COMPARATIVE STUDY OF OLANZAPINE AND QUETIAPINE IN PSYCHOTIC DISORDERS

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ABSTRACT

BACKGROUND

Psychotic disorders are a group of chronic debilitating psychiatric illness characterised by loss in touch with reality and disorders of thought, behaviour, appearance and speech. The second generation atypical antipsychotic olanzapine has been reported to be the commonly prescribed antipsychotic. However, olanzapine can cause adverse effects like weight gain, hyperglycaemia, diabetes, dyslipidaemia and metabolic syndrome. Quetiapine, another second generation antipsychotic has good efficacy and has become well established in the treatment of schizophrenia and manic episodes. There are reports on adverse effects of hyperglycaemia and diabetes with quetiapine, but these are comparatively lesser than olanzapine.

The aim of the study is to compare the efficacy of olanzapine and quetiapine in patients with psychotic disorders.

MATERIALS AND METHODS

It was an unicentric, open label, prospective and comparative clinical study. Subjects (n=80) who were diagnosed with psychotic disorder were randomly assigned to receive olanzapine (group 1) or quetiapine (group 2). The efficacy of the two drugs was assessed on the basis Brief Psychiatric Rating Scale (BPRS) scores at baseline, 1 week and 6 weeks. UKU scale (Udvalg Kliniske Undersogelser) and laboratory investigations were used to assess the safety profile.

RESULTS

The two study groups had comparable sociodemographic profile. Both the groups showed significant reduction in psychotic symptoms as compared from baseline to 1 week and 6 weeks ($p<0.001$). The intergroup comparison of the efficacy of the two groups did not show any statistically significant results. There was statistically insignificant differences in the occurrence of adverse effects in both the groups. Sedation (50% in both the groups) was the most common adverse effect in both the groups. The use of concomitant medications was comparable in both the groups. Benzodiazepines (56.3% in the olanzapine group and 51.9% in the quetiapine group) were the most common concomitant medication.

CONCLUSION

Olanzapine and quetiapine were effective in reducing psychotic symptoms. Both the drugs are equally efficacious. Quetiapine can be used as an alternative to olanzapine in managing psychotic disorders. Both groups had comparable safety profile and the adverse effects were tolerable. Benzodiazepines were the most common concomitant medication.

KEYWORDS

Olanzapine, Quetiapine, BPRS, UKU, Psychotic Disorders.

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BACKGROUND

Psychosis is defined as a loss of ego boundaries or a gross impairment of reality testing[1] in which a person's perception, thoughts, mood and behaviour are significantly altered.[2,3] Psychotic symptoms are conventionally characterised to be the main features of schizophrenia and other non-affective psychotic disorders, while affective psychoses and secondary psychoses are often regarded as disorders where there are associated psychotic symptoms.[4]

The symptoms of psychosis and schizophrenia are usually divided into 'positive symptoms', which include hallucinations (perception in the absence of any stimulus), delusions (fixed, firm and falsely held beliefs), disorganised behaviour; 'negative symptoms' (such as emotional apathy, lack of drive, poverty of speech, social withdrawal and self-neglect).[2] The lifetime prevalence of any psychotic disorder was reported to be 3.48%, non-affective psychotic disorders 2.29%, schizophrenia 1.00% and affective psychoses to be 0.62%.[4]

The introduction of antipsychotic drugs has led to massive changes in the disease management and identifying the pathophysiology of psychotic disorders.[5] Recent reports have shown second generation atypical antipsychotic olanzapine to be the most commonly prescribed antipsychotic.[6-10] However, various studies revealed that olanzapine can cause adverse effects like hyperglycaemia, diabetes,[11-14] dyslipidaemia[11,15,16,17] and metabolic syndrome.[18,19] Being associated with adverse effects, whether the fact that olanzapine is commonly prescribed is just is a question that whether it could be replaced with other safer drug.

Quetiapine, a newer member of the Second Generation Antipsychotics (SGAs) has good efficacy and has become well established in the treatment of schizophrenia and manic episodes.[20] There are reports on adverse effects of hyperglycaemia and diabetes with quetiapine, but these are comparatively lesser than olanzapine.[21]

Both the drugs are potent, 5HT blocker and have low D_2 occupancy.

In the recent years, various studies have evaluated the efficacy and safety profile of these drugs. While various studies[21-25] reported olanzapine to be more effective than quetiapine and other SGAs, other studies[20,26] reported quetiapine to be more effective than olanzapine and other SGAs. However, there are also studies,[27] which demonstrated comparable effectiveness of both the drugs.[28-30]

With this background and taking into account that not much effective research has been conducted in this direction of Kumaon region in the State of Uttarakhand, India. Our study is an effort to evaluate the efficacy of pharmacological therapy in psychotic disorders. Therefore, the present study was undertaken to compare the atypical antipsychotic, quetiapine with olanzapine in terms of efficacy and safety profile in our tertiary setup hospital, Haldwani, Uttarakhand, India.

MATERIALS AND METHODS

The study was a unicentric, open label, prospective, comparative clinical study, which was undertaken for a study period of 1 year, i.e. from October 2015 to October 2016 after duly taking permission from the institutional ethical committee in the Department of Pharmacology and Psychiatry, Government Medical College, and Dr. Susheela Tiwari Government Hospital, Haldwani, Uttarakhand.

Inclusion and Exclusion Criteria- All the patients diagnosed with psychotic disorder between 18-60 years were included in the study. Patients or patients' relatives not willing to participate in the study were excluded from the study. Pregnant and lactating mothers, patients with history of metabolic syndrome, severe cardiac, hepatic, renal diseases and other comorbid illnesses were excluded.

After meeting inclusion and exclusion criteria, due written informed consent was obtained from the patient or patient's relatives before the recruitment.

Group Design- The study had two treatment groups-

Group 1- Patients in group 1 were given tablet olanzapine in starting dose of 10 mg[31] orally per day and titrated to 15 mg[31] orally per day on the fourth day and the same dose maintained further till 6 weeks.

Group 2- Patients in group 2 were given tablet quetiapine in starting dose of 100 mg[31] orally per day and titrated to 400 mg[31] orally per day on the fourth day and the same dose maintained further till 6 weeks.

Concomitant medications as prescribed by clinician were used during the clinical course of individual patient.

Assessment- Evaluation of the patient was done at 1st visit (baseline), 2nd visit (1 week) and 3rd visit (6 weeks) and included the following-

Sociodemographic Profile Assessment- The sociodemographic profile of the patients was assessed at baseline (1st visit).

Clinical Evaluation- After taking the detailed history of the patient, clinical evaluation of the signs and symptoms was done. General examination included observing signs of pallor, icterus, cyanosis, clubbing, lymphadenopathy, oedema and recording the weight and vitals (blood pressure, pulse rate, respiratory rate and temperature). This was followed by examination of the central nervous system, cardiovascular system, respiratory symptom and the abdomen.

Assessment of Efficacy- Assessment of efficacy of the treatment drugs was done by Brief Psychiatric Rating Scale (BPRS)[32] expanded version. BPRS score was recorded for each patient before starting of the therapy at 1st visit (baseline), 2nd visit (1 week) and 3rd visit (6 weeks).

Assessment of Safety Profile- The safety profile of the drugs was measured using UKU (Udvalg Kliniske Undersogelser)[33] side effect rating scale. The causality assessment of the adverse effects was done by WHO causality assessment scale.[34] The adverse effects of the drug were then reported to the Indian Pharmacopoeia Commission.

Laboratory Investigations- The laboratory investigations were used to rule out any comorbid illness as well as for monitoring the safety profile of drugs. The following baseline

investigations were done on 1st visit and in the subsequent 2nd and 3rd visits- Haemoglobin levels, Total Leucocyte Count (TLC), Differential Leucocyte Count (DLC), Fasting Blood Sugar (FBS), Electrocardiogram (ECG), thyroid profile, Liver Function Test (LFT), Kidney Function Test (KFT) and lipid profile.

Statistical Analysis- The data thus collected were first filled in Microsoft excel (Office 2010) and then transferred to SPSS Version 21 for statistical analysis. Differences in the mean values of the BPRS score between the study groups were evaluated by independent sample t-test. The within group comparison of the mean values of the BPRS score in the subsequent visits was analysed by paired t-test. Non-parametric test was used to test the significance for qualitative data. The confidence interval percentage was 95% and the result was considered significant at p value less than 0.05.

Figure 1. Flow Chart of Patients' Recruitment

RESULTS

Out of 109 eligible participants, 52 patients and 57 patients were enrolled for the olanzapine and quetiapine trial, respectively. The flow chart (Figure 1) outlines the algorithm of the study patients' recruitment. In the olanzapine group, out of 52 patients, 12 patients were excluded from the study due to loss to follow up. A total of 17 patients were excluded from the quetiapine group out of the 57 patients due to loss to follow up. Our study was therefore, done on 80 patients with psychotic disorders. These 80 patients were followed up at 1 week (2nd visit) and 6 weeks (3rd visit).

Sociodemographic Profile- The sociodemographic profile of the study patients had been descripted in Table 1. Both the groups had comparable sociodemographic profile.

Efficacy- We assessed the psychotic symptoms of the study patients with BPRS at 0, 1 and 6 weeks. There was no statistically significant difference in the mean total BPRS scores at baseline, 2nd visit (1 week) and 3rd visit (6 weeks) (Table 2) between the two groups. Our results give impression that the two drugs have comparable efficacy profile. In the olanzapine group, the within group comparison of mean total BPRS scores from baseline to 2nd visit (1 week) and endpoint (6 weeks) suggested highly significant reduction ($p<0.001$) in psychotic symptoms (Table 3). Similarly, in our quetiapine group, there was highly significant ($p<0.001$) reduction in the psychotic symptoms from baseline to the 2nd visit (1 week) as well as at endpoint (6 weeks) (Table 3). Our study results give impression of progressive recovery by treatment in both the groups (Figure 2, 3).

We also assessed the change (difference between the total BPRS score at the baseline and endpoint) to further compare the efficacy of olanzapine and quetiapine. There was no statistically significant difference in the mean change in between the two groups (Table 4).

	Olanzapine Group n(%)	Quetiapine Group n(%)	Significance (p)
Gender*			
Male	22 (55)	19 (47.5)	0.502
Female	18 (45)	21 (52.5)	
Mean Age# (Mean ± SD)	34.5 ± 10.8	36.1 ± 10.2	0.498
Education*			
No schooling	6 (15)	3 (7.5)	
I to VIII	8 (20)	13 (32.5)	0.316
IX and above	26 (65)	24 (60)	
Marital Status*			
Married	19 (47.5)	24 (60)	0.370
Family history of psychiatric illness	8 (20)	9 (22.5)	-
History of substance abuse	6 (15)	14 (35)	-
Locality			
Rural	30 (75)	28 (70)	-

Table 1. Sociodemographic Characteristics of the Study Patients

*Chi-square test; #Unpaired t-test.

Visit	Olanzapine Group (Mean ± SD)	Quetiapine Group (Mean ± SD)	Significance
1st Visit	73.6 ± 11.2	76.9 ± 10.1	p=0.170
2nd Visit	65.9 ± 10.5	68.9 ± 9.3	p=0.176
3rd Visit	46.3 ± 7.1	48.4 ± 4.9	p=0.136

Table 2. Mean Total BPRS Scores of the Study Patients at Each Visit

Unpaired t-test; $p<0.05$=significant.

Visit	1st Visit (Baseline) Mean ± SD	2nd Visit Mean ± SD	3rd Visit Mean ± SD	Significance
Olanzapine group	73.6 ± 11.2	65.9 ± 10.5	46.3 ± 7.1	p=<0.001* p=<0.001**
Quetiapine group	76.9 ± 10.1	68.9 ± 9.3	48.4 ± 4.9	p=<0.001* p=<0.001**

Table 3. Comparison of the Mean Total BPRS Scores Within the Group

*1st visit vs. 2nd visit mean total BPRS score; **1st visit vs. 3rd visit mean total BPRS score; Paired t-test; $p<0.05$=significant.

Group	Olanzapine Group (Mean ± SD)	Quetiapine Group (Mean ± SD)	Significance
Change in total BPRS scores from 1st visit to 3rd visit	27.3 ± 11.6	28.5 ± 9.3	p=0.611

Table 4. Change in Total BPRS Scores from 1st Visit (Baseline) to 3rd Visit

Unpaired t-test, $p<0.05$=significant; mean change is the mean of the difference between the total BPRS score at the 1st visit (baseline) and 3rd visit.

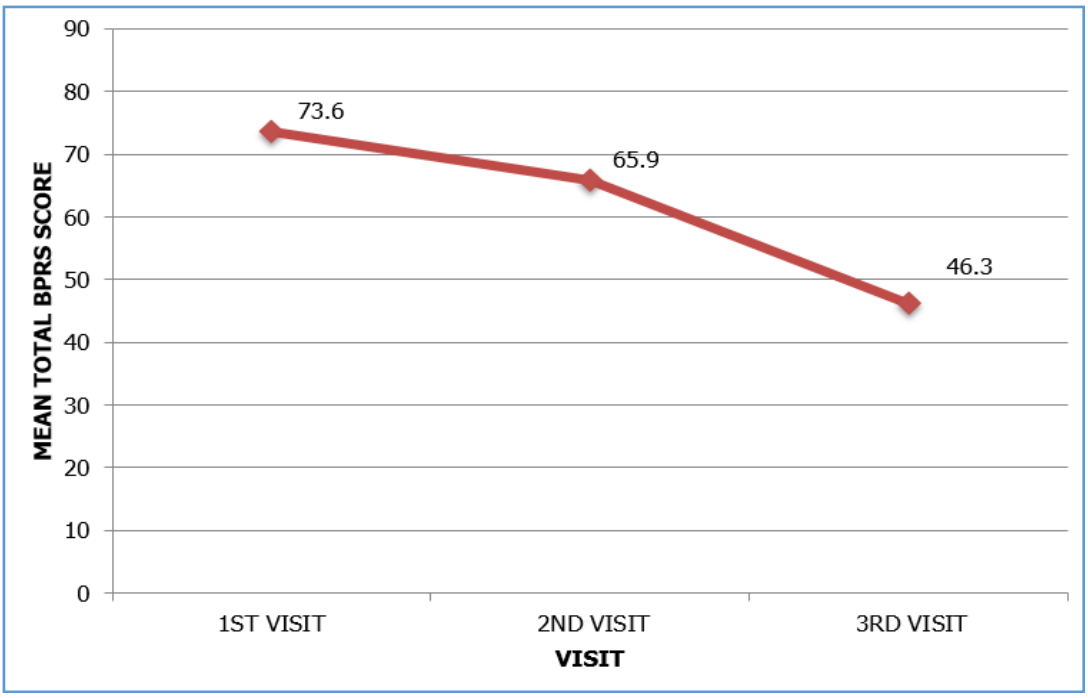

Figure 2. The Mean Total BPRS Scores of the Study Patients at Each Visit in the Olanzapine Group

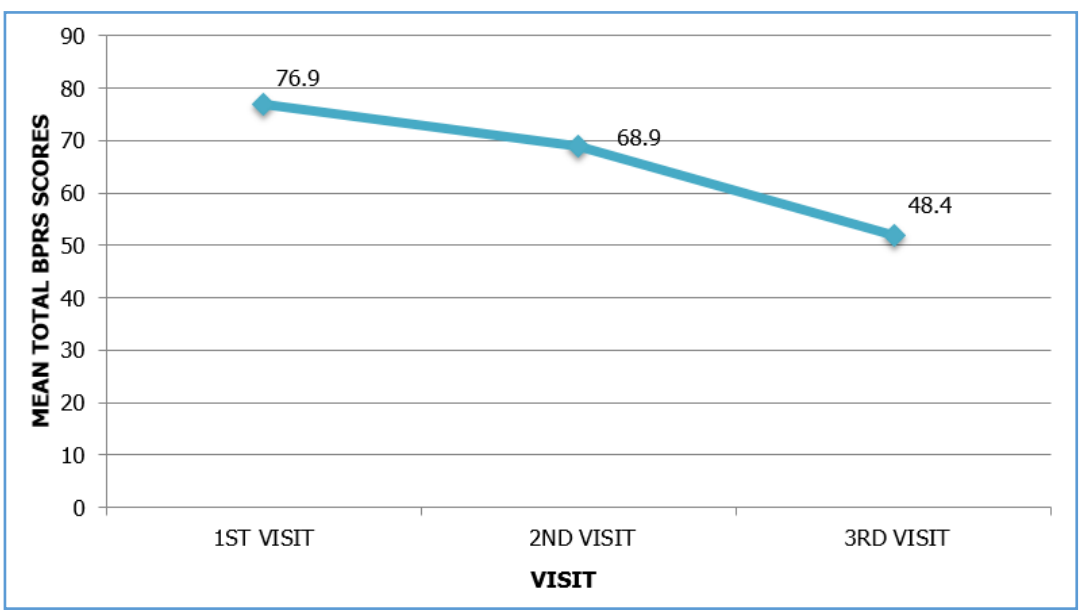

Figure 3. Mean Total BPRS Scores of the Study Patients at Each Visit in the Quetiapine Group

Safety Profile- About 50% (20 patients) and 40% (16 patients) of the study patients had adverse effects in the olanzapine and quetiapine groups, respectively (Table 5). There was no statistically significant difference in the number of patients with adverse drug effects between the two groups. The most common adverse effect in both the groups was sedation (Table 6). There was no significant within group changes in the mean haemoglobin levels, mean fasting blood glucose, total cholesterol, triglyceride values, thyroid profile, ECG, liver function test and kidney function test in the study patients.

Concomitant Medication- Concomitant medications were used in 70% (28 patients) and 57.5% (23 patients) in the olanzapine and quetiapine groups, respectively (Table 7). This data included patients with more than 1 concomitant medication. There was no statistically significant difference in the number of patients with concomitant medication between the two groups. The concomitant medications used in the study patients in both the groups have been described in Table 8. Out of concomitant medications, benzodiazepines were the most common concomitant medication used in both the groups (56.3% and 51.9% in the olanzapine and quetiapine group, respectively). Clonazepam was the most commonly prescribed benzodiazepine (72.2% in the olanzapine group and 64.3% in the quetiapine) (Table 9).

Group	Olanzapine Group n (%)	Quetiapine Group n (%)	Total n (%)	Significance
Number of patients with adverse effects	20 (50)	16 (40)	36 (45)	p=0.369
Number of patients without adverse effects	20 (50)	24 (60)	44 (55)	
Total	**40**	**40**	**80**	

Table 5. Number of Patients with Adverse Effects of Drugs in Both the Groups

Chi-square test; p<0.05=Significant.

Adverse Drug Effects	Olanzapine Group n (%)	Quetiapine Group n (%)	Total n (%)
Asthenia/lassitude	1 (3.8)	1 (5)	2 (4.3)
Sleepiness/sedation	13 (50)	10 (50)	23 (50)
Tremor	1 (3.8)	2 (10)	3 (6.5)
Orthostatic dizziness	1 (3.8)	1 (5)	2 (4.3)
Weight gain[a]	7 (27.0)	4 (20)	11 (23.9)
Tension headache	2 (7.8)	2 (10)	4 (8.7)
Vomiting	1 (3.8)	0	1 (2.3)
Total	**26**	**20**	**46**

Table 6. Adverse Drug Effects Observed in the Study Patients

a. Weight gain is not clinically significant.
b. Some patients reported multiple adverse effects.
Note- Percentage calculated out of total number of adverse effects in the respective group.

Group	Olanzapine Group n (%)	Quetiapine Group n (%)	Total n (%)	Significance
Number of patients with concomitant medication	28 (70)	23 (57.5)	51 (63.8)	P=0.245
Number of patients without concomitant medication	12 (30)	17 (42.5)	29 (36.2)	
Total	**40**	**40**	**80**	

Table 7. Number of Patients with Concomitant Medications in Both the Groups

Chi-square test; p<0.05=Significant.

Concomitant Medication	Olanzapine Group n (%)	Quetiapine Group n (%)
Benzodiazepines	18 (56.3)	14 (51.9)
Antiepileptics	4 (12.4)	6 (22.2)
Anticholinergics	2 (6.3)	2 (7.4)
Antidepressants	3 (9.4)	1 (3.7)
Lithium	1 (3.1)	0
Multivitamin	0	1 (3.7)
Muscle relaxant	0	1 (3.7)
Antiemetic	1 (3.1)	0
Antiallergic	2 (6.3)	1 (3.7)
Antimicrobial	1 (3.1)	1 (3.7)
Total	**32**	**27**

Table 8. Concomitant Medications Used During the Study

Note- Percentage calculated out of total number of concomitant medications in the respective group.

Drug	Olanzapine Group n (%)	Quetiapine Group n (%)
Clonazepam	13 (72.2)	9 (64.3)
Lorazepam	5 (27.8)	5 (35.7)
Total	**18**	**14**

Table 9. Benzodiazepines Used as Concomitant Medication in Both the Groups

DISCUSSION

Our study was a unicentric, open label, prospective, comparative clinical study. The study was conducted on a total number of 80 patients with psychotic disorders. These 80 patients were then followed up at 1 week (2nd visit) and 6 weeks (3rd visit). The two treatment groups received olanzapine (group 1) and quetiapine (group 2). The

sociodemographic profile in both the groups were comparable.

With respect to efficacy, in the olanzapine group, the within group comparison of mean total BPRS scores from baseline to endpoint (6 weeks) suggested highly significant reduction ($p<0.001$) in psychotic symptoms. This findings of our study suggest that olanzapine was effective in reducing the psychotic symptoms. This efficacy of olanzapine in psychotic disorders observed in our study is in accordance to CATIE trial,[21] which reported olanzapine to be effective in schizophrenia. Lieberman JA et al 2003[35] found that not only olanzapine was effective in treating psychotic symptoms, but it had several relative advantages in therapeutic response. Another double-blind comparative study[36] reported olanzapine to be with greater efficacy. A pilot study by Gobbi G et al 2014[28] had also reported olanzapine to be effective in psychosis. Another study done by Suresh K. et al 2016[37] in southern part of India had highlighted the better efficacy of olanzapine.

Similarly, in our quetiapine group, there was highly significant ($p<0.001$) reduction in the psychotic symptoms at the endpoint (6 weeks). This implies that quetiapine is effective in reducing psychotic symptoms. A study done by Mullen J et al 2001[38] reported that quetiapine is as effective as other SGAs in treating psychotic symptoms. Joseph P et al 2007 also demonstrated comparable efficacy of quetiapine with other SGAs.[27] Jon A. Shaw et al 2004[39] suggested quetiapine to be effective treatment of youths with psychotic disorders. K. P. Good et al 2002[40] reported improvement in cognitive functioning in patients with first-episode psychosis during treatment with quetiapine. According to Riedel M et al 2007,[20] quetiapine has become well established in the treatment of schizophrenia and manic episodes because of its good efficacy. A study done by Buckley PF et al 2004[41] had reported the efficacy of quetiapine for the treatment of schizophrenia. A meta-analytic study of efficacy by Schulz S et al 2003[42] also narrated the efficacy of quetiapine.

There was no statistically significant differences between the two groups in the mean total BPRS scores at baseline, 2nd visit and 3rd visit. We also assessed the change (difference between the total BPRS score at the baseline and endpoint (6 weeks) to further compare the efficacy of olanzapine and quetiapine. There was no statistically significant difference in the mean change in between the two groups. This finding suggests that both olanzapine and quetiapine are equally efficacious in reducing psychotic symptoms. This observation is in accordance with the study done by Joseph P. et al,[27] which demonstrated comparable effectiveness of olanzapine and quetiapine in early psychosis. Another pilot study by Gobbi G et al[20] compared the effects of olanzapine and quetiapine in patients with psychosis and found that quetiapine and olanzapine equally decreased impulsive and psychotic symptoms after 8 weeks of treatment. Saccheti et al 2004[29] in their study of comparison study reported comparable efficacy of olanzapine and quetiapine. Tandon R et al 2005[30] reported no evidence of differential efficacy among the SGAs, risperidone, olanzapine, quetiapine, ziprasidone and aripiprazole. However, CATIE trial[21] reported olanzapine to be more effective than quetiapine and other SGAs. Whereas, a study done by Johnsen E et al 2010[26] reported quetiapine to be more effective than olanzapine and other SGAs. Another study by Reidel M et al 2007[20] reported greater improvement in the quetiapine group than olanzapine.

None of the participants experienced serious adverse events. Sedation was the most common adverse effect in both the groups (13 adverse effects, 50% in the olanzapine group and 10 adverse effects, 50% in the quetiapine group). Studies relate the blockade of histaminic, H_1 receptors by antipsychotics to its sedative effect.[43] In the present study, there were no significant changes in the haemoglobin levels, DLC, TLC, thyroid profile, liver function test, kidney function test and ECG in both the groups.

There was statistically insignificant difference in the use of concomitant medications in the study patients between the two groups. Among the concomitant medications, benzodiazepines (56.3% in the olanzapine group and 51.9% in the quetiapine group) were the most common concomitant medication used. This is in line with previous studies done by Vares M et al 2011.[44] Among the benzodiazepines, clonazepam (72.2% in the olanzapine group and 64.3% in the quetiapine group) was the most commonly prescribed.

CONCLUSION

Olanzapine and quetiapine were effective in reducing psychotic symptoms. Both the drugs are equally efficacious. Quetiapine can be used as an alternative to olanzapine in managing psychotic disorders. Both groups had comparable safety profile and the adverse effects were tolerable. Sedation was the most common adverse effect in both the groups. There was statistically insignificant difference in the use of concomitant medications in both the groups. Benzodiazepines were the most commonly used concomitant medication, out of which, clonazepam was the most commonly prescribed.

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