ORIGINAL RESEARCH PAPER

Psychiatry

METABOLIC SYNDROME IN PATIENTS WITH PSYCHOSIS USING SECOND-GENERATION ANTIPSYCHOTICS

KEY WORDS:

Dr. Sarath Chandra Ivaturi Associate Professor, Department of Psychiatry, Katuri Medical College and Hospital, Guntur.

Dr. Sri Ramya* Assistant Professor, Department of Psychiatry, Katuri Medical College and Hospital, Guntur. *Corresponding Author

Dr. Syed Zainab Junior Resident, Department of Psychiatry, Katuri Medical College and Hospital, Guntur.

ABSTRACT

Background: Persons with Schizophrenia are more likely to die from cardiovascular illness and are at a greater risk of developing obesity, diabetes mellitus (DM), hypertension (HTN), and dyslipidemias. Though the SGA were quite effective, their safety advantages have been questioned because of their propensity to induce weight gain and alter glucose, lipid metabolism.

Objectives:

1. To study the incidence of metabolic syndrome (MS) due to selected SGA
2. To compare any differences in the metabolic profile of patients on various antipsychotics.

Methodology: A Study was done for about a year among 120 Drug Naive patients with the diagnosis of schizophrenia or acute psychosis as per ICD 10 criteria, attending psychiatry OPD and were selected by systematic sampling method into four groups. With the Group (A) receiving Olanzapine, group (B) Risperidone, group (C) Quetiapine, group (D) Aripiprazole. Each group consisting of 30 patients. After 12 weeks of medication, Patients were screened for the MS using NCEP- ATP III criteria. Data was collected and analyzed using SPSS software, ANOVA was used to assess the significance of the difference of mean values of different parameters in between groups.

Results: In the study concerning age group, majority of patients belong to 20-30(41.67%) yrs. There were no significant gender differences with 54.17% males and 45.80% females. Among 120 patients, 13(10.83%) patients developed MS after three months of continuous antipsychotic drug therapy. Among those who received Olanzapine and Risperidone, five patients from each group developed MS, and three patients who received Quetiapine fulfilled the criteria of MS. No patient on Aripiprazole developed MS.

Conclusion: The psychiatrist needs to be aware of the potential metabolic side effects of antipsychotic medication and to include them in the risk/benefit assessment when choosing a specific antipsychotic. Multidisciplinary assessment of psychiatric and medical conditions is needed.

INTRODUCTION:

Patients suffering from schizophrenia have about a 20 percent reduction in life expectancy and are at a greater risk of developing obesity, type 2 diabetes mellitus (DM), Hypertension (HTN) and dyslipidemias.

Second-generation antipsychotics (SGA) are safer and more efficacious than FGA in reducing negative symptoms. Though the SGA were quite effective, their safety advantages have been questioned because of their propensity to induce weight gain and alter glucose and lipid metabolism.[1]

The etiology of metabolic syndrome in psychiatric patients is multifactorial that can be by the disease itself or can be associated with lifestyle, dietary habits, antipsychotic drug therapy.

The present study was taken up to compare the incidence of MS and its constituents on drug-naive schizophrenics on various SGA.

AIMS and OBJECTIVES:

1. To study the incidence of metabolic syndrome due to selected second-generation antipsychotics.
2. To compare any differences in the metabolic profile of patients on various antipsychotics.

METHODOLOGY:

After obtaining ethics committee clearance, the study was done for about a 1year period from August 2020 to August 2021 at the Department of Psychiatry, Katuri Medical College and Hospital, Guntur.

120 Drug naive patients with the diagnosis of schizophrenia or acute psychosis as per ICD 10 criteria attending psychiatry OPD were sampled systematically and were assigned into four groups A, B, C&D with the 1st Group(A) receiving Olanzapine, 2nd group (B) receiving Risperidone, 3rd group (c) receiving Quetiapine, 4th group(D) Aripiprazole. Each group consisted of 30 patients.

Patients receiving more than one antipsychotic medication; Patients with a known diagnosis of type 1 or type 2 DM and HTN; history of alcohol dependence or any major endocrine disorder and patients on treatment for any severe medical or surgical illness; Pregnant and lactating women; Non-complying patients were not included in the study.

After obtaining written informed consent from the patients and informants, Particulars and history were obtained using study proforma.

The patient's blood was collected after fasting state (overnight fast of 12 – 14hours) for lipid studies and fasting blood glucose. Waist circumference was measured and noted, blood pressure was recorded, and the blood sample was collected and sent to The Department of biochemistry KMC&H for baseline measurement.

After 12 weeks of antipsychotic medication, Patients were screened for the metabolic syndrome using NCEP- ATP III criteria[2] (National Cholesterol Education Program, Adult Treatment Panel III) which are as follows:

a. Central obesity: Waist circumference ≥ 102cm and ≥ 88cm respectively in males and females.
b. Hypertriglyceridemia: Triglycerides ≥ 150 mg/dl
c. Low High density lipoprotein(HDL) cholesterol: < 40

mg/dl and < 50mg/dl respectively in males and females.

d. Hypertension: Blood pressure ≥ 130mmHg systolic or ≥ 85mmHg diastolic.
e. Fasting plasma glucose ≥ 100mg/dl.

Statistical Analysis:

The data was analyzed using SPSS software version 17.0. Descriptive results were expressed as mean and SD of various parameters in different groups.ANOVA was used to assess the significance of the difference of mean values of different parameters in between groups. A Chi-square test was done for the comparison of distribution between the groups. P-value was used to calculate the significance in between groups. P <0.05 was considered as significant and P> 0.05 was considered as non-significant.

RESULTS:

Table 1 Socio-demographic variables of the study sample.

Variable	Number	Percentage%
Age (in years)		
21-30	50.00	41.67
31-40	38.00	31.67
41-50	23.00	19.17
>51	9.00	7.87
Gender		
Male	65	54.17
Female	55	45.83
Occupation		
Employed	59	49.17
Unemployed	61	50.83
Education		
Uneducated	37	30.83
6th class	62	51.67
10th class	12	10.00
Graduation	9	7.50
Marital status		
Unmarried	79	65.83
Married	13	10.83
Separated/divorced	28	23.33
Socioeconomic status(SES)		
Low	64	53.33
Medium	56	46.67
Family history of psychiatric illness		
Present	16	13.33
Absent	104	86.67

Table 2 Incidence of MS

Drug	Metabolic syndrome	Percentage	P-value
Olanzapine(group a)	5/30	16.6	0.04
Risperidone(group b)	5/30	16.6	
Quetiapine(group c)	3/30	10	
Aripiprazole(group d)	0	0	
Total(120)	13	10.83%	

Table 3 Mean changes in waist circumference, SBP, DBP

Drug	Mean changes in waist circumference in males	Mean changes in waist circumference in females	Mean changes in SBP	Mean changes in DBP
Olanzapine	3.95±0.78 (0.0001)	3.78±1.05 (0.0001)	2.61 (0.0001)	4.75 (0.0001)
Risperidone	1.51±1.09 (0.0001)	2.19±0.56 (0.0001)	2.58 (0.0020)	-1.00 (0.100)
Quetiapine	0.63±0.53 (0.0001)	0.29±0.56 (0.0008)	1.43 (0.0080)	0.37 (0.37000)
Aripiprazole	-0.26±0.53 (0.01)	-0.85±3.8 (0.14)	-0.97 (0.0040)	-2.25 (0.00200)

Table 4- Change in FBS, Triglycerides, and Change in HDL in males and females.

Drug	mean change in FBS	mean change in triglyceride	Male		Female	
			change in hdl	p value	change in hdl	p value
Olanzapine	22.9±12.8 (0.0001)	41.31±32.3 (0.0001)	-23.01±5.79	0.0001	-24.49±8.36	0.0001
Risperidone	12.3±17.6 (0.0006)	22.74±31.71 (0.0001)	-13.93±14.29	0.0001	-15.38±11.9	0.0001
Quetiapine	6.4±8.2 (0.0003)	8.46±25.02 (0.07)	-5.62±8.25	0.001	-6.34±9.63	0.001
Aripiprazole	0.78±5.4 (0.43)	-2.11±6.2 (0.06)	2.43±5	0.01	0.43±4.8	0.62

DISCUSSION-

In our study majority of patients belong to the 21-30yrs age group (41.67%).There were no significant gender differences in the sample with 54.17% males and 45.80% females. The majority were unemployed (50.83%), 51.67 % of individuals had a primary level of education, 53.33% of individuals belong to Low SES,65.83% were married. 13.33 %of individuals had a positive family history of psychiatric illness. The purpose of the study was to find the incidence of MS in drug naïve patients with psychosis, which was 10.83% and was similar to the findings of the study done by shivgautam[3] et al., where the incidence of MS was 11.6% and is a contrast to high rates (56.2%)of incidence in the study done by grover et al.,2019.[4] The prevalence rate of MS is in the reported range from 9 to 68% in various previous studies from different ethnic groups and that from India (De Hert et al.,2006)[5]; (Tirupati and Chua,2007;)[6],(Grover et al.,2011)[7]

In the current study, out of 13(10.83%) patients who developed MS,16.6%(5/30) of patients belonging to the Olanzapine group and Risperidone group developed MS.10% (3/30)of patients who received Quetiapine fulfilled the criteria of MS.While no patient on Aripiprazole developed MS (0%).This difference between the four treatment groups is statistically significant. while in the study done by Sandeep Grover et al[7], where the MS is maximum in people who were treated with clozapine(54%) followed by Olanzapine (16.2%), Risperidone(17.4%), Aripiprazole (4.4%), Quetiapine (1.15%).These differences might be due to us not considering the patients using clozapine in our study.

There were no significant gender differences in the incidence of MS in our study. There were studies done by Meyer and Stahl in (2009)[8] and Lee et al.,(2011)[9] showing females and males having a higher prevalence of MS respectively.

Patients on Olanzapine had a higher mean change in waist circumference in our study and was similar to that of Almeras[10] et al.,(2004) who studied anthropometric and metabolic indices associated with SGA. In which Olanzapine had a significantly high change in waist circumference compared to those treated with Risperidone Increased mean change in SBP was significant for all 4 drugs except for Aripiprazole, whereas an increased change in DBP was significant for only Olanzapine and Aripiprazole in our study which is similar to study done by Gupta[11] et al.,(2003) there was a prevalence of 29% for hypertension among 208 patients treated with antipsychotic medication. Therefore treatment options include decreasing or dividing doses or switching to another antipsychotic medication with a lesser anti-adrenergic effect.[12]

FBS levels in our study were found significantly high for Olanzapine, Risperidone, Quetiapine and no significant rise for Aripiprazole which is similar to a study conducted among antipsychotic-naïve schizophrenia patients by Nielsen et al., in which patients treated with ziprasidone and Aripiprazole has a lower risk of diabetes when compared to those treated

with Olanzapine (84%)or clozapine(91%).[13] Olanzapine and clozapine had the greatest tendency for glucose metabolic disturbance among SGA according to Muench et al.[14]

In our study mean change in Triglyceride levels showed an increase for A, B, C groups in which Olanzapine showed a maximum increase. A significant increase was among Olanzapine and Risperidone groups only. Our findings were similar to the CATIE[15] trial, Olanzapine, Quetiapine having an elevating effect on the triglycerides levels of schizophrenic patients but the reducing effect was found in Risperidone and ziprasidone. Our findings were also similar to the study done by Lieberman et al.,2005 where Risperidone, ziprasidone, and Aripiprazole were the least likely antipsychotic medications to induce dyslipidemia and adverse effects on lipid levels.[1]In another study by Llorente et al., Quetiapine has an intermediate effect on worsening the lipid profile.[16] High triglyceride levels and an increase in lipid levels are the most frequent side effects of SGA according to a study done by Mc Evoy et al[17]and Grover et al.(2012)[18]. In our study, the mean change in HDL level for both males and females was significantly higher with Olanzapine (-23.01) followed by Risperidone and Quetiapine. It is similar to a study done by McQuaid etal comparing Olanzapine and Aripiprazole in schizophrenic patients showed worsening of lipid profile after 26 weeks for the Olanzapine group[19].Sheitman et al.,(1999) re-examined the lipid profile of 9 patients with Schizophrenia, after initiating treatment with Olanzapine. Though they did not observe a change in cholesterol or lipoprotein levels, the triglyceride levels increased from a mean of 170 mg/dl to 240 mg/dl. [20] A study done by Menzies (2004) raised CHD risk, estimated that 67% of his patients had a two-fold risk in patients having hyperlipidemia associated with SGA use.[21]

CONCLUSIONS

Out of 120 patients,10.83% of patients developed MS after three months of continuous antipsychotic drug therapy.16.6% of patients belonging to the Olanzapine group and Risperidone group developed MS.10% of patients who received Quetiapine fulfilled the criteria of MS. In comparison to individual components of MS, Olanzapine showed impairment in all the components of MS and was statistically significant. Patients on Risperidone showed impairment with the statistically significant increase in components of waist circumference, SBP, triglycerides, and decrease in the DBP and HDL levels. Patients on Quetiapine showed impairment of waist circumference, SBP, FBS, HDL. Aripiprazole showed a protective action against MS with a reduction of waist circumference, SBP, DBP, triglyceride, and an increase in HDL levels.

REFERENCES:

1. Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Swartz MS, et al. Effectiveness of Antipsychotic Drugs in Patients with Chronic Schizophrenia. The new England Journal of Medicine 2005; 353(12): 1209-1223.
2. National Cholesterol Education Program, Adult Treatment Panel III
3. Shiv Gautam and Parth Singh Meena Drug-emergent metabolic syndrome in patients with schizophrenia receiving atypical (second-generation) antipsychotics Indian J Psychiatry. 2011 Apr-Jun; 53(2): 128–133. DOI:10.4103/0019-545.82537PMCID:PMC3136014
4. Grover et al (2019)Relationship of Metabolic syndrome and Neurocognitive deficits in patients with schizophrenia (science direct.0165178119305323)
5. De Hert, M.A., van Winkel, R., Van Eyck, D., Hanssens, L., Wampers, M., Scheen, A., Peuskens, J., 2006. Prevalence of the metabolic syndrome in patients with schizophrenia treated with antipsychotic medication.
6. Tirupati, S., Chua, L.E., 2007. Body mass index as a screening test for metabolic syndrome in schizophrenia and schizoaffective disorders. Australasian Psychiatry.
7. Grover et al (2011) Prevalence of metabolic syndrome in subjects receiving Clozapine: a study from India. Indian Journal of Pharmacology 43, 591–595.
8. Meyer, J.M., Stahl, S.M., 2009. The metabolic syndrome and Schizophrenia. Acta Psychiatrica Scandinavica 119 (1), 4–14
9. Lee, N.Y., Kima, S.H., Jung, D.C., Kima, E.Y., Yu, H.Y., Sung, K.H., Kang, U.G., Ahn, Y.M., Kim, Y.S., 2011. The prevalence of metabolic syndrome in Korean patients with Schizophrenia receiving monotherapy with aripiprazole, olanzapine, or risperidone. Progress in Neuropsychopharmacology and Biological Psychiatry 35 (5)Gupta S, Steinmeyer C, Frank B, Madhusoodanan S, Lockwood K, Lentz B and Keller P (2003) Hyperglycemia and Hypertriglyceridemia in Real-World Patients on Antipsychotic Therapy. Am J Therapeutics 10:348-355
10. Almeras N, Depres J-P, Villeneuve J, et al. (2004) Development of an atherogenic metabolic risk factor profile associated with the use of atypical antipsychotics. J Clin Psychiatry 2004 65:557-64
11. Gupta A, Dadheech G, Yadav D, Sharma P, Gautam S.Metabolic issues in schizophrenic patients receiving antipsychotic Indian J Clin Biochem. 2014 Apr;29(2):196-201.DOI: 10.1007/s12291-013-0415-z.Epub 2014 Jan 23
12. Haddad PM, Sharma SG. Adverse effects of atypical antipsychotics: differential risk and clinical implications. CNS Drugs. 2007;21(11):911–936.
13. Nielsen J., Skadhede S. and Correll C. U. (2010) Antipsychotics associated with the development of type 2 diabetes in antipsychotic naive schizophrenia patients. Neuropsychopharmacology 35,1997–2004
14. Muench J. and Hamer A. M. (2010) Adverse effects of antipsychotic medications. Am. Fam. Physician 81, 617–22
15. Wani RA1, Dar MA1, Margoob MA1, Rather YH1, Haq I2, Shah MS1. Diabetes mellitus and impaired glucose tolerance in patients with schizophrenia, before and after antipsychotic treatment. J Neurosci Rural Pract. 2015 Jan;6(1):17-22.DOI: 10.4103/0976-3147.143182.
16. Llorente M. D. and Urrutia V. (2006) Diabetes, psychiatric disorders, and the metabolic effects of antipsychotic medications. Clin.Diabetes 24, 18–24
17. McEvoy, J.P., Meyer, J.M., Goff, D.C., Nasrallah, H.A., Davis, S.M., Sullivan, L., Meltzer, H.Y., Hsiao, J., Scott Stroup, T., Lieberman, J.A., 2005. Prevalence of the metabolic syndrome in patients with schizophrenia: baseline results from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia trial and comparison with national estimates from NHANES III. Schizophr. Res. 80, 19–32. https://doi.org
18. Grover, S., Aggarwal, M., Dutt, A., Chakrabarti, S., Avasthi, A., Kulhara, P., Somaiya, M., Malhotra, N., Chauhan, N., 2012. Prevalence of metabolic syndrome in patients with ACCEPTED MANUSCRIPT schizophrenia in India. Psychiatry Res. 200, 1035–1037. https://doi.org/10.1016/ j.psychres. 2012. 03.043
19. McQuade RD, Stock E, Marcus R, et al. (2004) A comparison of weight change during treatment with Olanzapine, or aripiprazole: results from a randomized, double-blind study. J Clin Psychiatry 65 (suppl 18):47-56
20. Sheitman B B, Bird Paula M, Binz Whitney, Akinli, Leyla and Sanches, Clare (1999) Olanzapine-Induced Elevation of Plasma Triglyceride Levels. Am J Psychiatry 156:1471-1472
21. Menzies R, Dyslipidaemia and Psychiatric Patients (2004)Can J Psychiatry 49(12):864