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Changes in Weight and Waist circumference in Patients Suffering from Schizophrenia onSecond Generation Anti-psychotics.

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Introduction:
Atypical antipsychotics are widely used in the treatment of many psychotic disorders. They are as effective as first-generation antipsychotics and also cause a lower incidence of EPS. Despite their uses, atypical antipsychotics do have some side effects. There is a high risk of metabolic syndrome. The current study highlights weight gain patterns in patients using second-generation antipsychotics.
AIM: To compare changes in the weight andwaist circumference in patients on second generation antipsychotics
Methodology:*A comparative study on changes in weight due to second-generation antipsychotics in a sample of 120, analyzed by recording kg/body weight and waist circumference of patients who were treated with Quetiapine, Olanzapine, Risperidone, and Aripiprazole. Baseline weight in kgs and waist circumference in centimetres was recorded before starting the drug and subsequent weight was recorded in a follow-up period of 12 weeks after the drug was started.*
Results:*Mean weight of the patients on the drugs considered in the study with Olanzapine was 61.13±7.21.The mean change in body weight from baseline by the end of duration in patients on Olanzapine showed a statistically significant weight gain of 5.8kg which was higher when compared the mean weight gain by Risperidone and Quetiapine. On contrary, patients in Aripiprazole (60.7±6.73) group had a weight loss of approximately 0.61kg though it was not statistically significant.A notable increase in waist circumference is observed with Olanzapine,Risperidone, and Quetiapine in both males and females.*
Conclusion:*Weight gain is an important factor in drug compliance. Among the anti-psychotics under study Olanzapine, Risperidone, Quetiapine, and Aripiprazole, significant weight gain and increase in waist circumference is noted with Olanzapine, Risperidone, Quetiapine but there is weight loss and decrease in waist circumference with Aripiprazole.*
Keywords:*weight gain, waist circumference, schizophrenia, second-generation antipsychotics.*

I. Introduction:

Atypical antipsychotics are considered a major advance over conventional antipsychotics, primarily because they offer effective treatment alternatives that are relatively free of extrapyramidal symptoms [(1)]. The tolerability profile of atypical drugs certainly benefits from a lower incidence of acute EPS effects, along with less certain or less uniform benefits in symptomatic hyperprolactinemia or tardive dyskinesia[(2)]. Antipsychotics affect neuropeptides associated with appetite control and energy metabolism. Leptin and adiponectin are the adipokines produced in white adipose tissue, which have been implicated in Antipsychotic Induced Weight Gain [(3)]. Anti-psychotic-induced weight gain can increase the risk of developing metabolic syndrome, diabetes, and cardiovascular disease [(4)]. Schizophrenia and metabolic disturbances may share certain genetic or pathobiological risks, antipsychotics, particularly those of the second generation, may further increase the risk of weight gain and metabolic disturbances in patients with schizophrenia[(5)]. Fontaine et al[(6)] estimated the expected impact of varying degrees of weight gain associated with antipsychotics. The current study highlights the pattern of weight gain due to second-generation antipsychotics in patients using them

II. Materials And Methods:

OBJECTIVE:
To compare changes in the weight and waist circumference in patients on various antipsychotics.
STUDY DESIGN:
The current study is a comparative follow up study.
STUDY AREA:
Department of Psychiatry, Katuri Medical College and Hospital, Guntur.

STUDY DURATION:
Study duration of 1year (December 2020-December 2021).
STUDY SAMPLE SIZE: 120
INCLUSION CRITERIA:
•Drug naive patients aged between 18 to 65 years suffering from schizophrenia as per ICD-10 criteria
•Patients who gave informed consent for the study.
•Patients with at least one informant who gave informed consent for the study.

EXCLUSION CRITERIA:
•Patients receiving more than one antipsychotic medication.
•Patients with known co-morbidities other than psychotic illness.
•Pregnant and lactating women.
•Non-complying patients.

PROCEDURE OF THE STUDY:

Drug naive patients with the diagnosis of schizophrenia as per ICD 10 criteriaattending psychiatry OPD were randomly assigned into four groups A, B, C, and D with the 1st Group(A) receiving Olanzapine,2nd group (B) receiving Risperidone,3rd group (c) receiving Quetiapine,4th group(D)Aripiprazole. The initial body weight and waist circumference of selected individuals was recorded. After 12 weeks of antipsychotic medication, body weight and waist circumference were recorded and compared with baseline recordings.

STATISTICAL ANALYSIS:

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

III. Results:

In thisstudy themajority of patients belong to the age group of 20-30(41.67%) yrs, 31.6% were between age groups 31-40 yrs, 19.17% were between 41-50 yrs and 6.7% were above 50 yrs of age. There were no significant gender differences in the sample with 54.17% males and 45.80% females. 49.17% of patients were employed and 50.83%were unemployed. Out of the total sample, 69.17% were literates. 13.33 %of individuals had a positive family history of schizophrenia. Of the total study sample 65.83% were married, 23.33%were separated or divorced and only 10.83% were single.

Table 1: SOCIODEMOGRAPHIC DATA

VARIABLE	**NUMBER**	**PERCENTAGE %**
AGE		
21-30	50	41.67
31-40	38	31.67
41-50	23	19.17
>51	9	7.87
GENDER		
MALE	55	54.17
FEMALE	65	45.83
OCCUPATION		
EMPLOYED	59	49.17
UNEMPLOYED	61	50.83
EDUCATION		
UNEDUCATED	37	30.83

6^{TH} CLASS	62	51.67
10^{TH} CLASS	12	10.00
GRADUATED	9	7.50
MARITAL STATUS		
MARRIED	79	65.83
UNMARRIED	13	10.83
SEPARATED	28	23.33
SOCIOECONOMIC STATUS		
LOW	64	53.33
MEDIUM	56	46.67
FAMILY HISTORY		
PRESENT	16	13.33
ABSENT	104	86.67

The total Study Sample consisted of 120drug-naive patients suffering from schizophrenia or psychosis. The sample was randomlydivided into 4 groups of 30 patients in each group namely groups A, B, C,and D with each grouppresscribed drugs Olanzapine, Risperidone, Quetiapine, and Aripiprazole respectively.

Table 2-SAMPLE SIZE

Drug	Number of patients
Olanzapine(group a)	30
Risperidone(group b)	30
Quetiapine(group c)	30
Aripiprazole(group d)	30
Total	120

WEIGHT GAIN:

The mean weight of the patients on the drugs considered in the study was Olanzapine(61.13±7.21), Risperidone(60.47±6.77), Quetiapine(60.47±7.12), Aripiprazole(61.1±6.85) at the baseline and end of 3 months of the initiation of the respective drug. The mean weight of patients after 3 months are Olanzapine(64.57±6.58), Risperidone(61.5±6.58), Quetiapine(61.00±7.40) and Aripiprazole(60.7±6.73).

TABLE. 3 MEAN BASELINE AND END-WEIGHT:

DRUG	BASELINE WEIGHT(KGS)	END WEIGHT(KGS)
OLANZAPINE	61.13±7.21	64.57±6.58
RISPERIDONE	60.47±6.77	61.5±6.58
QUETIAPINE	60.47±7.12	61.00±7.40
ARIPIPRAZOLE	61.1±6.85	60.7±6.73

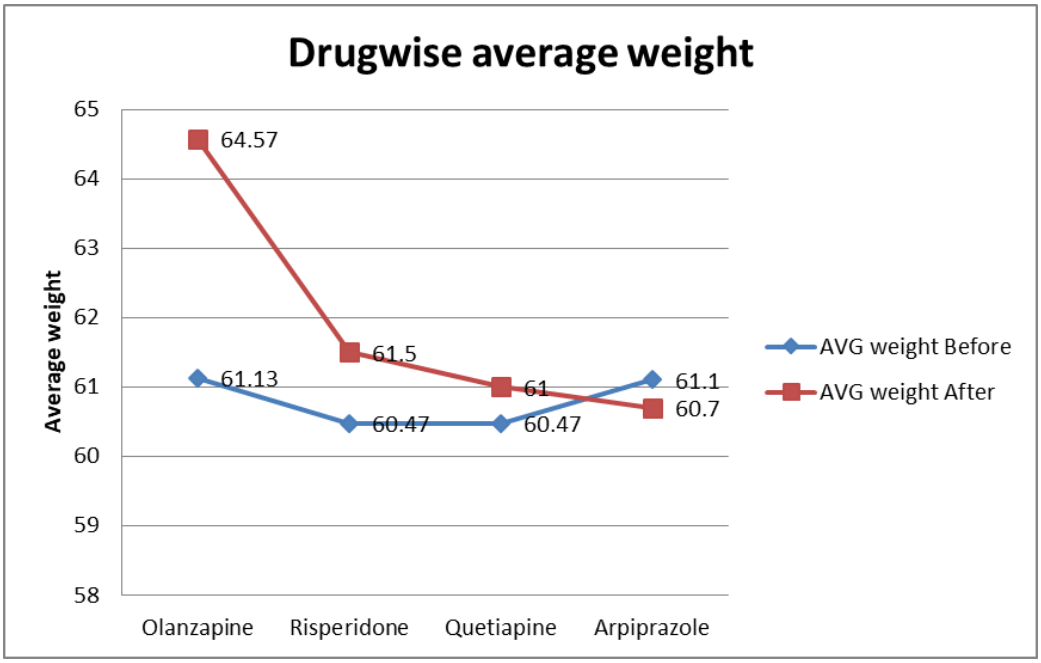

Figure:1

The mean change in body weight from baseline to the end of 3 months study is shown in Table 4. Patients on Olanzapine showed a statistically significant weight gain of 5.8 kg which was higher when compared to the mean weight gain by Risperidone(1.78±1.93) and Quetiapine(0.94±2.16). On contrary, patients in Aripiprazole (-0.61±2.27) group had a weight loss of approximately 0.61kg though it was not statistically significant.

TABLE 4. MEAN CHANGE IN BODY WEIGHT:

DRUG	CHANGE IN WEIGHT	P-VALUE
OLANZAPINE	5.89±5.05	0.0001
RISPERIDONE	1.78±1.93	0.0001
QUETIAPINE	0.94±2.16	0.02
ARIPIPRAZOLE	-0.61±2.27	0.15

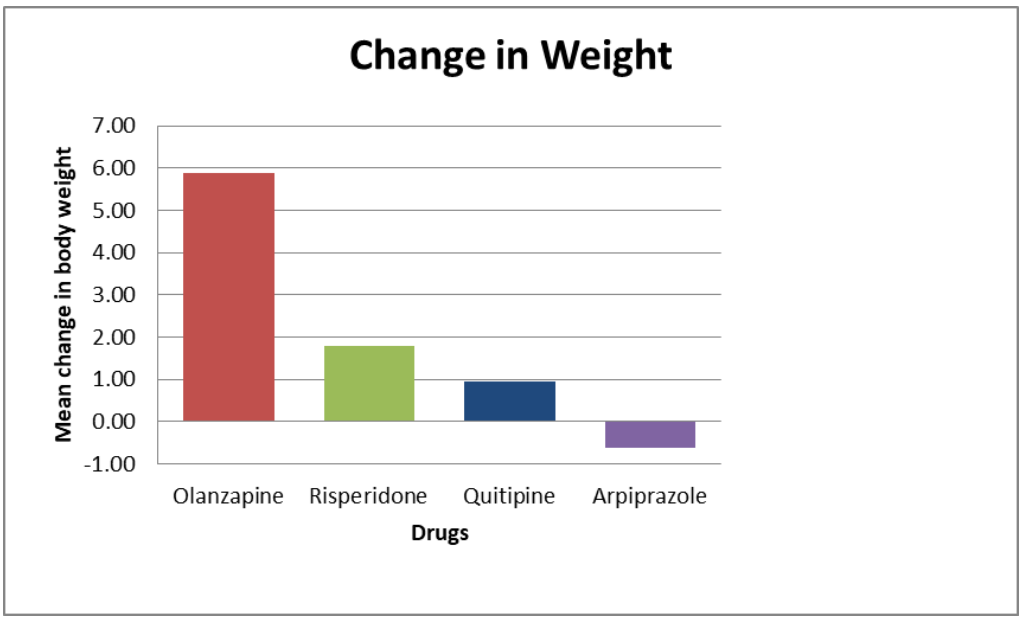

Figure:2

WAIST CIRCUMFERENCE:

The mean change in waist circumference level for both males and females is higher for Olanzapine when compared to the mean change in values of Risperidone, Quetiapineand Aripiprazole.This difference was found to be statistically significant in all 3 drugs in both males and females. There was a decrease in the waist circumference of patients both male and female on Aripiprazole. This difference was statistically significant for males (0.01) and not significant in the case for females (0.14).

TABLE:5 BASELINE AND END WAIST CIRCUMFERENCE IN MALES AND FEMALES.

DRUG	MALE(Cms)		FEMALE(Cms)	
	BASELINE	END	BASELINE	END
OLANZAPINE	77.47±1.97	78.2±2.5	77.7±3.00	79.62±3.95
RISPERIDONE	77.2±2.78	78.35±2.39	75.5±3.10	77.2±3.19
QUETIAPINE	78.29±3.15	78.79±3.26	78.3±3.5	78.44±3.61
ARIPIPRAZOLE	77.43±2.55	77.25±2.41	75.8±2.8	75.0±2.37

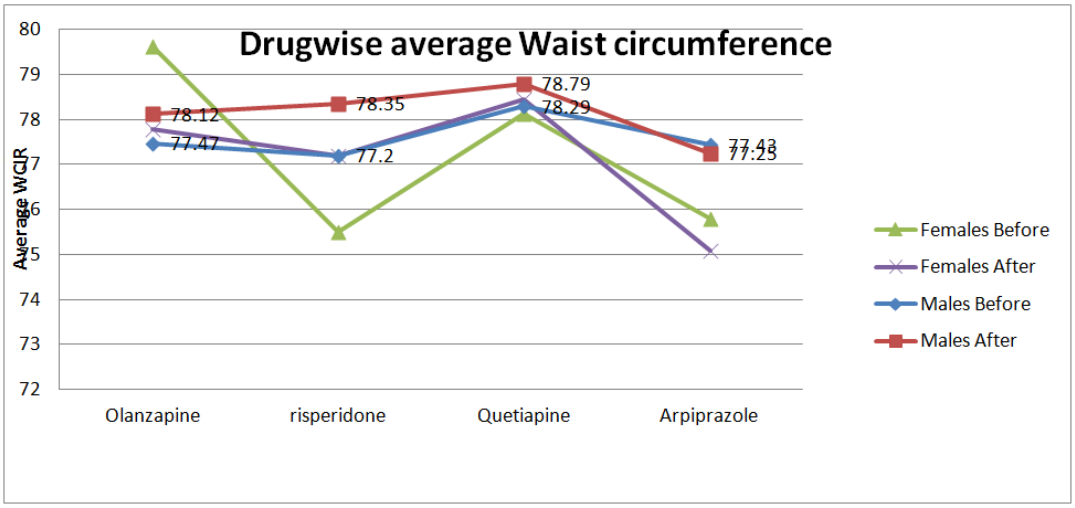

Figure: 3

TABLE: 6 MEAN CHANGE IN WAIST CIRCUMFERENCE

DRUG	MALE		FEMALE	
	CHANGE	P-VALUE	CHANGE	P-VALUE
OLANZAPINE	3.95±0.78	0.0001	3.78±1.05	0.0001
RISPERIDONE	1.51±1.09	0.0001	2.19±0.56	0.0001
QUTIAPINE	0.63±0.53	0.0001	0.29±0.56	0.0008
ARIPIPRAZOLE	-0.26±0.53	0.01	-0.85±3.8	0.14

IV. Discussion:

Gebhardt S[7] et al in their study found that low baseline BMI may predict a more rapid weight gain compared to heavier counterparts, who may ultimately gain more weight and reach a higher plateau and Younger age, lack of previous APD therapy, higher BMI, and non-smoking status are other potential risk factors for weight gain. In a 3yr prospective cohort study done by Perez- Iglesias[8] et al involving drug-naive patients, poor social functioning and lack of response to negative symptoms were correlated with weight gain due to anti-psychotics.

In a study done by Stefan Leucht et.al.,[9] standardized mean differences compared with placebo for weight gain varied between Haloperidol and Olanzapine. Current study has highlighted the weight gain pattern among second generation anti-psychotics.Simon[10] et al reviewed to investigate a possible correlation between SGA dose and magnitude of weight gain and founda dose-response relationship between clozapine and Olanzapine serum concentrations. The current study have not considered drug dose and weight magnitude but this is a comparison of weight gain with baseline and after 12weeks of using the drug. According to a study done by Kinon[11] et al., and colleagues the course of weight change in patients treated with Olanzapine over 1 year within 2 weeks of treatment approximately 15% of patients rapidly gained an average of 4% of their body weight. The present study has highlighted the difference in weight gain due to anti-psychotics at 12weeks after using the drug and a gain of 5.89±5.05 kgs was noted with Olanzapine.

McQuade [12] et al. in their study compared Aripiprazole and Olanzapine, especially in terms of significant weight gain. By the end of the trial, 37% of Olanzapine-treated patients reported significant weight

gain ($p<0.001$) compared to 14% of patients treated with Aripiprazole. In the current study, there is a weight loss of -0.61±2.27 with Aripiprazole. The findings of Olanzapine having a higher mean change in waist circumference was similar to that of Almeras[13] et al. who studied anthropometric and metabolic indices associated with atypical antipsychotic treatment, in an open-label, cross-sectional, multi-centre study.

According to a study done by Sung-Hwan Kim et.al, [14] abdominal obesity and dyslipidemia were dominant contributing factors to metabolic syndrome, especially in young psychiatric patients. In a study done by Hussein O.et.al[15], it was concluded that antipsychotic therapy was associated with increased abdominal obesity and increased waist circumference. Yamin Zhang et.al.,[16] concluded that there were significant changes in BMI, waist circumference, and lipid profile at baseline, 2, 4, and 6 weeks in patients taking antipsychotics. According to present study there was an increase in waist circumference noted with Olanzapine, Risperidone, Quetiapine and a decrease in waist circumference noted with Aripiprazole.

LIMITATIONS:

1)Short duration of follow up

2)Risk factors like family history of diabetes, smoking, exercise, and dietary habits have not been looked into.

3)Other atypical antipsychotics and newer antipsychotics were not included in the study.

V. Conclusion:

According to our study, Patients on Olanzapine,Quetiapine and Risperidone showed significant changes in weight gain as well as waist circumference, while patients on Aripiprazole had weight loss and loss of inches in waist circumference though not statistically significant.

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