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Original Article

METFORMIN IN THE PREVENTION OF METABOLIC SYNDROME ASSOCIATED WITH INITIATION OF ATYPICAL ANTIPSYCHOTIC THERAPY IN ADOLESCENTS AND YOUNG ADULTS-A RANDOMIZED, OPEN LABELLED, SINGLE CENTERED STUDY

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ABSTRACT

Objective: The aim of the study was to evaluate the effectiveness and safety of Metformin along with Risperidone to prevent antipsychotic-induced metabolic syndrome in first-episode schizophrenia patients.

Methods: This was a randomized, open labelled, prospective study conducted in the Department of psychiatry, Tirunelveli medical college. Around 96 patients diagnosed with first episode schizophrenia were randomized into 2 groups. Group 1 patients were given T. Risperidone (2 mg twice daily, n=48) and group 2 patients were given T. Metformin (500 mg twice daily, n=48) along with T. Risperidone for 6 mo.

The primary endpoint assessed was the proportion of patients developing metabolic syndrome at the end of 6 mo in both the groups. The secondary endpoints were the changes in body mass index (BMI), waist circumference (WC), fasting blood sugar (FBS) and triglycerides (TGL) from baseline to the end point.

Results: There was a significant reduction in BMI and WC at the end of 3 mo ($p<0.001$) and at the end of 6 mo ($p<0.001$) when compared to baseline in group II individuals. There was a significant reduction in FBS and TGL levels at the end of 6 mo of treatment ($p<0.001$) in group II individuals. There was the significant statistical difference between both the groups ($p<0.05$) in terms of BMI, WC, FBS, triglycerides. The treatment emergent adverse effects with Metformin were generally mild and did not lead to any discontinuation.

Conclusion: The use of Metformin along with Risperidone may have a better impact on the long-term cardiovascular morbidity and mortality of the schizophrenia patients.

Keywords: Schizophrenia, Metabolic syndrome, Atypical antipsychotics, Body mass index, Waist circumference, Fasting blood sugar, Triglycerides

INTRODUCTION

Schizophrenia is a debilitating brain disorder characterized by a chronic remitting and relapsing course of psychosis that is superimposed on persistent "deficit" features such as negative symptoms and cognitive dysfunction [1]. It has a worldwide prevalence [2] of 1% and is considered the prototype disorder for understanding the phenomenology of psychosis [3]. It is associated with a high morbidity and mortality resulting from strikingly high suicide rate of 10 % [4].

The introduction of Chlorpromazine in the late 1950s transformed and formed a new frontier in the clinical management of Schizophrenia. Initially, "conventional neuroleptics" were developed during that era, and they were found to control effectively and improve the disease symptomatology but were also associated with major drawbacks that include Parkinsonian-like movement disorders.

As a result, of these side effects, newer neuroleptics (termed "atypical antipsychotics") were introduced into clinical use [4]. Despite the concerns over extrapyramidal side effects and tardive dyskinesia are less with these groups of drugs, there has been a co-occurrence of atherogenic dyslipidemia with abdominal adiposity, impaired fasting glucose, insulin resistance or overt Diabetes Mellitus, and Hypertension that constitutes the cluster of clinical features known as the Metabolic syndrome [1].

Risperidone, which comes under the group of atypical antipsychotics, is a benzisoxazole derivative [5]. According to Clinical Antipsychotic Trials of Intervention Effectiveness study (CATIE study), 14% of patients receiving Risperidone had been found to have more than 7% increase in weight from baseline [1]. Also, a meta-analysis by Allison and coworkers has estimated that the mean increases in weight with Risperidone to be 2.1 kg [6]. It has been assumed that increased appetite and central Histamine H_1 antagonism along with the alteration of insulin sensitivity and direct impairment of metabolic dysregulation might be the underlying cause of weight gain [7]. These metabolic derangements not only affect the compliance but inevitably also are associated with substantial morbidity (Cardiovascular disease, Hypertension, and Diabetes) and mortality [8].

Lifestyle changes are found to be the safe and effective means of controlling weight in patients taking these drugs. However, these sorts of behavior and dietary modifications are difficult to be instituted in subjects with neuropsychiatric disorders [9].

Metformin, a member of the biguanide class of Oral hypoglycemic agents, increases storage of glycogen in skeletal muscles, lower rates of production of hepatic glucose, increases the sensitivity of insulin thereby reducing blood glucose levels [10]. In view of stemming down the metabolic derangements due to atypical antipsychotics and also due to the paucity of studies using Metformin along with Risperidone in our population, the present study has been designed to evaluate the effectiveness and safety of Metformin along with Risperidone in preventing antipsychotic-induced Metabolic syndrome in first-episode schizophrenia patients.

MATERIALS AND METHODS

Ethical consideration

The study was commenced after getting approval from the Institutional Ethical Committee [Ethical committee number: 309/PHARM/IEC/2013 dated 13/3/2013]. Written informed consent was obtained in the local vernacular language from every patient (or) his reliable caregiver before enrollment.

World health organization (WHO) clinical criteria for metabolic syndrome [11]

Insulin resistance, identified by one of the following

a) Impaired fasting glucose
b) Type 2 diabetes
c) Impaired glucose tolerance

Plus any two of the following

a) Plasma triglycerides ≥ 1.7 mmol/l
b) Antihypertensive medication and/or high blood pressure (≥140 mm Hg systolic (or) ≥ 90 mm Hg diastolic)
c) BMI>30 kg/m^2 and/(or) waist: hip ratio>0.9 in men,>0.85 in women
d) Urinary albumin excretion rate ≥ 20 µg/min (or) albumin: creatinine ratio ≥ 3.4 mg/mmol
e) HDL cholesterol<0.9 mmol/l in men (or)<1.0 mmol/l in women.

Study design

Open-labelled, randomized, prospective, comparative, single centered, parallel group study.

Study duration

Between March 2013-February 2014.

Study Centre

Department of Psychiatry, Tirunelveli Medical College Hospital, Tirunelveli.

Sample size

Total of 96 patients (48 in each group).

Inclusion criteria

1. Patients with 18 to 40 y of age who have been diagnosed with first episode schizophrenia based on Diagnostic and Statistical Manual of Mental disorders (DSM)-IV criteria and on treatment with T. Risperidone 2 mg twice a day for ≤ 2 mo.

Exclusion criteria

1. Uncooperative and aggressive patients

2. Patients with suicidal tendency

3. Pregnant and lactating women

4. Patients with history of liver disease/renal disease/ cardiovascular disease/diabetes mellitus/hypertension/ dyslipidemia/ substance abuse/seizure disorder/malignancy

5. Patients with diagnosis other than schizophrenia

6. Patients with mental retardation

7. Patients who are taking other drugs that may affect body weight (Carbamazepine, Lithium, and Topiramate, antidepressants, Valproate and hormone replacement therapy).

8. Patients on a special diet and who do exercise for weight loss

Screening

Based on the inclusion and exclusion criteria, the subjects were enrolled in the study after initial screening. Initial screening at baseline included clinical assessment, anthropometric measurements like weight, height and waist circumference and laboratory investigations like complete blood count, fasting blood sugar, serum urea, serum creatinine, liver function tests, routine urine analysis and fasting lipid profile.

Randomization and enrollment

Subjects who were initiated on T. Risperidone 2 mg orally twice daily for≤ 2 mo for first-episode schizophrenia were randomized using computer-generated table into two groups.

Group 1: Patients were given T. Risperidone 2 mg alone, orally, twice daily after food.

Group 2: Patients were given T. Metformin 500 mg orally, twice daily after food along with T. Risperidone.

T. Risperidone and T. Metformin remained at a fixed dose as baseline levels throughout the course of treatment. All subjects were under the care of another adult caregiver (or) their parents who monitored and recorded drug intake every day to confirm adherence.

Concomitant medications

Only T. Trihexyphenidyl (5-10 mg/day) for extrapyramidal symptoms (or) T. Lorazepam (1-3 mg/day) for insomnia (or) agitation were given when needed.

Compliance

The compliance in both the group of patients was assessed using a pill count. Patients were asked to return the empty strips when they come for receiving the drugs.

Efficacy parameters

Primary endpoint

A. The proportion of patients is developing metabolic syndrome at the end of 6 mo in both the groups.

Secondary endpoints

A. Changes in waist circumference (WC) from baseline to the endpoint (after 6 mo of treatment).
B. Changes in body mass index (BMI) from baseline to the end point.
C. Changes in fasting blood sugar (FBS) from baseline to the endpoint.
D. Changes in fasting triglycerides (TGL) from baseline to the endpoint.

All the above parameters were assessed in the fasting state. Fasting was confirmed with patients (or) caregivers at the time of assessment.

Parameter assessment

Body mass index measurement

Height

All subjects were instructed to remove their shoes and socks before the procedure. Subjects were instructed to stand on a level floor with the feet parallel and pointing forwards. Subjects were asked to stand unsupported by not touching the nearby wall (or) furniture. Subjects were asked to stand as tall as possible such that the lower border of the left orbit and the upper margin of the external auditory meatus remain horizontal. Subjects were instructed to breathe out gently during the measurement. The measure was placed on the subject's head to ensure that the spirit level is balanced. The measured height was expressed in centimeters.

Weight

The subjects were instructed to remove the shoes, excess clothing, and overcoats. Pockets containing keys and wallet were emptied. Any heavy jewelry worn by the subject was removed. Weight was measured using a manual weighing scale. The weighing scale platform was placed on an even floor surface. Before the subject stepped onto the platform, it was ensured that the viewfinder displayed [0.0] before the measurement. The subjects were instructed to stand still on the scale's platform. Subjects were asked to stand free without leaning on a chair (or)wall. Subjects were instructed to exhale gently during the measurement. The weight was measured in kilograms. Once the weight was recorded, the subjects were instructed to stand off the platform and re-apply them over clothes and shoes.

BMI calculation

BMI (or) Quetelet index was calculated using the formula.

[Weight (kg)/(height (m)) ^{2}]. BMI was graded as follows.

Underweight-<18.5

Normal-18.5 to 25

Overweight-25 to 30

Obese->30.

Waist circumference

The subjects were instructed about the procedure and permission acquired to remove the clothing as it may restrict the accurate measurement. A flexible measuring tape was used to measure the waist circumference in standing position. It was ensured that the tape was neither tight nor loose such that it fits snugly. Subjects were instructed to breathe out normally during the measurement, and the waist circumference was measured at a point midway between the lowest rib and greater trochanter with the subject's hands placed loosely by the side. Waist circumference was rounded off to nearby whole number and expressed in centimeters.

Blood investigations

Patients were previously instructed to come for follow-up visits with 10 h of fasting. The subjects were made to sit comfortably in a chair and informed about the procedure. After sterilizing our hands up to the elbows, a tourniquet was placed 3 to 4 inches above the selected puncture site neither tight nor too loose in the subjects not longer than 1 minute. Then after wearing the non-latex glove, the vein was palpated, and the area above it was cleaned, and air dried. The subject was asked to make a fist and the arm was firmly grasped to make the skin taut, and vein anchored such that at an angle of 15-30 degrees with the arm surface, the needle was inserted, and 2 ml of blood was withdrawn. Blood was collected in a sterilized, dry container for further investigation. Using the sample as obtained above, fasting blood sugar levels and fasting triglyceride levels were assessed using the autoanalyzer.

Follow up visits

Follow-up was done at the end of 3rd and 6th months of starting the treatment. Patients were reminded of their follow-up visits by a telephone call on the previous day. During the follow-up, anthropometric measurements such as weight, height, and waist circumference were recorded and fasting blood samples were taken to assess the blood sugar and triglycerides. Patients were given a diary after enrollment to record the adverse effects, and the diary was checked at every follow-up visit. Patients were also enquired about the use of concomitant medications through 3 and 6 mo.

Statistical analysis

Statistical analysis was performed with the help of statistical package SPSS (Statistical Package for the Social Sciences) version 11.

1. Baseline characteristics of both the groups were tabulated by descriptive statistics (mean, standard deviation) and frequency table. They were matched by unpaired student 't' test and Pearson's chi-square test.

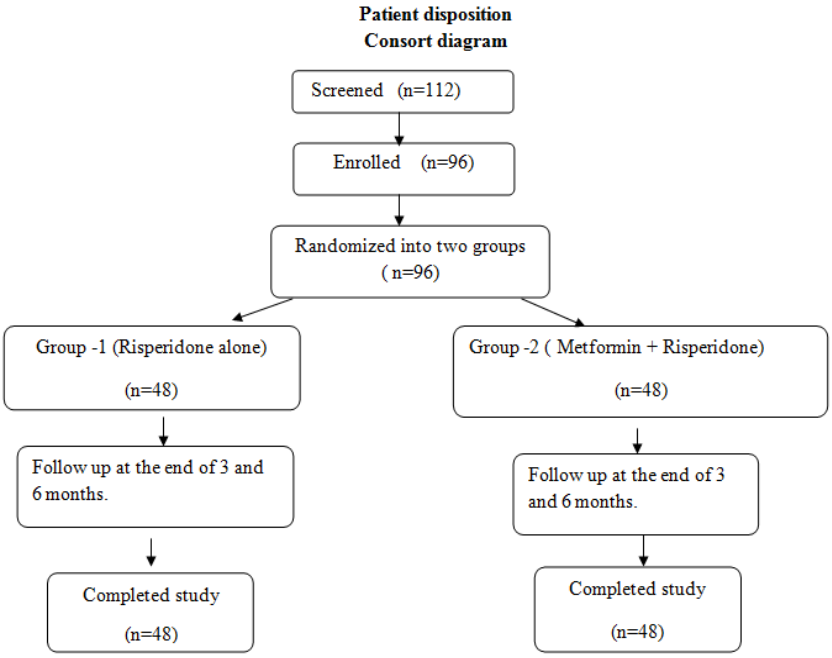
2. Between-group analysis was done using unpaired student 't' test at baseline, 3 mo and 6 mo.

3. The student paired 't' test was applied for analysis and interpretation within the group at varying intervals as mentioned above.

4. The categorical variable (development of metabolic syndrome) between two groups was compared by Chi-square test.

5. Adverse events were expressed in percentage.

The p values less than 0.05 ($p<0.05$) was considered as significant in two-tailed conditions.



RESULTS

For a period of one year from March 2013 to February 2014, around 112 patients newly diagnosed with schizophrenia were initially screened. Based on the inclusion and exclusion criteria, around 96 patients were enrolled for the study. They were randomly assigned through the computer generated table into 2 groups receiving either Risperidone alone (or) Metformin along with Risperidone. All the patients completed the study, and the results were analyzed.

Baseline characteristics

Baseline characteristics were similar in both the groups ($p>0.05$) except that the patients in group II had higher BMI levels ($p<0.001$) and larger waist circumference levels ($p=0.04$) (table 1).

Primary end point

According to the WHO criteria for metabolic syndrome [11], it was found that 10 patients in group I developed metabolic syndrome and 1 patient in group II developed metabolic syndrome. The Pearson

Chi-Square test was used to test the association between the two groups, and the p-value was found to be<0.05 implying a significant difference between the groups (table 2).

Secondary end points

There was a significant reduction in waist circumference at the end of 3 mo (p<0.001) and at the end of 6 mo (p<0.001) when compared to baseline with group II individuals (table 3).

Table 4 shows the statistical difference in waist circumference levels between both the groups at the end of 3 mo (p<0.001) and at the end of 6 mo (p<0.001). There was a significant reduction in BMI at the end of 3 mo when compared to baseline (p<0.001) in group II individuals. Also, the BMI reduction at the end of 6 mo with respect to baseline was also statistically significant (p<0.001) (table 5).

There was a significant statistical difference between both the groups at the end of 3 mo(p<0.001) and at the end of 6 mo (p<0.001) in terms of BMI (table 6).

Table 7 demonstrates a significant reduction in FBS levels at the end of 6 mo of treatment (p<0.001) in group II individuals.

There was a statistical difference in FBS levels between both the groups at the end of 3 mo (p<0.001) and at the end of 6 mo of treatment (p<0.001) (table 8).

Table 9 demonstrates no significant changes in TGL levels at the end of 3 mo (p=0. 49) with respect to baseline in Metformin group.

However, there was a significant reduction in TGL levels at the end of 6 mo (p<0.001) in group II individuals.

Table 10 shows a significant rise in TGL levels at the end of 6 mo compared to baseline in the group I individuals and similarly Metformin along with Risperidone has significantly caused a reduction in TGL levels at the end of 6 mo in group II individuals signifying the existence of a statistical difference between both the groups.

Table 1: Baseline characteristics

Baseline parameters		Group 1 (n=48)	Group 2 (n=48)	P value
Age (in yrs)		29.69±5.78	28.75±4.56	0.88
Gender	Male	26 (54)	28 (46)	0.68
	Female	22 (46)	20 (54)	
BMI (Kg/cm$^{2)}$		22.61±4.03	26.29±4.57	<0.001*
WC (Cms)		84.48±12.17	89.69±13.25	0.04*
FBS (Mg%)		90.46±23.47	99.52±30.54	0.1
TGL (Mg%)		146.42±66.26	164.10±81.64	0.25

n= Number of patients; 48 patients in each group; Data are expressed as mean values, with plus-minus values as standard deviation (SD), or as numbers with percentages in parentheses; P value finds by fishers exact test or by unpaired T-test; *Statistically significant; BMI-Body Mass Index; WC-Waist Circumference; FBS-Fasting Blood Sugar.

Table 2: Proportion of patients developing metabolic syndrome at the end of 6 mo in both the groups

Groups	Yes	No	P value
Group I	10	38	0.01*
Group II	1	47	

*Statistically significant.

Table 3: Change in waist circumference in group II patients (Risperidone+Metformin) with respect to baseline

Time	Mean	C. I	P value
Baseline	89.7	-	-
End of 3 Months	89	(-0.9 to-0.4)	<0.001*
End of 6 Months	87.8	(-2.3 to-1.6)	<0.001*

C. I-Confidence interval; *Statistically significant.

Table 4: Comparison of change in waist circumference from baseline between group I and group II.

Visits	Groups	Mean difference from baseline	C. I	P value
End of 3	Group I	2.50	(2.4 to 4)	
Months	Group II	-0.67		<0.001*
End of 6	Group I	3.75	(5 to 6.4)	
Months	Group II	-1.94		<0.001*

C. I-Confidence interval; *Statistically significant.

Table 5: Change in body mass index in group II patients with respect to baseline

Time	Mean	C. I	P value
Baseline	26.3	-	-
End of 3 Months	25.5	(-0.9 to-0.6)	<0.001*
End of 6 Months	24.8	(-1.8 to-1.3)	<0.001*

C. I-Confidence interval; *Statistically significant.

Table 6: Comparison of change in BMI from baseline between group I and group II

Visits	Groups	Mean difference from baseline	C. I	P value
End of 3	Group 1	0.99	(1.4 to 2)	
Months	Group 2	-0.71		<0.001*
End of	Group 1	1.93	(3.1 to 3.9)	<0.001*
6 Mo	Group 2	-1.53		

C. I-Confidence interval; *Statistically significant.

Table 7: Change in fasting blood sugar levels in group II patients with respect to baseline

Time	Mean	C. I	P value
Baseline	99.5	-	-
End of 3 months	102	(-2 to 7.1)	0.28
End of 6 Months	94	(-10 to-1.3)	<0.001*

C. I-Confidence interval; *Statistically significant.

Table 8: Comparison of change in fasting blood sugar levels from baseline between group I and group II

Visits	Groups	Mean difference from baseline	C. I	P value
End of 3 mo	Group 1	15.81	(6.3 to 20.3)	<0.001*
	Group 2	2.52		
End of 6 mo	Group 1	28.04	(26.3 to 41)	<0.001*
	Group 2	-5.58		

C. I-Confidence interval; *Statistically significant.

Table 9: Change in fasting triglyceride levels in group II patients with respect to baseline

Time	Mean	C. I	P value
Baseline	164.1	-	-
End of 3 Months	161.5	(-10 to 4.8)	0.49
End of 6 Months	150.3	(-19.8 to-7.7)	<0.001*

C. I-Confidence interval; *Statistically significant.

Table 10: Comparison of change in fasting triglyceride levels from baseline between group I and group II

Visits	Groups	Mean difference from baseline	C. I	P value
End of 3	Group 1	36.83	(22 to 57.1)	<0.001*
Months	Group 2	-2.58		
End of 6	Group 1	45.21	(43 to 75.1)	<0.001*
Months	Group 2	-13.77		

C. I-Confidence interval; *Statistically significant.

Adverse effects

Metformin was tolerated well by the study participants. The treatment emergent adverse effects with Metformin were mainly gastrointestinal side effects such as diarrhea and gastritis. They were reported by 5% of patients and were transient. It did not lead to the discontinuation of the drug. There were no reports suggestive of lactic acidosis (or) hypoglycemia.

DISCUSSION

Atypical antipsychotics are commonly used for managing schizophrenia spectrum disorders nowadays. However, their benefit-to-risk ratio is challenged by metabolic abnormalities and weight gain [12]. Adherence to medications is difficult and also physical interventions may not be possible in psychiatric patients. Net weight loss in chronic patients who have undergone indeterminate weight gain seems to be more difficult. But weight gain mitigation at early stages of treatment seems to be more easy and clinically advantageous. Adverse cardiometabolic effects of atypical antipsychotics may be minimized by several strategies such as a) healthy lifestyle intervention [13], b) switching to lower risk antipsychotics [14] and c) the addition of medication that may reduce body weight and/(or) lipid and glucose parameters [15].

Metformin has a well-established safety profile in both adolescents and young adults in contrast to the other weight reducing drugs which have potentially serious adverse effects. Importantly, Metformin is not metabolized by hepatic P_{450} enzymes. Hence significant drug-drug interactions are not reported. Also, there exist no specific interactions with antipsychotic medication [16]. Hence, the present study was aimed to evaluate the effectiveness and safety of Metformin along with Risperidone in preventing the occurrence of antipsychotic-induced metabolic syndrome in first-episode schizophrenia patients.

With regard to the primary endpoint, the development of metabolic syndrome was assessed in both the group of patients using the WHO criteria [11] for metabolic syndrome. Ten patients (21%) in group I and One patient (2%) in group II developed metabolic syndrome, thereby implying that Metformin seems to be effective in reducing the incidence of metabolic syndrome.

The secondary endpoints in our study were the individual components of metabolic syndrome (Changes in WC, BMI, FBS and TGL). Waist circumference has a better correlation with abdominal fat and is strongly associated with cardiovascular risk factors when compared to other parameters [17]. The increase in waist

circumference of every 2 inches is associated with an increase in mortality by 17% in men and 13% increase in women.

Recent studies suggest that the ability of subcutaneous fat depots to store excess energy is limited. This results in an "overflow" of excess energy to 'ectopic sites' such as skeletal muscle and liver and intra-abdominal adipose tissue. This excessive ectopic fat eventually leads to metabolic dysfunction in organs and so increase in intramuscular fat is found to be associated with skeletal muscle insulin resistance [18] and an increase in intrahepatic fat is associated with hepatic insulin resistance [19].

Metformin suppresses appetite and causes satiety through an increase in insulin sensitivity and reduction in hyperinsulinemia. GLP-1 (uncertain) released from L cells in the intestine via glucose-dependent insulin secretion lowers blood glucose levels and promotes satiety by slowing gastric emptying. In a study by Mannuci *et al.*, it was found that the reduced intake of food and weight loss in Metformin treated subjects might be related to the increase in GLP-1 levels [20].

In our study, within the group, group II showed mean waist reduction of (-1.9 cms) from the baseline at the end of 6 mo. This implies that the waist circumference reduction by Metformin will have a positive impact in preventing metabolic syndrome.

Waist circumference is a marker of central obesity, whereas BMI is a measure of overall adiposity [17]. BMI is strongly associated with cardiovascular mortality, which is partially due to the effect of obesity on lipoprotein metabolism, blood pressure and insulin resistance [21]. However, cardiovascular disease is better predicted by BMI coupled together with WC than with the BMI alone [22]. In our study, mean baseline BMI value got reduced from 26.29 to 25.5 at 3 mo and 24.8 at 6 mo of treatment. These results were similar to the study conducted in the USA by Morrison *et al.* which demonstrated significant (2.22 kg/m^2) reduction in BMI with Metformin in children taking Risperidone, Olanzapine, Quetiapine (or) Valproate [23]. Hence, both BMI and WC play a crucial role in the assessment of metabolic syndrome [17] and Metformin along with Risperidone has been found to decrease both waist circumference and BMI suggests its importance in the prevention of metabolic syndrome.

As we all know about the microvascular and macrovascular complications associated with long-term hyperglycemia, normalization of fasting blood sugar levels at the earliest is considered wise in the prevention of metabolic syndrome. In our study, fasting blood sugar levels did not show any statistical difference at 3 mo of treatment (p=0. 28) which was comparable to the results of the study by Carrizo *et al.* that interpreted that Metformin had no significant effect on FBS compared with placebo at 14 w of treatment [24]. But in our study at 6 mo of treatment, there was a significant reduction in FBS (p<0.001). This result was similar to the double-blind, placebo-controlled study conducted by Baptista *et al.* showing a significant FBS reduction after Metformin addition (p=0. 02) [25].

Elevated triglycerides along with increased waist circumference are termed as hypertriglyceridemic waist, which is found to have an association with arteriographic cardiovascular disease (CVD) [26]. Also, TG elevation is found associated with stroke and MI risk in National Health and Nutrition Examination Survey (NHANES)-III [27]. Metformin increases AMP-dependent Protein Kinase (AMPK) and hormone sensitive lipase activities in brown adipose tissue thereby lowering TGL by enhancing uptake of Very Low-Density Lipoprotein (VLDL)-TGL, lipolysis of intracellular TGL and subsequent fatty acid oxidation by mitochondria [28].

In our study, fasting triglyceride levels did not differ statistically at 3 mo when compared to baseline (p=0. 49) in group II individuals. However, the mean triglyceride level (164.1 mg%) at baseline dropped down (150.3 mg%) at 6 mo, suggesting there was the significant statistical difference at 6 mo (p<0.001). This result was similar to the study conducted by Shin *et al.* which showed a significant reduction in triglyceride levels after 12 w of treatment with Metformin [29].

Thus, our study has shown that Metformin is effective and safe in preventing the occurrence of the antipsychotic-induced metabolic syndrome in adolescents and young adults with first-episode schizophrenia.

Our study has some Limitations. First, as the duration of study is only 6 mo, we do not know whether the improved BMI, WC, FBG and TGL levels could be sustained.

Second, all our study participants were cared by their caregivers (or) parents and hence they could have better adherence with Metformin when compared to patients living independently with schizophrenia.

Hence, due to the feasibility of Risperidone and Metformin in our hospital setting and due to the paucity of trials using both these drugs, we conducted this study using Metformin and Risperidone. Further studies with more number of patients, long-term follow up and Metformin along with lifestyle intervention would provide more appealing results regarding the efficacy and safety of Metformin for the prevention of antipsychotic-induced metabolic syndrome.

CONCLUSION

To conclude, the use of Metformin along with Risperidone was safe and effective in the prevention of metabolic syndrome induced by atypical antipsychotics. This may have a better impact on the long term cardiovascular morbidity and mortality of the schizophrenia patients.

CONFLICTS OF INTERESTS

Declare none

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