Comparative study of olanzapine and risperidone in the control of positive and negative symptoms in the treatment of schizophrenia

Supriya Sharma[1,*], Yeshwant Deshmukh[2], Priya Ann Sam[3], Urmila Salve[4]

[1]PG Resident, [2]Professor, [3,4]PG Resident, Dept. of Pharmacology, MGM Medical College, Navi Mumbai, Maharashtra, India

***Corresponding Author:**
Email: bhanusharma1995@rediffmail.com

Abstract

Objective: To compare the efficacy of olanzapine and risperidone in the treatment of positive and negative symptoms of schizophrenia.

Materials and Methods: The study was conducted in MGM medical college Navi Mumbai between October 2012 to September 2014. The study included 110 patients of schizophrenia. The positive and negative symptoms were assessed with the help of the PANSS (positive & negative symptom score) scale.

Results: We observed that the mean percentage reduction in score in the positive scale of PANSS was 48.74% in the risperidone and 49.40% in the olanzapine group .The negative score reduced by 56.32% in the Risperidone group and by 61.59% in the olanzapine group on the PANSS.

Conclusion: olanzapine was superior to risperidone in controlling the positive as well as negative symptoms of schizophrenia clinically but the results were not statistically significant.

Keywords: Olanzaine, Risperidone, Schizophrenia.

Introduction

Schizophrenia is a clinical syndrome of variable but profoundly disruptive psychopathology that involves cognition, emotion, perception, and other aspects of behavior. The expression of these manifestations varies across patients and over time, but the effect of the illness is always severe and is usually long lasting. Schizophrenia is a severe form of mental illness affecting 7 per thousand of the adult population, mostly in the age group of 15-35 years. Though the incidence is low (3-10,000), the prevalence is high due to chronicity.[1] The discovery of antipsychotics in the 1950s revolutionized the treatment of schizophrenia and focused on the positive symptoms. The advent of the novel antipsychotics during the last 15 years represents a significant improvement over the effectiveness of conventional antipsychotics. Among the advantages of these second generation antipsychotics over first generation antipsychotics are reduced extra-pyramidal sideeffects,[2-3] reduced risk for tardive dyskinesia[4-5] and possibly beneficial effects on cognitive functioning[6] and negative symptomatology. Olanzapine is an atypical antipsychotic; it resembles clozapine in blocking multiple monoaminergic as well as muscarinic and H_1 receptors. The antipsychotic effect has been ascribed to a combination of Dopamine (D_2) and Seretonin ($5HT_{2a}$) receptor blockade.[7] The relative receptor binding affinity for olanzapine is: $5\text{-}HT_{2a}>D_4>\alpha_1=D_1=D_2=H_1>=M_1$.[8] Both positive and negative symptoms of schizophrenia appear to be benefited. It is an atypical antipsychotic whose antipsychotic activity has been attributed to a combination of D_2 and $5HT_2$ receptor blockade. In addition it has high affinity for α_1, α_2, and H_1 receptors: blockade of these may contribute to efficacy as well as side effects like postural hypotension.[7] The receptor binding affinity is $5\text{-}HT_{2A}> D_4=D_2=\alpha_1=H_1=M_1$.[8] Risperidone is more potent D_2 blocker than clozapine; extrapyramidal side effects are less only at low doses.[7]

Aim

To compare the efficacy of olanzapine and risperidone in the treatment of positive and negative symptoms of schizophrenia.

Materials and Methods

Study Area: The study was performed at the Department of Pharmacology in collaboration with Department of Psychiatry, MGM medical college, Kamothe, Navi-Mumbai. Here patients were offered outpatient consultation and admission when necessary.

Duration of the study: October 2012 to September 2014.

Sample Size: 110

Inclusion Criteria: 1) Patients fulfilling DSM 4 criteria for schizophrenia; 2) Age of the patients was 18 to 60yrs; 3) Patients were outpatients or inpatients hospitalised for less than or equal to 4 weeks at the time of treatment; 4) Those patients and their relatives who were willing to give consent for the treatment.

Exclusion Criteria: 1) Patients requiring ECT or hospitalization. Patients with hypertension, cardiac disorder; 2) Pregnant or nursing females; 3) Patients having any past history or physical disorder that is likely to deteriorate during participation; 4) Patients with suicidal tendencies; 5) Unable to provide informed consent.

The study was an open label, prospective, randomised comparative clinical trial. Ethics approval

from Institutional Ethics Review Committee (IERC) was obtained.

55 Patients received Olanzapine (5 to 20 mg) & 55 patients received the drug Risperidone (2 mg to 6mg). The two drugs were given according to the randomization table. The patients were evaluated at: Baseline and were followed up on 7th day (1 week), 14th day (2 weeks), 28th day (4weeks) and 42nd day (6 weeks). The patients were evaluated on POSITIVE & NEGATIVE SYDROME SCALE (PANSS).

Statistical Analysis

Data is presented using Descriptive statistics, Graphs and Charts. Further analysis was done using ONE WAY ANOVA TEST (The F test) & INDEPENDENT SAMPLE t-test. All means are expressed as mean ± standard deviation. The critical levels of significance of the results were considered at 0.05 levels i.e. $P < 0.05$ was considered significant.

Results

Results of Positive and Negative Syndrome Scale (PANSS SCALE)

These results denote the effect of olanzapine and risperidone on the positive and negative symptoms of schizophrenia. The decrease in the score denotes improvement in the symptoms.

Effect of Risperidone and Olanzapine on the Positive Scale

Table 1: Effect of Risperidone on Positive Scale of PANSS

Weeks	N	Mean	SD	SEM	F-stat	p-value
Baseline	55	40.582	7.044	0.950	241.313	< 0.001**
First	55	35.255	6.845	0.923		
Second	55	32.036	6.215	0.838		
Fourth	55	26.382	5.523	0.745		
Sixth	55	20.800	5.592	0.754		

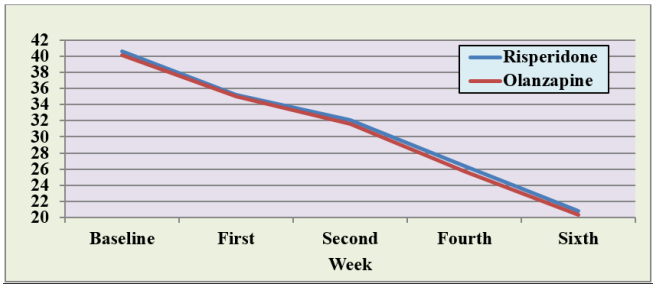
The result indicates that there is significant decrease in the score according to duration ($p< 0.001$). One –Way ANNOVA test (F-stat) was used since the variables (i.e. no of follow- ups) are more than 2 in number. The positive score at baseline was 40.582 (±7.044) which reduced to 32.036 (±6.215) at the end of the 2nd week. When the dose was increased on the 14th day the score further reduced to 20.800 (±5.592) at the end of 6th week. Risperidone reduced the positive symptoms by 48.74%.

Table 2: Effect of Olanzapine on Positive Scale of PANSS

Weeks	N	Mean	SD	SEM	F-stat	p-value
Baseline	55	40.164	6.986	0.942	243.741	<0.001**
First	55	35.036	6.529	0.880		
Second	55	31.582	5.865	0.791		
Fourth	55	25.745	5.296	0.714		
Sixth	55	20.320	5.301	0.715		

The result indicates that there is significant decrease in the score according to duration ($p< 0.001$). One –Way ANNOVA test (F-stat) was used since the variables (i.e. no of follow- ups) are more than 2 in number. The positive score at baseline was 40.164(±6.986) which reduced to 31.582(±5.586) at the end of 2nd week. When the dose was increased on the 14th day (2nd follow up) then the scores further reduced and the score on the positive scale was 20.320(±5.301) at the end of 6th week. Olanzapine reduced the positive symptoms of schizophrenia by 49.40%. Thus, we observe that the decrease in the positive symptoms is more in the olanzapine group than the risperidone group.

Graph 1: Effect on Positive Scale of PANSS



Effect of risperidone and olanzapine on the negative scale of PANSS

Table 3: Effect of Risperidone on Negative Scale of PANSS

Weeks	N	Mean	SD	SEM	F-stat	p-value
Baseline	55	35.636	7.145	0.963		
First	55	31.436	5.814	0.784		
Second	55	28.691	6.289	0.848	212.598	<0.001**
Fourth	55	21.891	6.571	0.886		
Sixth	55	15.564	8.066	1.088		

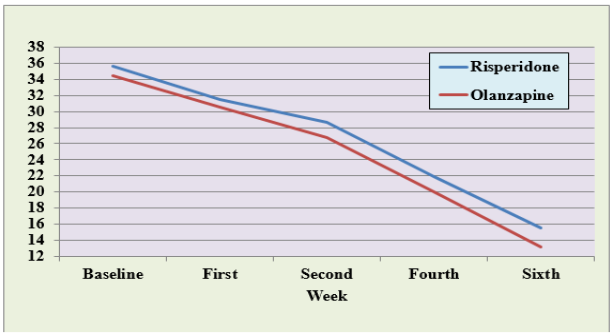
The result indicates that there is significant decrease in the score according to duration (p< 0.001).One –Way ANNOVA test (F-stat) was used since the variables (i.e. no of follow- ups) are more than 2 in number. The score on the negative scale in the risperidone group at baseline was 35.636 with a standard deviation of 7.145 which reduced to 28.691 with a standard deviation of 6.289at the end of 2nd week. When dose was increased on the 14th day the scores further reduced and at the end of the study the score on the negative scale was 15.564±8.066. Risperidone reduced the negative symptoms of schizophrenia by 56.32%.

Table 4: Effect of Olanzapine on Negative Scale of PANSS

Weeks	N	Mean	SD	SEM	F-stat	p-value
Baseline	55	34.418	7.312	0.986		
First	55	30.527	5.830	0.786		
Second	55	26.745	5.885	0.794	237.837	<0.001**
Fourth	55	20.036	6.313	0.851		
Sixth	55	13.218	7.781	1.049		

The result indicates that there is significant decrease in the score according to duration (p< 0.001). One –Way ANNOVA test (F-stat) was used since the variables (i.e. no of follow- ups) are more than 2 in number. The score on the negative scale in the olanzapine group at baseline was 34.418±(7.312) which reduced at the end of 6th week to 13.218±(7.781) after increase in the dose at the 2nd week. Olanzapine reduced the negative symptoms of schizophrenia by 61.59%. Thus, we observe that the decrease in the negative symptoms is more in the olanzapine group than the risperidone group.

Graph 2: Effect on Negative Scale of PANSS



Discussion

Effect on Positive Symptoms: We observed that the mean percentage reduction in score in the positive scale of PANSS was 48.74% in the risperidone and 49.40% in the olanzapine group.

Effect on Negative Symptoms: The negative score reduced by 56.32% in the Risperidone group and by 61.59% in the olanzapine group on the PANSS.

Tran P V et al (1997) did a Double blind comparison of olanzapine versus risperidone in the treatment of schizophrenia and other psychotic disorders. Olanzapine demonstrated significantly greater efficacy in negative symptoms (Scale for Assessment of Negative Symptoms summary score), as well as overall response rate (> or = 40% decrease in the Positive and Negative Syndrome Scale total score). The results of this study are in accordance with the results of our study.

Saeed Shoja Shafti and Mahsa Gilanipoor in 2014 conducted A Comparative Study between Olanzapine and Risperidone in the Management of Schizophrenia. Conclusion of the study is that while both of olanzapine and risperidone were equally effective for improvement of positive symptoms and insight, olanzapine showed superior efficacy with respect to negative symptoms.

The results on negative symptoms of schizophrenia are in accordance with our study.

Conclusion

In our study Olanzapine was superior to Risperidone in treating both the positive and negative symptoms of schizophrenia clinically. Statistically the decrease in the positive and negative scores of PANSS scale was more in the olanzapine group than risperidone group but the difference is not statistically significant.

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PANSS RATING FORM

Absent			Minimal	Mild	Moderate	Moderate severe	Severe	Extreme
P1	Delusions	1	2	3	4	5	6	7
P2	Conceptual disorganisation	1	2	3	4	5	6	7
P3	Hallucinatory behaviour	1	2	3	4	5	6	7
P4	Excitement	1	2	3	4	5	6	7
P5	Grandiosity	1	2	3	4	5	6	7
P6	Suspiciousness/ persecution	1	2	3	4	5	6	7
P7	Hostility	1	2	3	4	5	6	7
N1	Blunted affect	1	2	3	4	5	6	7
N2	Emotional withdrawal	1	2	3	4	5	6	7
N3	Poor rapport	1	2	3	4	5	6	7
N4	Passive/apathetic social Withdrawal	1	2	3	4	5	6	7
N5	Difficulty in abstract thinking	1	2	3	4	5	6	7
N6	Lack of spontaneity & flow of conversation	1	2	3	4	5	6	7
N7	Stereotyped thinking	1	2	3	4	5	6	7
G1	Somatic concern	1	2	3	4	5	6	7
G2	Anxiety	1	2	3	4	5	6	7
G3	Guilt feelings	1	2	3	4	5	6	7
G4	Tension	1	2	3	4	5	6	7
G5	Mannerisms & posturing	1	2	3	4	5	6	7

G6	Depression	1	2	3	4	5	6	7
G7	Motor retardation	1	2	3	4	5	6	7
G8	Uncooperativeness	1	2	3	4	5	6	7
G9	Unusual thought content	1	2	3	4	5	6	7
G10	Disorientation	1	2	3	4	5	6	7
G11	Poor attention	1	2	3	4	5	6	7
G12	Lack of judgement & insight	1	2	3	4	5	6	7
G13	Disturbance of volition	1	2	3	4	5	6	7
G14	Poor impulse control	1	2	3	4	5	6	7
G15	Preoccupation	1	2	3	4	5	6	7
G16	Active social avoidance	1	2	3	4	5	6	7