Research Article

Effect of Risperidone and Olanzapine on Obsessive Compulsive Symptoms in Patients with Schizophrenia

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Abstract

Aims and Objectives: To evaluate the response to treatment with antipsychotic drugs in both OC symptoms as well as underlying schizophrenia, in patients with schizophrenia who have obsessive compulsive disorder/symptoms. **Material & Methods:** All newly diagnosed cases of schizophrenia as per ICD10 criteria by the consultant psychiatrist were included in study. Patient enrollment, data collection and follow-up were done over a period of 12 months and data analysis was done over next 6 months. This was a prospective observational study which also evaluated the response to treatment with medications and follow up was done 12 weeks after initiation of treatment in each patient. All the patients who were diagnosed as schizophrenia, and those who were drug naïve, were subjected to inclusion criteria: The clinical features of the study patients further carefully analyzed for the presence of obsessive compulsive symptoms/ disorder (OCS/D) as per the ICD 10 criteria for obsessive compulsive disorder. The outcome of patients was assessed clinically with PANSS and CGI scores at 12 weeks for all patients. In schizophrenia patients with obsessive compulsive symptoms/disorder (Group A), the outcome was assessed with the help of YBOCS score at 12 weeks follow up visit. Results: Prevalence of OCD/S in schizophrenia according to our study was 24.7%. Mean baseline total YBOCS score was 23.96 ± 4.06 with mean YBOCS obsessions score being 12.85 ± 5.28 and mean YBOCS compulsion score being 10.92 ± 5.22. Severe OC symptoms were in 65.38% and 34.61% had moderate OC symptoms. The mean baseline PANSS score was 53.4 ± 13.5 in patients with OCD-schizophrenia and 53.6 ± 10.4 in patients with only schizophrenia. Both atypical antipsychotic drugs risperidone and olanzapine were equally effective in controlling OC symptoms in these patients as indicated by the significant p values ($p<0.001$). At the end of 3 months treatment with atypical antipsychotics the mean PANSS positive symptom score for group A was 12.2 ± 2.6 and for group B was 12.1 ± 3 which had no statistical difference ($U=993.5$, $p=0.802$) and the negative symptom score for group A patients was 8.6 ± 3.9 and for group B patient was 9.5 ±4.9 which also had no statistical significance ($U=979.5$, $p=0.626$). There was a statistically significant difference seen in the mean scores with a reduction in the scores at the end of 3 months for both the groups (t 15.714, $p<0.001$; t 16.624 $p<0.001$) respectively. Hence both the groups had more or less same severity despite the psychopathology of OCS in Group A patients both the groups had better improvement at the end of three months of treatment with

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no statistical difference(u=810,p=0.064) in two groups. **Conclusion:** The prevalence of OCD in schizophrenia was 24.7%. At the end of 3 months there was a marked reduction in obsessive compulsive symptoms on YBOCS on treatment with both Risperidone and Olanzapine.

Introduction

The Obsessive-Compulsive (OC) phenomenon in schizophrenia has been extensively described and debated over the years. Co-occurrence of Obsessive–Compulsive Symptoms (OCS) and psychotic illness was first recognized over a century ago. [1] In the early years, it was believed tShat these affective and anxiety symptoms are a reactive manifestation to the perceived external or internal stressors. [2]

The revival in interest in this area in recent years is a result of increased recognition of higher comorbidity rates and emergence or exacerbation of OC symptoms during treatment of psychosis with the atypical antipsychotics. [3, 4] There is an increasing evidence to point towards the fact that patients with OC symptoms disorder and schizophrenia (recently termed "schizo-obsessive" may represent a special category of the schizophrenia population. [5, 6]

Conventional first-generation antipsychotic medications are generally ineffective in the treatment of patients with OC schizophrenia. However, a number of recent treatment studies and anecdotal case reports have shown an adjunctive Selective Serotonin Reuptake Inhibitor (SSRI) may be an effective intervention. Furthermore, since the introduction of Second Generation Antipsychotic (SGA) medication there has been emergence of clinical evidence suggesting development of de novo or exacerbation of pre-existing obsessions and compulsive symptoms in well-established schizophrenia. [4] Thus there is a need of a study addressing these issues.

The issue is affected by lack of exact prevalence, especially in Indian population; the association of these symptoms with types of schizophrenia; the effect of OC symptoms on over all prognosis and outcome of these patients with treatment modalities including drugs and psychotherapy, thus strongly pointing towards need of a study addressing these issues.

Hence, the aim of our study is to evaluate the response to treatment with antipsychotic drugs in both OC symptoms as well as underlying schizophrenia, in patients with schizophrenia who have obsessive compulsive disorder/ symptoms.

Material and Methods

The study was approved by the Institutional Ethics committee of the parent institute. All participants were informed about the study protocol, clinical evaluation and the treatments involved in the study. Written informed consent was obtained from all participants. The study was performed in accordance with the provisions of the Declaration of Helsinki. This was Prospective observational study. Cases were enrolled from the patients attending outpatient clinic and patients admitted in the department of Psychiatry of a tertiary care teaching hospital.

Study population and sample size

All newly diagnosed cases of schizophrenia as per ICD10 criteria by the consultant psychiatrist were included in study.

There are approximately 350 newly diagnosed cases of schizophrenia per year. 30% of these patients who were drug naïve were selected after fulfilling the inclusion and exclusion criteria. The patients were enrolled after obtaining a written informed consent. Thus sample size calculated was therefore 105 new cases of schizophrenia.

Duration of study

Patient enrolment, data collection and follow-up were done over a period of 12 months and data analysis was done over next 6 months. Thus total duration of study was 18 months. This was a prospective observational study which also evaluated the response to treatment with medications and follow up was done 12 weeks after initiation of treatment in each patient.

Selection of cases

All patients attending outpatient clinic of department of Psychiatry and all patients admitted in the department of Psychiatry in the study duration were evaluated for features of schizophrenia as per ICD 10 criteria, which are as follows: All the patients who were diagnosed as schizophrenia, and those who were drug naïve, were subjected to following inclusion criteria.

Inclusion criteria

- Age group: Above 18 years.
- Clinically diagnosed cases of schizophrenia as per ICD10 criteria.
- No previous exposure to antipsychotic medications (drug naive).
- Informed consent of patient.

Exclusion criteria

The exclusion criteria were as follows:

- Patients having other medical comorbidities.
- Patients already diagnosed as having psychiatric illness and on medications.
- Already diagnosed cases of schizophrenia on treatment.

Patients with drug naïve schizophrenia fulfilling above criteria were included in the study. Written informed consent to participate in the study was taken from the patient's relatives, prior to enrolment. Complete history taking and thorough clinical evaluation was done in each patient as per protocol. The clinical features of the study patients further carefully analysed for the presence of obsessive compulsive symptoms / disorder (OCS/D) as per the ICD 10 criteria for obsessive compulsive disorder.

Out of the 105 schizophrenia patients included in our study, 26 patients satisfied the ICD10 diagnostic criteria for obsessive compulsive disorder. Thus the patients were divided into flowing two groups:

Group A: Patients of schizophrenia with obsessive compulsive symptoms/disorder (n=26).

Group B: Patients of schizophrenia without obsessive compulsive symptoms/disorder (n=79).

A semi structured proforma was used to collect information on the various demographic variables, phenomenological factors such as duration of schizophrenia, duration of OCD/ OCS, number of hospitalizations for the same and scales pertaining to the aims of the study. Severity of schizophrenia symptoms was assessed with The Positive and Negative Symptoms Scale (PANSS), severity of OCD was assessed on YBOCS and global severity and improvement was assessed using CGI scale.

Outcome measures

The outcome of patients was assessed clinically with PANSS and CGI scores at 12 weeks for all patients. In schizophrenia patients with obsessive compulsive symptoms/ disorder (Group A), the outcome was assessed with the help of YBOCS score at 12 weeks follow up visit.

Statistical analysis

All categorical variables were expressed as numbers and percentages. Continuous variables were expressed as mean ± standard deviation. Comparison of categorical variables between the two groups was done with Pearson's chi square test. Fisher's exact test was used for small numbers. Continuous variables were compared between the two groups with the student's t test for two independent samples. Mann Whitney U test was used for nonparametric data. Continuous variables at baseline and three months follow up were compared using paired t test for related samples.

Results and Discussion

We studied 105 adult drug naive patients of schizophrenia diagnosed as per ICD10 criteria. These patients were evaluated for presence of obsessive compulsive disorder/ symptoms. The severity of schizophrenia was estimated by PANSS, whereas the severity of OCD/S was studied by the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS). Patients with schizophrenia were divided into those with and without OCD/S. Various clinical features were studied between the two groups. Patient outcome was assessed with PANSS, YBOCS and Clinical Global Impressions (CGI) scale scores at 12 weeks follow up.

The results of our study and their significance are discussed.

We evaluated 105 patients with schizophrenia, out of whom 26 patients had OCD/S. Thus the prevalence of OCD/S in schizophrenia according to our study was 24.7% [Table 1]. Our finding correlated with the previous studies which noted the prevalence of OCD in Schizophrenia to be ranging from 25%-26.7%. [5, 6] The trend in the prevalence of OC phenomenon in schizophrenia is evolving since the coexistence of OCD and schizophrenia was first reported. The prevalence varied from as low as 1% to as high as 46%.The initial studies in the early 20th century showed that the prevalence rates were as low as 1% to 3.5%. [7-9] After the introduction of DSM criteria in the 80s, the proportion was steadily increasing. Using the DSM criteria several researchers have found the prevalence of OCS/D in patients of schizophrenia to be ranging from 10%-13%. [10-15] Rabe-Jablonska also found obsessive symptoms in 13% of adolescent schizophrenia patients. [14, 15] Initially, it was believed that the neurotic OC features work as a defense mechanism against frank psychotic manifestations. These early theories were based upon Freudian psychoanalysis. Several studies have now shown that the interaction of serotonin, dopamine and glutaminergic pathways is involved in the OC symptoms seen in schizophrenia.

Table 1: Prevalence of OCD/S in schizophrenia.

Group A Schizophrenia with OCD	Group B Schizophrenia without OCD	Total (n)
26(24.7%)	79(75.2%)	105

The above table shows that the mean baseline total YBOCS score was 23.96 ± 4.06 in our study with mean YBOCS obsessions score being 12.85 ± 5.28 and mean YBOCS compulsion score being 10.92 ± 5.22.The severity of obsessive compulsive symptoms can be defined on the basis of the total YBOCS score as: subclinical (YBOCS score 0-7); mild (YBOCS score 8-15); moderate (YBOCS score 16-23); severe (YBOCS score 24-31); and extreme (YBOCS score 32-40). [11] In our study, out of 26 patients having OCD/S with schizophrenia, 17 (65.38%) patients had severe OC symptoms and 9 (34.61%) patients had moderate OC symptoms. In our study, out of 26 patients having OCD/S with schizophrenia, 65.38% (17 patients) had severe OC symptoms and 34.61% (9 patients) had moderate OC

symptoms [Table 2]. Our findings were on higher side to several previous studies where the mean baseline severity on OCD on YBOCS was in a range of 14 ± 6.3 to 17.3±4.9. [16,17] A slightly higher mean total score was found by Agrawal et al [18] at 30.3 ± 4.9 whereas most studies have reported the mean total YBOCS score to be ranging from about 14 to 20. Researchers like GulcanGulec et al found a baseline mean YBOCS score of 16.75 ± 11.64, MJ Lee et al have observed baseline YBOCS score of 14.00 ± 6.34, de Haan et al found mean baseline YBOCS score of 17.7 ± 9.1 whereas Hemrom et al found it to be 17.7 ± 9.1 respectively. [16,17,11]

Table 2: Severity of OC symptoms as per YBOCS scores at baseline.

Baseline YBOCS score	Mean	Standard deviation
YBOCS Obsessions score	12.85	5.28
YBOCS Compulsions score	10.92	5.22
YBOCS Total score	23.96	4.06

Severity of schizophrenia symptoms as per PANSS score in both groups at baseline

It can be seen from the above table that the mean baseline PANSS score was 53.4 ± 13.5 in patients with OCD-schizophrenia and 53.6 ± 10.4 in patients with only schizophrenia [Table 3]. It was also observed that the patients with OCD-schizophrenia had higher positive symptoms (mean PANSS score 17.1 ± 4.5) than schizophrenia patients without OCD (mean PANSS score 15.1 ± 4.4). The mean negative symptom score for group A patient was 10.7 ±8.5 and that for group B patient was 11.8 ± 9.2 which had no statistical significance.(t=-0.527, p 0.599).

Table 3: Comparison of PANSS scores at baseline in both groups.

Baseline PANSS score	Group A (n=26) [Mean ± SD]	Group B (n=79) [Mean ± SD]	Sum of ranks		Mann Whitney U value	P value
			Group A	Group		
Positive symptoms score	17.1 ± 4.5	15.1 ± 4.4	1619	3946	786	0.072
Negative symptoms score	9.6 ± 7.2	11.7 ± 9.2	1354	4211	1003	0.802
General symptoms score	25.5 ± 4.6	26.8 ± 4.1	1142.5	4422.5	791.5	0.079
PANSS Total score	52.3 ± 12.8	54.1 ± 10.3	1270.5	4294.5	919.5	0.424

The general symptom score for group A and group B patient was 25.5 ± 4.6 and 26.8 ± 4.1 respectively which also had no statistical significance (t-1.268, p 0.208). Agarwal et al found the mean PANSS scores in patients of schizophrenia with OCD to be 54.8 ± 8.6, [18] MJ Lee et al reported the scores as 61.4 ± 14.78, [17] whereas a higher mean of 86.7 ± 20.0 has been reported.

Our findings are in keeping with the above researchers. Furthermore, we also observed the association between positive schizophrenia symptoms and OCD in schizophrenia where most of the patients with paranoid symptoms had OC symptoms. Such a correlation has also been observed in previous studies. [19, 20]

Clinical outcome of patients in both Groups at the end of 3 months on treatment

All the patients in both the groups were treated with atypical antipsychotic medications Tab risperidone (2mg to 6 mg) or Tab olanzapine (5 mg -20mg) which were available from the hospital dispensary. There was nearly an equal proportion in both groups for both the oral drugs [Table 4].

However, it is important to note that none of the patients in the OCD-schizophrenia group required electroconvulsive therapy or shifting to typical antipsychotics which was seen in nearly 10% of the patients requiring the same in the schizophrenia group without OCS.

This also shows good tolerability and efficacy of both risperidone and olanzapine in schizophrenia patients with OCD/S.

Various previous research has also found atypical antipsychotics to be effective in symptomatic improvement of OC symptoms in schizophrenia patients with co morbid OCD/S. [21]

Table 4: Outcome on treatment

Patientstreatment	Group A (n=26)	Group B (n=79)
	1.Oral Antipsychotic Medication	
Risperidone	14 (53.8%)	45 (57%)
Olanzapine	12 (46.2%)	34 (43%)
Shift to haloperidol	0 (0%)	8 (10.1%)
2. Electro Convulsive Therapy (ECT)	0 (0%)	9 (11.4%)

Improvement of patients in Group A on YBOCS at the end of 3 months

When the patients of OC with schizophrenia were assessed for improvement in their OC symptoms on the YBOCS scale at the end of 3 months then a statistically significant difference was noted on the YBOCS obsession score($t=12.359$, $p<0.001$),YBOCS compulsion score($t=9.29$, $p<0.001$),and total YBOCS score($t=24.154$, $p<0.001$) from the baseline scores Agrawal et al observed the mean YBOCS score at 12 weeks follow up to be 14.1 ± 10.9 from 30.3 ± 4.9 at baseline [Table 5]. [18]

Table 5: Improvement of patients in group A on YBOCS.

Parameter	Baseline score	Score at 3 months	t value	P value	95% confidence interval
YBOCS Obsessions score	12.85 ± 5.28	7.27 ± 3.32	12.36	<0.001	4.648 to 6.506
YBOCS Compulsions score	10.92 ± 5.22	6.42 ± 3.26	9.29	<0.001	3.502 to 5.498
YBOCS Total score	23.96 ± 4.06	13.73 ± 2.45	24.15	<0.001	9.358 to 11.103

Furthermore, it was observed that, out of 26 patients having OCD with schizophrenia, 18(69.23%) patients had mild OC symptoms and 8 (30.76%) patients had moderate OC symptoms. No patient had severe OC symptoms. Our findings were on the higher side at baseline and after 3 months but there was a significant reduction of symptoms on treatment with antipsychotics

Improvement of patients in Group A on YBOCS after treatment with APDs at the end of 3 months

The comparison of mean YBOCS score at baseline and after three months in patients having OCD with schizophrenia showed that both atypical antipsychotic drugs risperidone and olanzapine were equally effective in controlling OC symptoms in these patients as indicated by the significant p values ($p<0.001$) [Table 6]. There was no worsening of OC symptoms found in these patients as both drugs have been known to cause worsening or de novo OCS. We found that the symptoms reduced significantly and hence an antiobsessive agent was not required. In some of previous studies, symptomatic improvement in the OC features on treatment with atypical antipsychotics has been observed. For example, Jacobson et al observed symptomatic improvement in OC symptoms in patients treated with risperidone. [21] OCS that is part of a psychotic process has been successfullytreated with clozapine monotherapy. A meta-analysis has also shown that risperidone and haloperidol significantly improve the refractory OC symptoms in OCS with schizophrenia. Agrawal et al have shown significant improvement in OC features in these patients with fluoxetine. [18] Seed at et al also observed that the second generation antipsychotics were more frequently used for patients in OCD with schizophrenia compared to pure schizophrenia patients. [11] However, there are is no randomized controlled trial comparing risperidone and Olanzapine for controlling OC symptoms in comorbid OCD and schizophrenia.

Table 6: Efficacy of APDs in improvement in O C symptoms from baseline as per YBOCS.

Drug	Baseline score(mean ± SD)	Score at 3 months (mean ± SD)	t value	p value	95 % Confidence Interval
		YBOCS Obsessions			
Risperidone	12.07± 7.04	6.93 ± 4.37	6.395	<0.001	3.405 to 6.88
Olanzapine	13.75±1.76	7.67±1.49	23.41	<0.001	5.511 to 6.655
		YBOCS Compulsions			

Risperidone	10.57±6.22	6.36± 3.81	6.048	<0.001	2.709 to 5.72
Olanzapine	11.33±3.98	6.50±2.64	7.071	<0.001	3.329 to 6.338
		YBOCS Total Score			
Risperidone	22.64±4.30	13.29±2.4	15.4	<0.001	8.044 to 10.67
Olanzapine	25.50±3.28	14.25±2.52	25.23	<0.001	10.268 to 12.232

Improvement of patients in both Groups on PANSS at the end of 3 months

At the end of 3 months treatment with atypical antipsychotics the mean PANSS positive symptom score for group A was 12.2 ± 2.6 and for group B was 12.1 ± 3 which had no statistical difference (U=993.5, p=0.802) and the negative symptom score for group A patients was 8.6 ± 3.9 and for group B patient was 9.5 ± 4.9 which also had no statistical significance (U=979.5, p=0.626) [Table 7]. On the other hand the mean general symptom score at 3 months follow up in group B (22.8 ± 3.6) was significantly higher than that in group A (20.8 ± 2.4) [U=661.5, p=0.006]. Similarly, the mean total PANSS score at 3 months follow up in group B (43.3 ± 6.3) was significantly higher than that in group A(39.7 ± 6.5) [U=698.5, 0.015]. Thus, our data shows that the response of general schizophrenia symptoms and overall total schizophrenia symptoms to atypical antipsychotics was better in patients having comorbid OCD and schizophrenia than patients having schizophrenia alone.

Table 7: PANSS score of both groups at 3 months.

PANSS score at 3 months	Group A (n=26) [Mean ± SD]	Group B (n=79) [Mean ± SD]	Sum of ranks		Mann Whitney U value	p value
			Group A	Group B		
Positive symptoms score	12.1 ± 2.6	12.1± 3	1411.5	4153.5	993.5	0.802
Negative symptoms score	8.1± 3.2	9.5 ± 4.8	1330	4234.5	979.5	0.626
General symptoms score	20.8 ± 2.4	22.8 ± 3.6	1012.5	4552.5	661.5	0.006
PANSS Total score	39.7 ± 6.5	43.3 ± 6.3	1049.5	4515.5	698.5	0.015

Thus the above two tables show that there is significant improvement in the positive and negative symptoms of schizophrenia in all the study patients. Furthermore, the general symptom score is significantly low in schizophrenia patients with OCD/S compared to pure schizophrenia patients [Table 8].

Table 8: Comparison of PANSS score at baseline and at 3 months in Schizophrenia patients (n=105) paired t test.

PANSS	Baseline score [mean ± SD]	Score at 3 months [mean ± SD]	t value	P value	95% Confidence Interval
Positive symptoms score	15.64±4.502	12.11± 2.939	11.2	<0.001	2.9 to 4.14
Negative symptoms score	11.50±9.031	9.31±4.640	4.645	<0.001	1.25 to 3.12
General symptoms score	26.46±4.272	22.33±3.444	14.12	<0.001	3.54 to 4.7
PANSS Total score	53.58±11.188	42.43±6.458	14.7	<0.001	9.64 to 12.65

In a longitudinal follow up study of OC symptoms in schizophrenia, the mean PANSS score at six weeks follow up was 72.5 ± 24.0 and the mean PANSS score at three years was 65.6 ± 15.2. [22] This indicates that the follow up PANSS score in our study is less than this study, showing more improvement of schizophrenia in our study. Thus our study showed that the atypical antipsychotic drugs Risperidone and Olanzapine are effective in controlling symptoms of schizophrenia as well as the associated obsessive compulsive symptoms.

Severity of illness as per CGI scale

On comparing the severity of illness between the two groups as per the clinical global impression scale then there was a statistically significant difference seen in the mean scores with a reduction in the scores at the end of 3 months for both the groups (t 15.714,p<0.001.; t 16.624 p<0.001) respectively. Hence both the groups had more or less same severity despite the psychopathology of OCS in Group-A patients [Table 9].

Table 9: Severity of illness as per clinical global impression scale.

Groups	Baseline score [mean ± SD]	Score at 3 months [mean ± SD]	t value	p value	95% Confidence Interval
Group A	4.962± 0.52	3.269± 0.45	15.71	<0.001	1.47 to 1.91
Group B	5.303± 0.92	3.810 ±1.11	16.62	<0.001	1.31 to 1.67

On assessing the global improvement in clinical status and behaviour of the patients as per CGI in both the groups had better improvement at the end of three months of treatment with no statistical difference(u=810,p=0.064) in two groups. Also therapeutic efficacy of both Risperidone and Olanzapine did not show statistically significant difference in both the groups. Thus both the drugs were efficacious in both schizophrenia patients with OCD/S and without OCD/S [Table 10].

Table 10: Change in CGI at 3 months in both groups.

CGI	Group A (n=26)	Group B (n=79)	p value	Mann Whitney U value
Global improvement [Mean ±SD]	2.582 ±0.726	2.269±0.452	0.064	810
Sum of ranks	4404	1161		
Efficacy Index [Mean± SD]	5.769 ±1.608	6.329 ±2.055	0.227	892
Sum of ranks	1243	4322		

Also therapeutic efficacy of both Risperidone and Olanzapine did not show statistically significant difference in both the groups. Thus both the drugs were efficacious in both schizophrenia patients with OCD/S and without OCD/S. Similarly, Shafti et al observed that risperidone and olanzapine were both equally effective in alleviating schizophrenia symptoms as per CGI scale. [23] Riedel et al also noted improvement in schizophrenia symptoms as per CGI scale with atypical antipsychotics. [24] Thus, the observations of our study are in agreement with these two studies. Different studies on obsessive compulsive disorder [25, 26] and schizophrenia [27-30] were reviewed.

Conclusions

To conclude, the prevalence of OCD in schizophrenia was 24.7%. At the end of 3 months there was a marked reduction in obsessive compulsive symptoms on YBOCS on treatment with both Risperidone and Olanzapine. Significant improvements in symptoms of schizophrenia were seen in patients of both groups as assessed by PANSS at the end of 3months on treatment with atypical antipsychotics (risperidone and olanzapine). There was significantly greater improvement in general symptom score and total PANSS score in group A patients compared to group B patients. At the end of 3 months, all patients had a significant reduction in the severity of illness and therapeutic effects with atypical antipsychotics whereas group A schizophrenia patients with co morbid OCD/S had better global improvement in functioning as assessed by CGI.

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