antagonism.[4] They enhance patient's quality of life with fewer relapses and reduced hospital stay, number of physician visits and overall care costs.[5]

However, atypical antipsychotics enhance 5HT2C mediated effects on food intake as well as influence lipid and glucose metabolism via disinhibition of prolactin secretion.[6] Thus, they appear to cause metabolic side effects at a greater frequency and increased severity and thereby increase the incidence of metabolic syndrome from 15% in baseline drug naïve schizophrenia patients to 40%, which is twice that of the general population.[7]

Limited number of studies have been done so far regarding the metabolic syndrome in psychiatric patients and the role of atypical antipsychotics in its causation.

To our knowledge, no study related to this aspect of antipsychotics has been reported from India. Hence, this study was carried out to find out the prevalence and monitor the metabolic side effects in patients taking two different antipsychotic agents, i.e. Haloperidol and Risperidone.

**AIM**

To compare and analyse the metabolic side effects of Risperidone and Haloperidol in newly diagnosed drug naive schizophrenic disorder patients attending Govt. Stanley Medical College Hospital during initial 6 months of therapy.

**MATERIALS AND METHODS**

Prospective, comparative, open labelled, parallel grouped study.

**Inclusion Criteria**

Newly diagnosed drug naïve Schizophrenic patients according to WHO ICD-10 criteria aged between 18 - 45 years attending psychiatric OPD, Stanley Medical College Hospital, for the period of 1st January 2016 - 30th June 2016 were recruited after obtaining informed consent.

**Exclusion Criteria**

Patients with previous exposure to antipsychotic drugs, known hypersensitivity to Risperidone, Haloperidol, patients with chronic liver and renal disorders, known diabetic and/or hypertensive patients, patients showing biochemical evidence of dyslipidaemia, patients with abnormal ECG changes, obese patients, patient's family members who are not willing to give informed consent were excluded from the study.

Patients were randomly allocated into Group A and Group B after getting informed consent from the patient family members. The study was conducted after Regional Ethical Committee approval.

Group A: Risperidone 4 - 6 mg daily.
Group B: Haloperidol 5 - 10 mg daily.

Acute schizophrenic patients receive Risperidone 4 - 6 mg bd or Haloperidol 5 - 10 mg bd along with trihexyphenidyl 2 mg bd; during stabilisation phase patients receive Risperidone 4 mg bd and haloperidol 5 mg bd along with trihexyphenidyl; during the maintenance phase patients receive lesser doses according to the degree of improvement. Both groups were supplemented initially with lorazepam or diazepam.

Weight gain, BP and blood sugar were assessed every month and lipid profile was assessed at the end of 3rd month and 6th month during the 6 months duration of the study.

**RESULTS**

**Demographic Profile**

Around 80 newly diagnosed schizophrenia patients were enrolled in the study, which lasted for 9 months. Of which 20 patients lost for followup; 30 patients in Group A who were prescribed Risperidone and 30 patients in Group B who were prescribed Haloperidol were followed up for the emergence of metabolic side effects during the first 6 months of therapy.

| | **Haloperidol** | **Risperidone** |
|---|---|---|
| | **Number and Percentage** | **Number and Percentage** |
| **Education Status** | | |
| Uneducated | 6 (20) | 5 (16.6) |
| Primary School | 10 (33.3) | 12 (40) |
| High School | 9 (30) | 6 (20) |
| Degree | 5 (16.6) | 7 (23.3) |
| **Occupation Status** | | |
| Student | 4 (13.3) | 4 (13.3) |
| Unemployed | 18 (60) | 19 (63.3) |
| Self Employed | 8 (26.6) | 7 (23.3) |
| **Socioeconomic Status** | | |
| Low | 20 (66.6) | 20 (66.6) |
| Lower Middle | 6 (20) | 6 (20) |
| Upper Middle | 4 (13.3) | 4 (13.3) |
| **Marital Status** | | |
| Single | 7 (23.3) | 5 (16.6) |
| Married | 16 (53.3) | 19 (63.3) |
| Separated | 7 (23.3) | 6 (20) |
| **Family H/O Mental Illness** | | |
| Yes | 11 (36.6) | 11 (36.6) |
| No | 19 (63.3) | 19 (63.3) |

***Table 1. Sociodemographic Features between Haloperidol and Risperidone Group***

In this study, 65% were females and 35% were males; 44% of the patients were between 20 - 30 years of age and 56% were between 31 - 45 years.

Of the 60 patients 36% completed primary education, 25% high school education, 20% were degree holders and 19% were uneducated; 62% were unemployed, 25% were self-employed and 13% were students.

In this study 67% of the patients belonged to low socioeconomic status, 20% were from lower middle and 13% were from upper middle status; 58% were married, 20% were single and 22% were separated; 40% had a family history of mental illness and 59% had none.

| | Group | | | | P value |
|---|---|---|---|---|---|
| | Risperidone | | Haloperidol | | |
| | Mean | SD | Mean | SD | |
| Weight - 0 visit | 64.40 | 5.87 | 64.07 | 5.52 | 0.0618 |
| Weight - 3 Months | 66.98 | 6.19 | 66.67 | 5.84 | |
| Weight - 6 Months | 69.27 | 6.07 | 68.48 | 6.04 | |
| SBP 0 visit | 123.80 | 9.20 | 123.80 | 9.20 | 0.332 0.335 |
| DBP 0 visit | 79.00 | 4.88 | 79.00 | 4.88 | |
| SBP 3 Months | 123.80 | 9.20 | 123.80 | 9.20 | |
| DBP 3 Months | 79.00 | 4.88 | 79.00 | 4.88 | |
| SBP 6 Months | 128.90 | 7.08 | 124.27 | 9.74 | |
| DBP 6 Months | 83.13 | 4.83 | 81.67 | 6.69 | |
| FBS 0 visit | 100.20 | 7.82 | 100.20 | 7.82 | 0.000** 0.002* |
| PPBS 0 visit | 129.30 | 8.29 | 129.30 | 8.29 | |
| FBS 3 Months | 119.87 | 11.45 | 109.87 | 7.08 | |
| PPBS 3 Months | 167.77 | 21.38 | 145.70 | 17.09 | |
| FBS 6 Months | 135.40 | 11.80 | 119.87 | 11.45 | |
| PPBS 6 Months | 185.13 | 20.70 | 167.10 | 21.30 | |
| TC 0 visit | 177.23 | 12.00 | 177.23 | 12.00 | 0.094 |
| TC 3 Months | 197.40 | 15.91 | 188.07 | 15.23 | |
| TC 6 Months | 206.23 | 23.49 | 197.40 | 15.91 | |
| LDL 0 visit | 124.30 | 13.89 | 119.77 | 12.09 | 0.000** |
| LDL 3 Months | 139.00 | 9.38 | 124.30 | 13.89 | |
| LDL 6 Months | 158.30 | 16.34 | 139.00 | 9.38 | |
| HDL 0 visit | 48.83 | 4.73 | 48.83 | 4.73 | 0.322 |
| HDL 3 Months | 48.83 | 4.73 | 48.83 | 4.73 | |
| HDL 6 Months | 50.07 | 4.84 | 48.83 | 4.73 | |
| TG 0 visit | 133.47 | 16.79 | 133.47 | 16.79 | 0.006* |
| TG 3 Months | 171.40 | 35.08 | 149.30 | 23.38 | |
| TG 6 Months | 197.80 | 36.93 | 171.40 | 35.08 | |

***Table 2. Statistics, the Weight, BP, Blood Sugar and Lipid Levels were Compared between the Two Groups at the beginning of the Study at 3rd Month and at 6th Month***

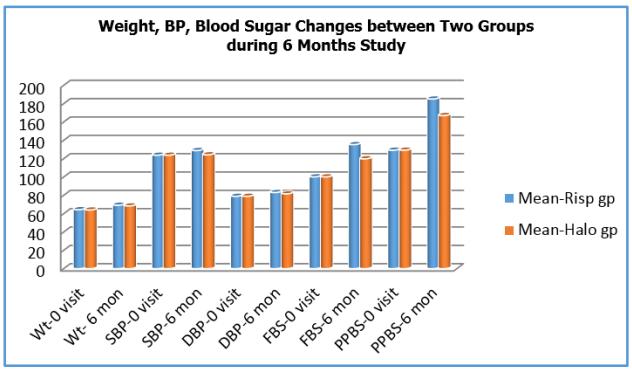


***Figure 1. Weight, BP, Blood Sugar Changes between Two Groups during 6 Months Study***

At the beginning of the study (0 visit), the mean body weight of the Risperidone group was 64.40 and that of haloperidol group was 64.07. By the end of 6 months, it increased to 69.27 and 68.48 respectively with p value of 0.618 which is statistically not significant.

The mean Systolic BP/Diastolic BP in Risperidone group increased from 123.80/79.00 to 128.90/83.13; whereas in Haloperidol group the mean Systolic BP/Diastolic BP increased from 123.80/79.00 to 124.27/81.67 with the p value of 0.332/0.335 which is statistically not significant.

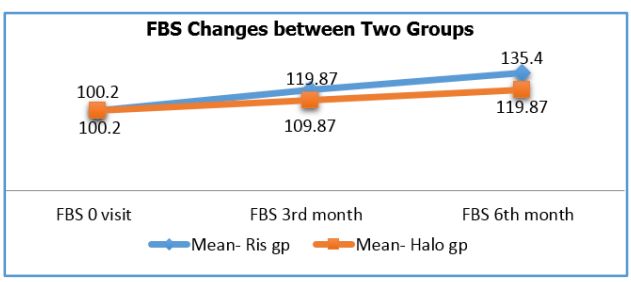


***Figure 2. FBS Changes between Two Groups***

The mean Fasting Blood Sugar levels in Risperidone group at the start of the study was 100.20, at 3rd month it raised to 119.87 and at the end of 6 months it reached 135.40; whereas in haloperidol group the FBS value was 100.20 at the beginning, which gradually raised to 109.87 and 119.87 by 3rd and 6th month.

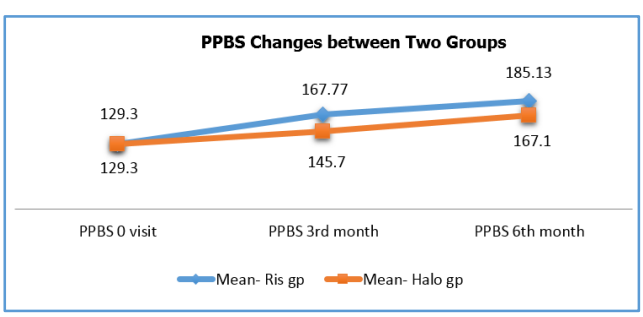


***Figure 3. PPBS Changes between Two Groups***

The mean post prandial blood sugar level in risperidone group at the start of the study was 129.30, which was same as haloperidol group. By 3rd month, it raised to 167.77 in Group A and 145.70 in Group B. At the end of the study, the PPBS values reached 185.13 and 167.10 in Group A and

Group B respectively with the p value of 0.000/0.002, which was statistically highly significant for FBS and significant for PPBS.

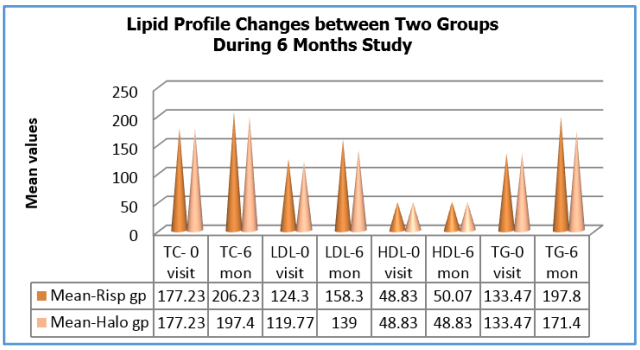


***Figure 4. Lipid Profile Changes between Two Groups during 6 Months Study***

The total cholesterol mean in Risperidone group increased from 177.23 to 206.23 and in Haloperidol group from 177.23 to 197.40 with the p value of 0.094, which is not significant.

The LDL cholesterol mean in Risperidone group increased from 124.30 to 158.30 and in Haloperidol group from 119.77 to 139.00 with the p value of 0.000**, which is highly significant.

The HDL cholesterol mean in Risperidone group increased from 48.83 to 50.07 and in Haloperidol group from 48.83 to 48.83 with the p value of 0.322, which is not significant.

The Triglycerides mean in Risperidone group increased from 133.47 to 197.80 and in Haloperidol group from 133.47 to 171.40 with the p value of 0.006, which is statistically significant.

Intra group analysis was done for Group A and B using Paired sample statistics.

| Parameters | Mean -0 Visit | Mean-6 Months | SD -0 Visit | SD-6 Months | P value |
|---|---|---|---|---|---|
| Weight | 64.40 | 69.27 | 5.870 | 6.068 | <0.01 ** |
| FBS | 100.20 | 135.40 | 7.819 | 11.796 | |
| PPBS | 129.30 | 185.13 | 8.289 | 20.698 | |
| TC | 177.23 | 206.23 | 11.999 | 23.494 | |
| LDL | 124.30 | 158.30 | 13.894 | 16.335 | |
| TG | 133.47 | 197.80 | 16.788 | 36.935 | |

***Table 3. Paired Sample Statistics- Risperidone-Intra Group Analysis***

The rise in mean weight (64.40 to 69.27), FBS (100.20 to 135.40), PPBS (129.30 to 185.13), TC (177.23 to 206.23), LDL (124.30 to 158.30) and TG (133.47 to 197.80) was statistically significant in Risperidone group with a p value of < 0.01.

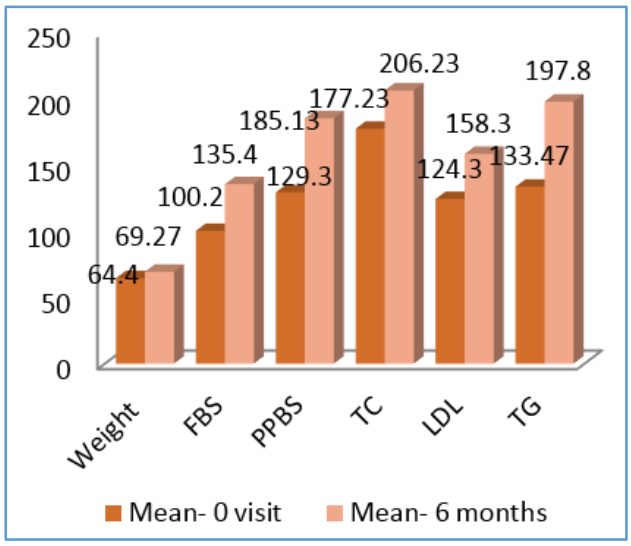


***Figure 5. Risperidone-Intra Group Analysis***

| Parameters | Mean- 0 Visit | Mean- 6 Months | SD- 0 Visit | SD- 6 Months | p value |
|---|---|---|---|---|---|
| Weight | 64.07 | 68.48 | 5.521 | 6.038 | < 0.05* |
| FBS | 100.20 | 119.87 | 7.819 | 7.084 | |
| PPBS | 129.30 | 167.80 | 8.289 | 21.30 | |
| TC | 177.23 | 197.40 | 11.999 | 15.915 | |
| LDL | 119.77 | 139.00 | 12.091 | 9.381 | |
| TG | 133.47 | 171.40 | 16.788 | 35.080 | |

***Table 4. Paired Sample Statistics- Haloperidol-Intra Group Analysis***

The rise in weight gain (64.07 to 68.48), FBS (100.20 to 119.87), PPBS (129.30 to 167.80), TC (177.23 to 197.40), LDL (119.77 to 139.00) and TG (133.47 to 171.40) was significant in haloperidol group, though not to the extent seen in risperidone group.

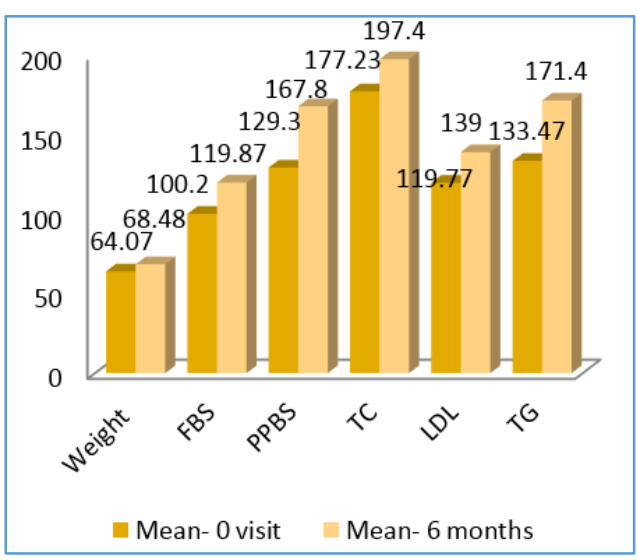


***Figure 6. Haloperidol-Intra Group Analysis***

## DISCUSSION

Metabolic syndrome, as of now is considered to be caused by variety of factors. As stated by Shiv Gautham and Parthi Singh in their study, most of excess mortality in schizophrenia is attributable to physical illness with cardiovascular being the major contributor.[8]

Persons with schizophrenia were reported to have twice likely chance of developing cardiovascular accidents than the general population. Though schizophrenia per se has risk of insulin resistance and cardiovascular complications, the role of antipsychotics to this contribution was described by Jonathan M. Ameil in his study "Addressing cardiometabolic risk during treatment with antipsychotic medications."[9]

In our study both the groups during the 6 months followup period showed mild increase in body weight with no significant change in systolic and diastolic BP. Highly significant rise in fasting blood sugar and significant rise in postprandial blood sugar levels were seen in Risperidone group similar to one such study by John Newcomer, where he observed the changes in fasting blood glucose levels in schizophrenia patients treated with atypical antipsychotics were more significant than typical antipsychotics.[10]

Regarding lipid profile, Risperidone group showed highly significant rise in LDL cholesterol levels and significant rise in Triglycerides than Haloperidol group similar to a study conducted by Moreno et al.[11]

In our study apart from comparing the emergence of metabolic side effects in patients on risperidone and haloperidol, intra group analysis was also done which also showed significant rise in these levels, but the rise was statistically more significant in Risperidone group than in Haloperidol group.

### Limitations

The sample size was small. Though family history of psychiatric illness was taken, specific importance to presence of chronic metabolic disorders have not been elicited.

## CONCLUSION

This study showed that patients in both the groups had weight gain, rise in blood sugar, LDL cholesterol and Triglycerides level, but the rise was significant in patients on Risperidone when compared to those on Haloperidol during the 6-month followup.

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