Research Article

Comparative evaluation of effect of Olanzapine and Quetiapine on body weight and body mass index (BMI) in psychotic patients at a tertiary care teaching hospital in Nepal

Vijay Kaul[1], Shaktibala Dutta[2], Mirza Atif Beg[2], Shalu Bawa[2], Nand Kishore Singh[3], Srihari Dutta[4], Mohammad Anjoom[5]

[1]Department of Psychiatry, Nepalganj Medical College, Nepalgunj, Nepal.
[2]Department of Pharmacology, Shri Guru Ram Rai Institute of Medical & Health Sciences (SGRRIM&HS), Dehradun, Uttarakhand, India.
[3]Department of Psychiatry, Shri Guru Ram Rai Institute of Medical & Health Sciences (SGRRIM&HS), Dehradun, Uttarakhand, India.
[4]Immunization Health Specialist, Unicef, New Delhi, India Country Office, India.
[5]Department of Pharmacology, Shri Guru Ram Rai Institute of Medical & Health Sciences (SGRRIM&HS), Dehradun, Uttarakhand, India.
Correspondence to: Mirza Atif Beg, E-mail: mabeg1997@gmail.com

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Abstract

Background: Atypical antipsychotics are currently the most frequently prescribed class of drugs for psychotic illness. Weight gain and obesity are more problematic with atypical antipsychotics than with typical antipsychotics. Since weight gain contributes to non-compliance with treatment and may lead to medical morbidity, it is important to know and compare the weight gain associated with the use of most commonly prescribed atypical antipsychotics olanzapine and quetiapine at our set up.

Objective: Comparative evaluation of changes in body weight and body mass index (BMI) of psychotic patients treated with olanzapine and quetiapine in a tertiary care teaching hospital in Nepal.

Materials and Methods: This study was conducted in the Department of Neuropsychiatry, Nepalgunj Medical College & Teaching Hospital, Nepalgunj, for a period of 6 months between July to December 2014. A total of 40 patients suffering from psychotic disorders were included in the study and randomly allocated in two groups: Group-I (20 patients) received tablet olanzapine (10–15 mg/day) and Group-II (20 patients) received tablet quetiapine (200–600 mg/day). Patients were followed upto 6 weeks. All values were expressed in mean ± SD. The changes in body weight and BMI were measured at 0 and 6 weeks. Statistical analysis was done by using paired and unpaired *T*-test. p value < 0.05 was considered significant.

Result: Mean weight in group receiving olanzapine at 0 and 6 weeks was 54.59 ± 6.72 kg and 58.75 ± 6.76 kg, respectively and in quetiapine group was 55.37 ± 5.63 kg and 57.18 ± 5.93 kg, respectively ($p < 0.0001$). The mean BMI in olanzapine group at 0 and 6 weeks was 22.99 ± 3.65 kg/m² and 24.79 ± 3.74 kg/m², respectively ($p < 0.01$) and in quetiapine group was 22.18 ± 1.70 and 22.95 ± 1.82 kg/m², respectively ($p < 0.01$). At 6 weeks, the intergroup comparison was done with respect to weight gain and BMI in both the groups which was insignificant ($p > 0.05$).

Conclusion: Both olanzapine and quetiapine showed increase in body weight and BMI in psychotic illness patients during the study period. But intergroup comparison revealed no significant difference between the groups.

KEY WORDS: Olanzapine, quetiapine, weight gain, body mass index

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Introduction

Atypical antipsychotics are currently the most frequently prescribed class of drugs for psychotic illness.[1] Previous studies indicate that these agents provide antipsychotic efficacy with a lower risk of extrapyramidal symptoms (EPS) than typical antipsychotics.[2] Although the use of atypical antipsychotics offers many benefits, these drugs appear to be

associated with varying degrees of metabolic adverse effects, such as weight gain, impaired glucose metabolism and dyslipidemia.[3,4]

A national survey in the USA, which evaluated the patterns of use and emerging adverse effect profile of atypical antipsychotics, found that 70% patients were prescribed an atypical antipsychotic drug and only 30% were prescribed typical antipsychotic. Thirty-four percent of the patients on atypical antipsychotics reported weight gain in comparison to 16% on typical antipsychotics; weight gain was more evident in females (54%).[5]

Weight gain due to psychotropic agents is very complex and may involve several different mechanisms. The molecular mechanisms responsible for antipsychotic-induced weight gain are not fully known. There is ample evidence, however, that binding to certain neurotransmitter receptors may at least partly explain antipsychotic associated weight gain.[6] Low-potency typical antipsychotics (e.g., chlorpromazine) pose a moderate risk of weight gain, whereas high-potency typical antipsychotics (e.g., haloperidol) have not been shown to cause significant weight gain.[7] Overall, weight gain and obesity are more problematic with atypical antipsychotics than with typical antipsychotics. Atpyical antipsychotic medications induce changes in appetite and food intake, most likely because of interaction with serotonergic, histaminergic, and dopaminergic neurotransmitter systems inducing increase in appetite and food intake. Therefore, the effects on weight and body mass index (BMI) likely will progress with time. Duration of antipsychotic use thus is thought to constitute an important factor contributing to weight gain.[8,9]

Olanzapine, a thienobenzodiazepine, is an atypical antipsychotic drug with a high affinity for the serotoninergic receptors 5-HT2 and 5-HT6, and a low affinity for 5-HT3 receptors in vitro. It also has a high affinity for dopaminergic receptors, mainly D2, D3, and D4; muscarinic M1–5; (alpha-1) α-1 adrenergic; and histaminergic H1 receptorsin vitro. It has a half-life of about 45 h, depending on the rate of metabolism. The most common side effects are somnolence and weight gain.[10]

Quetiapine is a dibenzothiazepine derivative, an atypical antipsychotic, with a relatively broad receptor-binding profile. It has major affinity to cerebral serotonergic (5HT2A), histaminergic (H1), and dopaminergic D1 and D2 receptors, moderate affinity to α-1 und α-2-adrenergic receptors, and minor affinity to muscarinergic M1 receptors; it demonstrates a substantial selectivity for the limbic system. This receptor occupancy profile with relatively higher affinity for the 5HT2A receptor compared with the D2 receptor is in part responsible for the antipsychotic characteristics and low incidence of extrapyramidal side effects of quetiapine. The efficacy of quetiapine in reducing positive and negative symptoms of schizophrenia has been proven in several clinical trials with placebo-controlled comparators. Quetiapine has also demonstrated robust efficacy for treatment of cognitive, anxious-depressive, and aggressive symptoms in schizophrenia. Long-term trials show sustained tolerability for a broad spectrum of symptoms. In comparison with other antipsychotics, quetiapine has a favorable side-effect profile.[11]

Psychotropic-induced weight gain is a common cause of medication non-adherence, which can lead to illness relapse, hospitalization, and worsened outcomes. Therefore, it is imperative to have a thorough understanding of psychotropic-induced weight gain, including the relative incidence between psychotropic agents and the pharmacological basis for the adverse effect.[12,13] Weight-gain liabilities and new-onset metabolic side effects occupy middle-ground among newer antipsychotics. Since weight gain contributes to noncompliance 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 antipsychotics olanzapine and quetiapine.

Materials and Methods

This study was conducted in the Department of Neuropsychiatry, Nepalgunj Medical College & Teaching Hospital, Nepalgunj, for 6 months from July to December 2014. All consecutive patients who attended the neuropsychiatry OPD of both sexes were included for the study. The cases were patients who were diagnosed as suffering from schizophrenia, schizoaffective disorder, or acute and transient psychosis, according to ICD 10 system (World Health Organization, 2008) who further had no comorbidity. Patients already suffering from the illness and not on olanzapine or quetiapine earlier were also included. Written informed consent was obtained from the patients/legal guardians after the full explanation of the study protocol. Exclusion criteria were use of psychoactive substances, metabolic and endocrine disorders, severe debilitation, known case of other psychiatric illness as described by ICD 10 (World Health Organization, 2008), occasional use of benzodiazepines, suicidal tendency, refusal to participate, history of drug reaction, breast feeding, and suspected pregnancy.

Study Design

Subjects were assigned in alternate group according to the serial number of attendance into olanzapine (n = 20) and quetiapine (n = 20) groups. Tablet olanzapine was administered at a dose of 10–15 mg once a day and tablet quetiapine was administered at a dose of 200–600 mg once a day. Patients were diagnosed as acute and transient psychotic disorder (n = 16), schizophrenia (n = 17), schizoaffective disorder (n = 7) according to ICD 10 system. The severity of psychotic symptoms as measured by Scales for the Assessment of Positive Symptoms (SAPS) and Scales for the Assessment of Negative Symptoms (SANS). The treatment was carried out by the neuropsychiatrist. The patients who would be added another antipsychotic agent or whose antipsychotic treatment was suspended were to be dropped from the study. Patients were allowed to add tablet Benzhexol 2 mg twice or thrice daily as per requirement after evaluation by a qualified psychiatrist. Drug compliance was monitored rigorously (every patient was provided a diary and advised to cut one number every day, patients/guardians were regularly contacted through mobiles), but no drug blood levels were monitored due to lack of facility locally. The patients were given a standard Nepali

diet schedule which amounted to about 2000 kcal/day. The patient was allowed to add extra diet according to the choice. Weight and BMI were recorded at baseline and at 6 weeks. A weight was measured in morning before food, with departmental weighing machine each time. Patients were assessed on the extra pyramidal side effects and other ADRs. Statistical analysis was done using paired and unpaired *T*-test. *p*-Value < 0.05 was considered significant.

Result

A total of 40 patients were included in the study, 8 patients dropped out from the study due to varying reasons: 4 patients requested therapy change, 3 patients were lost to follow up and 1 patient was uncooperative. Overall, 32 patients completed the study: 16 patients in olanzapine group and 16 patients in quetiapine group (Figure 1). The mean age of the patients in the study drug groups was 25.28 ± 4.26 years. All values were expressed in mean ± SD. The male:female ratio was 15(46.8%):17(53.2%). The baseline mean height, mean weight, and mean BMI were 156.09 ± 6.59 cm, 54.98 ± 6.21 kg, and 22.59 ± 2.87 kg/m^2 (Table 1). The comparison in changes in weight and BMI was done between 0 and 6 weeks in both the study groups. In olanzapine group, the mean weight at 0 week was 54.59 ± 6.72 kg and at 6 weeks was 58.75 ± 6.76 kg ($p < 0.001$) and in quetiapine group the mean weight at 0 and 6 weeks was 55.37 ± 5.63 kg and 57.18 ± 5.93 kg, respectively ($p < 0.001$) (Table 2). The mean BMI in olanzapine group at 0 and 6 weeks was 22.99 ± 3.65 kg/m^2 and 24.79 ± 3.74 kg/m^2, respectively ($p < 0.01$) and in quetiapine group was 22.18 ± 1.70 and 22.95 ± 1.82 kg/m^2, respectively ($p < 0.01$) (Table 2). At 6 weeks, the intergroup comparison was done with respect to weight gain and BMI in both the groups which was insignificant ($p > 0.05$) (Figure 2).

Discussion

This study was done to compare the effects of olanzapine and quetiapine on body weight and BMI in psychotic illness patients. A total of 32 patients completed the study: 16 patients in olanzapine group and 16 patients in quetiapine group. The mean age of the patients in the study drug groups was 25.28 ± 4.26 years. The male:female ratio was 15(46.8%):17(53.2%). The baseline mean height, weight, and BMI were 156.09 ± 6.59 cm, 54.98 ± 6.21 kg, and 22.59 ± 2.87 kg/m^2, respectively. We compared the changes in weight and BMI between 0 and 6 weeks in both the study groups. A highly significant increase in mean weight was seen in both olanzapine and quetiapine groups at the end of 6 weeks ($p < 0.001$). The changes in BMI were also significant in both olanzapine and quetiapine treated patients at the end of 6 weeks ($p < 0.01$). At 6 weeks, the intergroup comparison was done with respect to weight gain and BMI in both the groups which was insignificant ($p > 0.05$).

The mean age of the patients in our study was 25.28 ± 4.26 years. The results from previous studies have concluded that the majority of mental health disorders manifest around the age of mid-20s which should be considered as extensions of adolescent disorders.[14] A slightly higher proportion of females were affected with psychotic illness in our study as compared to males. This finding was comparable to study by Van Os et al.[15] found slightly increased incidence rates for women in psychosis. But this was in contrast to other study where no gender difference has been seen in prevalence of schizophrenia.[16] According to our study, it is important to note that more women than men seek help for psychological or medical problems as has been seen in a previous study.[17] Both the study groups showed highly significant gain in weight and BMI during the study period. The mean increase in weight in olanzapine group was 4.16 kg and in quetiapine group was

Table 1: Baseline characteristics

Variables	No (% age)
Age	25.28 ± 4.26
Male:Female	15 (46.8%): 17 (53.2%)
Height (cm)	156.09 ± 6.59
Weight (kg)	54.98 ± 6.21
Body mass index (kg/m^2)	22.59 ± 2.87

All values are expressed in mean ± SD.

Table 2: Comparison of change in weight and body mass index (BMI) over the study period

Parameter	Drug groups	0 weeks	6 weeks	*p*-value
Change in weight	Olanzapine ($n = 16$)	54.59 ± 6.72	58.75 ± 6.76	<0.001
	Quetiapine ($n = 16$)	55.37 ± 5.63	57.18 ± 5.93	<0.001
Change in BMI	Olanzapine ($n = 16$)	22.99 ± 3.65	24.79 ± 3.74	<0.01
	Quetiapine ($n = 16$)	22.18 ± 1.70	22.95 ± 1.82	<0.01

All values are expressed in mean ± SD.

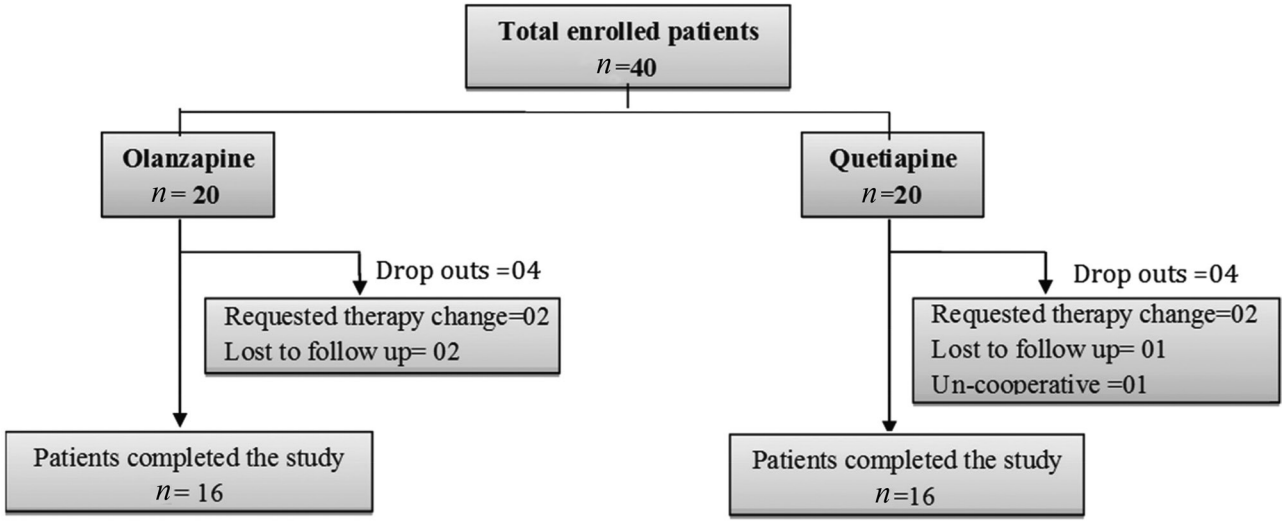

Figure 1: Flowchart of patients who completed the study.

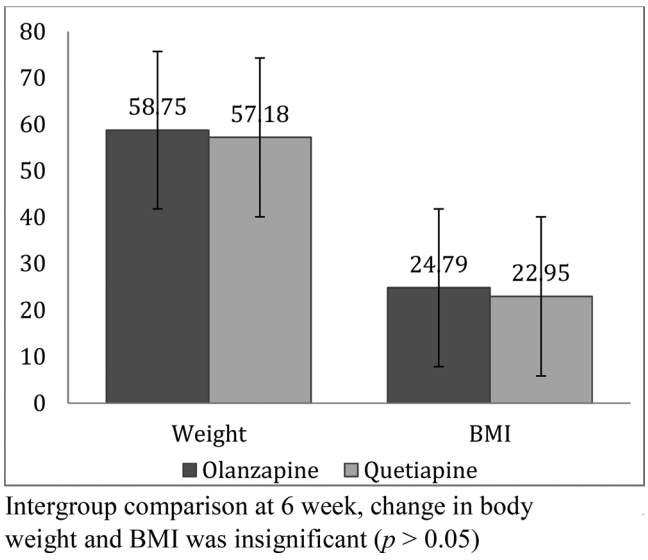

Figure 2: Intergroup comparison at 6 weeks.

1.82 kg. Of the atypical antipsychotics, olanzapine has the most significant effect on weight. This finding was consistent with previous studies which have shown highest weight gain in patients treated with olanzapine, quetiapine, and clozapine.[18–20]

The capability of antipsychotics to cause weight gain roughly correlates with their affinity for histamine-1 and serotonin-2C receptors. Olanzapine is a potent antagonist of these receptors, and is associated with the most weight gain. Quetiapine has high affinity for histamine-1 receptors, but much lower affinities for dopamine-2 and serotonin-2C receptors, and it causes moderate weight gain.[21] In our study the increase in body weight and BMI was measured, these parameters were increased in both the olanzapine and quetiapine groups. This was also seen in previous studies.[22–24] Although mean weight and BMI increased more with olanzapine-treated patients, intergroup comparison at 6 weeks showed no significant difference between the two groups. This was similar to previous study which showed no significant difference between olanzapine and quetiapine in respect to change in body weight and BMI in psychotic illness patients.[25]

Study Limitations

The study was an open label study. Both doctors and patients were aware of the treatments. Hence more chances of bias. The sample size was very small and no sample size calculation was done. Patients were followed up only for 6 weeks.

Conclusion

Both olanzapine and quetiapine showed increase in body weight and BMI in psychotic illness patients during the study period. But intergroup comparison revealed no significant difference between the groups. A longer duration study with larger sample size could have yielded different results.

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