

ORIGINAL ARTICLE

ANTIPSYCHOTIC TREATMENT AND WEIGHT GAIN: DOES RISPERIDONE BEHAVE DIFFERENTLY IN PAKISTANI PSYCHIATRIC PATIENTS?

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Background: Studies from the Western world have shown that antipsychotic medications in psychiatric patients result in weight gain and other metabolic diseases. This study was undertaken to investigate whether any one of the five most commonly prescribed antipsychotics, (risperidone, olanzepine, trifluoperazine, quetiapine and haloperidol) could behave differently in terms of causing weight gain among patients attending the psychiatric outpatient clinics in a tertiary care hospital in Karachi, Pakistan. **Methods:** For this retrospective cohort study, data were collected from outpatient records of the Aga Khan University Hospital, from 2003 to 2007. Demographic and clinical data were analysed. Repeated measures ANOVA, using a linear mixed model approach was used to assess weight gain over time due to the use of antipsychotic medications. **Results:** A total of 124 subject records (68 males and 56 females) were evaluated. One-way ANOVA revealed that the groups being prescribed with antipsychotics were comparable with respect to age, duration of treatment and weight measurements. Frequencies were calculated which showed that weight increases significantly over time with respect to the prescribed antipsychotic medications, except for risperidone. Repeated measures ANOVA using the linear mixed model approach showed that the serial weight measurements were significantly different across the follow up times ($p < 0.05$). **Conclusion:** Four of the commonly prescribed antipsychotic drugs do result in an increase in weight; however risperidone has no such effect, making it an option in treating psychiatric disorders without worrying for any gain in weight. In view of the increased prevalence of obesity and other metabolic diseases, measures should be taken towards careful prescription of antipsychotic medications.

Keywords: Schizophrenia depression weight gain obesity antipsychotics risperidone

INTRODUCTION

The introduction of antipsychotic medications was a major breakthrough in the field of psychiatry. In spite of the high prevalence of psychiatric disorders, like schizophrenia¹ and depression², clinicians have been able to contain these disorders with reasonable success. However, the metabolic adverse effects due to the use of these drugs are a cause of concern, especially in developing countries, and a major focus of psychiatric research.³

One important metabolic side effect of many antipsychotics is the gain in weight.⁴ Various studies have shown that treatment with antipsychotics results in weight gain.⁵⁻⁹ The mechanism for this weight gain are not well understood, though some factors, like sedation, decreased satiety, lack of movement and a series of endocrinological changes, resulting in increased appetite and food intake, might be playing a role.⁹⁻¹¹ In addition, reports suggest that role of central 5-hydroxytryptamine₂ (5-HT₂) receptors might also be involved in some manner, leading to increased appetite and subsequent weight gain.¹²

Overweight and obesity are issues of concern for both developed and developing countries, especially with respect to their association with hypertension, diabetes mellitus, metabolic syndrome and dyslipidemia. In the United States, the prevalence of

obesity increased from 23% in 1990 to 31% in 2000, with no decline in obesity rates across 2000 and 2002.^{13,14} Obesity is common in psychiatric disorders, like schizophrenia.¹⁵ This adds to their risk of developing any of the above mentioned metabolic diseases.¹⁶⁻¹⁹

In Pakistan, obesity has been found to be frequently associated with diabetes mellitus, hypertension, and other metabolic cardiovascular disorders, which are highly prevalent in the country.²⁰⁻²² Antipsychotic induced weight gain is proposed to be a mechanism by which these medications can increase the risk for insulin resistance, hyperglycaemia and dyslipidemia.²³

The increasing proportion of psychiatric illnesses in Pakistan has been reported quite recently.² This shows that clinicians are now more involved in seeing and treating such patients and caution is necessary as psychiatric patients are known to have the worse physical health due to co-morbid somatic diseases.^{3,24}

In our previous communication⁵ we have shown that treatment with antipsychotics does result in statistically significant weight gain. However, the follow up in that study was for 6 months only. Our purpose for this research was to investigate whether any of the commonly prescribed antipsychotic medications could

cause little or no weight gain over a period of 1 year, regardless of their disease presentation, among patients attending the psychiatric outpatient clinics in the Aga Khan University Hospital, Karachi.

MATERIAL AND METHODS

This retrospective cohort study was carried out at The Aga Khan University Hospital and involved patients visiting the psychiatry outpatient clinics, during the period of 2003–2007, and prescribed with antipsychotic medications. The patients were identified through the University’s Psychiatric Assessment System (PAS) database which records the general and clinical information of all patients seen in the outpatient settings.⁵

The patients were categorised on the basis of the commonly prescribed antipsychotic medications. The doses [medians (IQR)] were as following:

- Risperidone= 2 (2.5) mg/day
- Olanzapine= 10 (6.3) mg/day
- Quetiapine= 200 (250) mg/day
- Haloperidol= 10 (4.8) mg/day
- Trifluoperazine= 2 (3) mg/day

Information was recorded on variables like age, gender, psychiatric diagnoses, associated co-morbid and the prescribed antipsychotic medications.

Serial measurements for weight were recorded in SI units, at every follow up of the patient in the clinic, as advised by the attending psychiatrist. For research purpose, we had categorised these time frames as baseline (or first visit) and after 1, 2, 3, 6 and 12 months of follow up. We included those patients whose serial weight measurements were on either one of the commonly prescribed antipsychotic medications.

Frequencies were recorded in means (±SEM) for quantitative variables and percentages for categorical variables. One way analysis of variance (ANOVA) was employed to compare the groups with respect to age, duration of treatment and the serial measurements for weight. Repeated measures ANOVA, using a mixed model approach, was employed to examine the trend of weight gain over the follow up times. Data analyses were performed using SPSS-16 and *p*<0.05 was considered significant.

RESULTS

A total of 124 records of patients were identified. Table-1 summarises the frequencies of clinical characteristics. The mean age was calculated as 34.61±1.44 years. About 55% of the subjects were males and remaining were females. A mean combined weight was calculated for all follow up times which ranged from 63 Kg, at baseline to 69 Kg at the last follow up. Majority of the patients were diagnosed as having schizophrenia (52%), followed by depression (16%). About 9% of the subjects

were hypertensive, and hypercholesterolemia and diabetes mellitus were found among 2% of the subjects.

Table-1: Frequencies of demographic and clinical characteristics of patients at baseline

Variable	N (%)
Age (years) Mean±SEM	34.61±1.44
Gender	
Male	68 (55)
Female	55 (44)
Psychiatric diagnosis	
Schizophrenia	64 (52)
Depression	20 (16)
Bipolar disorders	11 (9)
Others	28 (23)
Associated co-morbid conditions	
Hypertension	11 (9)
Hypercholesterolemia	2 (2)
Diabetes mellitus	3 (2)
Antipsychotics prescribed	
Risperidone	75 (61)
Olanzapine	23 (19)
Quetiapine	14 (11)
Haloperidol	7 (6)
Trifluoperazine	5 (4)

Sixty-one percent of the subjects were prescribed with risperidone, followed by olanzapine (19%), quetiapine (11%), haloperidol (6%) and trifluoperazine (4%). One way ANOVA showed that the groups prescribed with these medications were comparable with respect to age, duration of treatment and weight measurements (*p*>0.05).

Starting from a total of 124 subjects at baseline, 92 were identified at 1 month of follow up, 60 were identified at 2 months, 47 were identified at 3 months, 48 were identified at 6 months and 29 were identified at 1 year of follow up. An increasing trend in weight is observed over the follow up times, with respect to all of the prescribed antipsychotics, except risperidone (Table-2). Maximum weight gain was observed with the use of olanzapine (29%), followed by trifluoperazine (28%), quetiapine (24%), and haloperidol (13%).

From the 29 (23%) subjects identified till 1 year, 52% have received risperidone, followed by 17%, 14%, 10% and 7% for olanzapine, trifluoperazine, quetiapine and haloperidol, respectively (data not shown).

Mixed model analyses showed that weight was significantly different over the various follow up times (*p*-value 0.001), adjusted for age, gender, and psychiatric diagnoses. Figure 1 shows the trend of weight gain with respect to the prescribed antipsychotic medications, using the best fit model. It is noteworthy that the pattern of recorded weight for the group which received risperidone did not show any increase, whereas the pattern seems to be increasing in the other groups.

Table-2: Mean±SEM for the weight (Kg) of patients taking the prescribed antipsychotic over the follow up times

Medicines	Months					
	Baseline	At 1 st	At 2 nd	At 3 rd	At 6 th	At 12 th
Risperidone	63.9±2.1	65.3±2.3	66.9±2.8	65.2±3.9	65.1±4.1	62.7±4.5
Olanzapine	62.5±3.2	67.1±4.0	74.7±5.6	68.9±3.8	66.4±3.1	80.9±8.9
Quetiapine	70.5±4.8	65.3±3.4	74.8±8.0	78.9±7.5	72.4±6.5	87.7±5.7
Haloperidol	62.2±3.8	59.1±5.2	62.5±4.6	70.3±0.1	69.6±11.9	70.1±9.0
Trifluoperazine	48.9±7.5	49.7±7.1	44.3±17.7	51.0±7.1	51.2±7.1	62.6±0.5

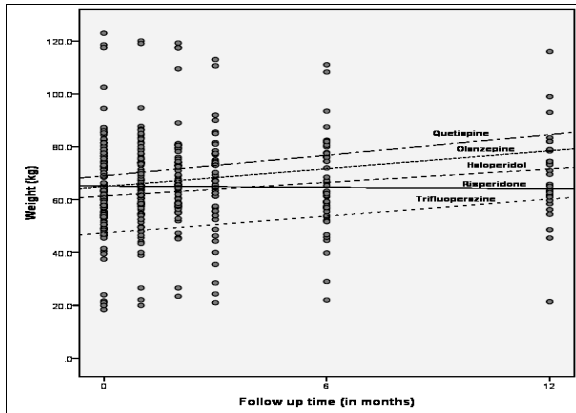


Figure-1: Patterns of mean weight over the period of 12 months following use of antipsychotic medication
(Trends of weight gain generated using best fit; 0 months indicate initiation of anti-psychotic medication)

DISCUSSION

The main aim of the study was to investigate whether any of the commonly prescribed antipsychotic medications could cause little or no weight gain over a period of 1 year of follow up. To our knowledge, no such study has been conducted in the context of our population. Our findings show that with exception to risperidone, almost all antipsychotics induce weight gain among psychiatric patients in Pakistan.

The mean age of our population of interest was 34 years. This is to no surprise to us as majority of the population suffering from psychiatric disorders lie in this age group. In a recent study², conducted among Pakistani population, the mean calculated age was around 35 years, and about 46% of the population were suffering from depression.

In the present study we found that 55% of our subjects were males and remaining were females. The notion is pretty obvious as the males are the main ‘bread-earners’ and experience life cycle changes with respect to employment, economic and family well-being, and thus are at a greater risk of psychiatric disorders. In other studies^{2,25}, females are reported to be the main sufferers of psychiatric illnesses. However, Pakistani females are hesitant towards seeking health care for a comparatively stigmatising disease, thus few females approach clinics for check-up. In a research study by Ascher-Svanum *et al*, the adverse effects of

gain in weight, upon using antipsychotics, have shown to have more profound consequences among females.²⁶ This, though not being a primary objective of this research, offers a new avenue to elaborate the negative effects of weight gain among females, upon using antipsychotics, in the perspective of a developing country, like Pakistan.

Reports suggest that weight gain is more prominent due to the use of second generation antipsychotics (SGA), compared to the first generation.^{26,27} In our research, we found olanzapine (an SGA) to induce maximum weight gain, and haloperidol inducing the least. Similar results have been reported by Allison *et al*. and Kraus *et al*.^{6,28} It is noteworthy that risperidone did not result in significant weight gain in our population. In research conducted elsewhere risperidone does result in gain in weight, though not as much as compared to olanzapine.^{6,11,29} This points to the fact that response to risperidone could vary from one population to another. Clinical trials over a long follow up time and using a large sample size would be required to obtain conclusive evidence in this regard.

It would be important to mention a couple of limitations of this study. As this was a retrospective cohort analysis we relied on the readily available information on records, with no means for quality assessment. However, we tried to capture maximally the recent records which are more accurate and error free. As pointed elsewhere, it is likely that the patients might have received other antipsychotics before their first presentation in the clinical set-up of the University Hospital.⁵ Also, we were unable to assess for compliance on the prescribed medications. However, subsequent weight gain in 4 out of 5 groups of patients indirectly shows that the subjects were pretty compliant with the prescribed treatment.

The serial measurements for weight at the designated time frames, for any medication group may have been missing, which is a usual feature in the real clinical setups. This may also have contributed in obtaining a non-significant weight gain due to the use of risperidone. In order to rectify this, the linear mixed model approach was employed, a robust technique which analyses data in a relational format and allows analyses for the variable number of follow ups for each subject.³⁰

In this research, risperidone, due to its comparatively non-significant effect on gain in weight offers an option to clinicians and psychiatrists to prescribe among psychiatric patients. Although the mixed model approach used takes into account every serial weight measurement, irrespective of the follow up time yet it would have been better to have had balanced categories of patients on antipsychotics. Large scale prospective studies are warranted to unravel the underlying mechanism of this effect of risperidone.

Moreover, role of gender also needs to be evaluated in future research in this part of the world.

CONCLUSIONS

Use of risperidone for over a period of 1 year does not cause any significant weight gain. In view of the prevalent proportions of obesity, diabetes mellitus, dyslipidemia, and other cardiovascular events in Pakistan, weight gain among psychiatric patients undergoing treatment is a cause of concern. Risperidone may offer an option to clinicians and psychiatrists in treating psychiatric disorders in overweight/obese patients. Measures should be taken towards controlled prescriptions of antipsychotics to psychiatric patients, so that the quality of their already affected life could be improved.

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