Research Article

A study on Olanzapine induced weight gain among patients of Schizophrenia at a Tertiary Care Medical College Hospital in Deccan Plateau

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Abstract

Objective: The introduction of atypical antipsychotics was a big step forward in the treatment of schizophrenia and other psychoses. However, they are liable to cause weight gain and hence further put the patient at risk of metabolic disorders. Our aim was to evaluate the weight gain associated with the use of olanzapine, in relation to age and gender, in patients of Schizophrenia. **Materials and methods:** One hundred patients fulfilling the ICD-10 criteria for schizophrenia, were included in this study to evaluate weight gain as an adverse effect of treatment with olanzapine in relation to age, gender, dose and body mass index (BMI). Sociodemographic data and baseline weight along with height (to calculate the BMI) were recorded before the initiation of treatment. The patients were administered a flexible dose of olanzapine (5—15 mg) as monotherapy. Pregnant patients, smokers, patients with history of endocrine disorders, CVS disease and chronic alcoholics were excluded from the study. The increase in weight as a neuroleptic side-effect of olanzapine was recorded and analysed in relation to age, gender, dose and BMI. **Observations and results:** Of the patients receiving olanzapine, 66.6% had a weight gain of 1–5 kg over a period of 4 weeks. The weight gain was not related to the dose of the drug or BMI. The increase in weight was significantly related to age ≥45 years and female sex, indicating that women ≥45 years of age are more prone to gain weight with olanzapine therapy in comparison with women <45 years and men of any age group. **Conclusion:** The potential for weight gain associated with the use of olanzapine is high in females more than 45 years of age. The potential of olanzapine to cause long-term complications will need further study.

***Keywords*:** Weight gain, olanzapine, body mass index, age, gender

Introduction

The introduction of second-generation or atypical antipsychotic drugs has led to a therapeutic advance in the treatment of schizophrenia. As there are less neurological side effects, compared to typical antipsychotics, they are more commonly being used in clinical practice (Conley and Mahmoud, 1999). Based on the side-effect profile, atypical anti-psychotics have become the preferred choice and most of the recent guidelines also recommend the use of atypical agents as the first line of treatment for schizophrenia (Tollefson et al., 1997; Lehman et al., 2004).

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Introduced in 1950s, the atypical antipsychotic drugs were a huge step forward in the treatment of schizophrenia and other psychoses. These novel antipsychotics demonstrated an improved therapeutic profile compared with that of conventional antipsychotics in terms of effectiveness and adverse effect profile (Green, 1999; Berstein, 1992). Anti-psychotic drugs of the second generation have side effects such as weight gain, lipid abnormalities and disturbance of glucose regulation. This increases the risk of the metabolic syndrome, recognizable features of which include central obesity, glucose intolerance/insulin resistance, hypertension and dyslipidaemia (Kraus et al., 1999). Olanzapine has been rated as the agent, next only to clozapine, which leads to the metabolic syndrome (McEvoy et al., 1999; American Diabetes Association, 2004). Accordingly, clinicians are now focusing away from concerns of motor effects and their

emphasis has shifted to weight gain, drug-induced glucose imbalance and other emerging metabolic effects associated with the use of atypical antipsychotics.

A national survey in the USA, which evaluated the patterns of use and emerging adverse effect profile of atypical antipsychotics, found that 70% of patients were prescribed an atypical antipsychotic drug and only 30% a typical antipsychotic. Thirty-four per cent of the patients on atypical antipsychotics reported weight gain in comparison to 16% on typical antipsychotics; weight gain was more evident in females (54%) (Eder et al., 2001; Weiden et al., 1991).

Since weight gain contributes to non-compliance with treatment and may lead to medical morbidity, it is important to know and study the causes of weight gain associated with the use of the atypical antipsychotic olanzapine.

Olanzapine, a thienobenzodiazepine, is an atypical antipsychotic drug with a high affinity for the serotoninergic receptors 5-HT_2 and 5-HT_6, and a low affinity for 5-HT_3 receptors *in vitro.* It also has a high affinity for dopaminergic receptors, mainly D2, D3 and D4; muscarinic M1–5; α_1 adrenergic; and histaminergic H1 receptors *in vitro* (Wang et al., 1987; Gómez et al., 2000). The drug reaches peak plasma levels in 5–8 hours and is metabolized through cytochrome p450 cyp1a2 and p450 cyp2d6. It has a half-life of about 45 hours, depending on the rate of metabolism. The recommended dosage is 20 mg daily, but higher doses have been used. The most common side-effects are somnolence and weight gain (Jain et al., 2006). In India, olanzapine is the most common medication followed by risperidone (Chakravarty et al., 2016).

Materials and methods

The study was conducted at GSL Medical College, a tertiary care hospital in Rajahmundry, Andhra Pradesh and its peripheral centers. One Hundred consecutive outpatients who presented at the Department of Psychiatry from January 2015 to October 2015 and who were newly diagnosed as having schizophrenia or its subtypes according to the ICD-10 criteria, patients who were not on any antipsychotic medications for the past three months were included in the study. Initially, Institutional Ethical Committee approval was obtained to conduct the present study. Known patients of diabetes mellitus, cardiovascular disease & thyroid disorders, pregnant patients, smokers and chronic alcoholics were excluded from the study. All the eligible study subjects, fulfilling the selection criteria were initially screened by the Psychiatrist. Informed consent was taken from the patients or their legal caretakers before initiation of the study. A complete baseline investigation was done; clinical symptoms were examined; and the weight and body mass index (BMI) were recorded in a predesigned proforma. The patients were started on olanzapine monotherapy (in doses of 5–15 mg; mean dose 8.375 mg); only benzodiazepines were used as concomitant medication. The patients' weight was recorded weekly till the end of the fourth week. The change in weight was recorded and data on weight gain with respect to age, gender, BMI and dose were analyzed.

Statistical analysis

Statistical analysis was performed using the SPSS for Windows statistical package software. All data were expressed as mean ± SD. The results were evaluated statistically using one way ANOVA followed by student *t*-test for comparison of results. Statistical significance was set at the $p < 0.01$ level.

Observation and results

Of the 100 subjects, only 82 (41 men and 41 women) completed the study, owing mainly to loss of follow up. The median age of the patients was 43.8 years (age range: 18–58 years). The patients were divided in two groups according to age (Table 1). There were 41 patients in each group; group I had 22 men (53.7%) and 19 women (46.3%) less than 45 years of age, and group II had 19 men (46.3%) and 22 women (53.7%) more or equal to 45 years of age.

Table 1. Distribution of the patients according to age and gender (*n*=82)

Gender	less than 45 years	More or equal to 45 years	Total patients
Male	22	19	41
Female	19	22	41
Total	41	41	82

Of the 82 patients who completed the study, 60 (73.2%) gained weight; 25 patients (30%) (mean weight gain: 2.3±2.7 kg) were less than 45 years of age, whereas 35(42.6%) (mean weight gain: 3.5±2.11 kg) were more than or equal to 45 years. The two groups were compared and the results were statistically significant at $p<0.01$, indicating that patients more than or equal to 45 years of age are more prone to gain weight (Table 2 and 3).

Table 2. Distribution and comparison of weight gain according to age (*n*=82)

Age Groups	Patients who gained weight	Patients with no weight gain	Total	Mean weight gain
Less than 45	25	16	41	2.3±2.7 kg
More and equal to 45	35	6	41	3.5±2.11 kg
Total	60	22	82	-

Among women, 32 (78.1%) gained weight; 12 (29.3%) were less than 45 years of age (mean weight gain: 1.52±1.41 kg) and 20 (48.8%) were more than or equal to 45 years (mean weight gain: 2.75±1.29 kg). When the two groups

were compared using the *t* test, the results were statistically significant (p<0.01), indicating that women more than 45 years of age are more prone to gain weight (Table 3). Among men, 28 (68.3%) gained weight; 13 (31.7%) were less than 45 years of age (mean weight gain: 0.87±0.95 kg) and 15 (36.6%) were more than or equal to 45 years of age (mean weight gain: 0.71±0.69 kg). The two groups were compared using the *t* test; the results were not statistically significant (p>0.1), indicating that men are prone to gain weight irrespective of the age (Table 3 and 4).

Table 3. Distribution and comparison of women according to weight gain and age (*n*=41)

Age groups	Patients who gained weight	Patients who did not gain weight	Total	Mean weight gain
Less than 45	12	7	19	1.52±1.41 kg
More or equal to 45	20	2	22	2.75±1.29 kg
Total	32	9	41	-

Table 4. Distribution and comparison of men according to weight gain and age (*n*=41)

Age groups	Patients who gained weight	Patients who did not gain weight	Total	Mean weight gain
Less than 45	13	9	22	0.87±0.95 kg
More or equal to 45	15	4	19	0.71±0.69 kg
Total	38	9	41	-

When change in weight was compared on the basis of gender, 34.1% of men gained weight in comparison with 39.1% of women, which was statistically not significant (*p*>0.1), indicating that weight gain with respect to gender was not significant.

Discussion

Weight gain with olanzapine, has been reported in many studies conducted earlier and our results abide by that (Melkersson et al., 2000; Nemeroff, 1997). The principal findings of this study were that 73.2 % of the patients exhibited a change in weight; the majority were more than 45 years of age. There was no significant difference among the genders. This is in agreement to the finding of the study by Melkersson et al (2000), who reported weight gain and increase in BMI during olanzapine treatment but did not find any difference when compared on basis of gender (Allison et al., 1999; Guille et al., 2000; Farver, 2001). Wetterling et al. (1999), had contrary findings. They concluded that the young and non-obese show the highest weight gain. The finding that there is no significant gender difference in weight gain was contrary to that reported by Gopalaswamy and Morgan (1985). Kinon et al. (1998)reported that men are more prone to gain weight, which is not similar to our findings. Our findings are also contrary to the findings by Jain et al. (2006), who concluded that women more than 40 years, on olanzapine therapy had a tendency to gain more weight.

The association of olanzapine with weight gain and the potential for long-term complications is well documented. Hence it is necessary for physicians using the drug to monitor metabolic changes occurring during the treatment, so that adequate measures can be initiated to prevent significant morbidity and mortality as patients with schizophrenia already have a tendency to gain weight and acquire related medical disorders.

Limitations

The main limitation of this study is that there was no control group used. Also, the duration of the study was short. The blood sugar, lipid profile, BMI changes, other anticholinergic side effects were not noted during the study. This study is part of an ongoing research.

Conclusion

The results of the study revealed that there is a significant gain in weight with olanzapine, which is related to age more than or equal to 45 years, but unrelated to gender. Of the 60 patients who gained weight, 37 (61.7%) reported an increase in appetite. The association of atypical antipsychotics with weight gain and their potential to cause long-term complications is well documented in literature. Clinicians are encouraged to monitor weight, plasma glucose and lipid parameters in patients receiving olanzapine. Also further studies comparing the potential of other atypical antipsychotics to cause weight gain in comparison to olanzapine can give a better therapeutic option.

Conflict of Interest: NIL

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