

Treatment Response on Positive Symptoms of Schizophrenia with Olanzapine and Risperidone

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Abstract

Introduction: Positive symptoms become perceptible in patients as schizophrenia progresses. If schizophrenia goes untreated catatonic motor behaviors are develops. Now a day's catatonia which is a type of disturbed behavior is observed, with less frequency than in past years due to advances in treating schizophrenia. Treatment of schizophrenia by olanzapine and risperidone shows diverse outcomes.

Objectives: To assess the response on positive symptoms of schizophrenia by olanzapine and risperidone.

Materials and Methods: This study was conducted in Department of Pharmacology and Department of Psychiatry of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka during the period from September 2013 to January 2015. A total of 179 schizophrenia patients fulfilling the inclusion criteria were enrolled and of them 75 patients completed the study, where 40 were in olanzapine treated group and 35 were in risperidone treated group in a 12-weeks assessment where Scale for Assessment of Positive Symptoms (SAPS) was applied. After statistical analysis of scores between intergroup and intra group $p < 0.05$ was considered significant.

Results: Treatment with both the olanzapine and risperidone were remarkably effective for progress of positive symptoms of schizophrenia patients but in olanzapine treated group the score was reduced more than that of risperidone treated group and the difference was significant ($p < 0.05$).

Conclusion: Olanzapine has responded better on positive symptoms of schizophrenia patients than that of risperidone.

Key-words: Schizophrenia, Positive Symptoms, Olanzapine, Risperidone.

Introduction

Now a day's, schizophrenia is well known psychiatric disorder for its chronic recurrences¹. Schizophrenia patients may present with positive and/or negative symptoms. The positive symptoms represents with distortion or exaggeration of functions that are normally present, whereas negative symptoms represents with deficiency of mental functions that are normally present. Positive symptoms include hallucinations, delusions, bizarre or disorganized behavior. Disorganized thinking and behavior becomes apparent in patients' speech patterns as schizophrenia progresses and in

severe cases patients interpret reality abnormally. Usually in initial state of psychosis patient develops positive symptoms and if treated early the prognosis is better. If untreated or improper treatment the negative symptoms may start to develop. After developing negative symptoms the prognosis is poor than that of positive symptom patients. With this treatment about 30-40% patients may show signs of poor response to conventional antipsychotics² and among them approximately 50% may suffer from serious side effects³. Therefore the aim of new drug development for schizophrenia treatment has shifted to synthesize compounds capable to improve both positive and negative symptoms, which are commonly insensitive to classical antipsychotics and to synthesize compounds that create slight or no extrapyramidal side effects. Initially, first generation antipsychotics seemed to be more efficient than second generation but later by meta-analysis of effects of first generation antipsychotics with second generation, the first generation drugs were found to be more effective in schizophrenic patients⁴. Olanzapine is a thienobenzodiazepine and has high affinity to serotonin, histamine, α_1 -adrenergic and dopamine receptors^{5,6}. It has shown that olanzapine has better efficacy and less side effects compared to haloperidol in controlled clinical trials and some studies reveals that it has better efficacy in schizophrenia patient management^{7,8,9}. Risperidone is a benzisoxazole derivative and has greatest affinity for serotonin, histamine, α_1 adrenergic and dopamine sites. In few other trials, risperidone has been shown to be better to typical antipsychotics⁹.

In the treatment of psychotic disorders both the risperidone and olanzapine have shown well tolerability and efficacy^{6,7,9,10}. A variety of study for comparing these two atypical antipsychotics has resulted in various outcomes. For example, Tran et al., and Gureje et al had found olanzapine to have a risk vs benefit advantage compared to risperidone^{10,11}. In a study, advantage of olanzapine was due to its better efficacy and improvement of symptoms in older patients¹⁰. But symptoms, better maintenance of treatment and finally lower incidence of extrapyramidal side effects, hyperprolactinemia and sexual dysfunction¹⁰. Also, Edgell et al¹² and Rascati et al¹³ found that olanzapine treated patients were more likely to continue treatment than risperidone treated patients. Feldman et al¹⁴ also, found olanzapine to be more efficacious than risperidone in progress of older patients. On the other hand, in parallel comparisons, Taylor et al¹⁵ Kasper et al¹⁶ and Conley and Mahmoud¹⁷, found equal clinical outcome for both of olanzapine and risperidone treated patients. Based on aforesaid controversies and result, in present study, the efficacy on positive symptoms of schizophrenia of risperidone and olanzapine were compared for additional persuasive evidence.

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Materials and Methods

Present study was carried out in Department of Pharmacology and Department of Psychiatry of BSMMU during the period from September 2013 to January 2015. Samples were collected up to November 2014. Patients with schizophrenia attending the outpatient department or admitted in the inpatient department of psychiatry, BSMMU were recruited in the study. Patients were diagnosed as schizophrenic, by psychiatrists of BSMMU according to diagnostic protocol which fulfilled DSM-5 criteria (Diagnostic and Statistical Manual of Mental Disorders, 2013). Patients receiving antipsychotic drugs within last 30 days, having serious cognitive deficit and having serious infection or terminal illness were excluded from the study. A total of 179 patients fulfilling the inclusion criteria were enrolled and of them 75 patients completed the study, where 40 were in olanzapine treated group and 35 were in risperidone treated group. In this 12 weeks study the patients were assessed by means of SAPS at baseline and at 4, 8 and 12 weeks. Olanzapine and risperidone were prescribed according to practice guidelines at a dose of 5-20 mg/day and 4-16 mg/day orally respectively. Data were collected on variables of interest using a semi-structured questionnaire (research instrument) by interviewing. Collected data was checked daily and edited into Excel sheet. Data were processed and analyzed using computer software SPSS (Statistical Package for Social Sciences) version 16.0. Patients were compared on baseline characteristics by means of 't'-tests. Treatment efficacy was analyzed by unpaired 't'-test and paired 't'-test was used to compare the continuous data between and within groups respectively. The level of significance was set at 5% and $p < 0.05$ was considered significant.

Results

Table-I shows, in olanzapine and risperidone treated groups at baseline mean \pm SD of SAPS score were 62.51 ± 3.06 and 61.11 ± 3.45 respectively. The difference in SAPS score between olanzapine and risperidone treated group at baseline was not significant ($p > 0.05$). Table-II shows, in olanzapine treated group SAPS score was reduced from 62.51 ± 3.06 to 58.1 ± 5.5 , 49.5 ± 5.5 , 40.5 ± 6.3 after 4, 8 and 12 weeks of drug treatment respectively. Whereas in risperidone treated group SAPS score was reduced from 61.11 ± 3.45 to 59.9 ± 4.9 , 51.7 ± 4.4 and 45.7 ± 5.5 after 4, 8 and 12 weeks of drug treatment respectively. Table-III shows, in olanzapine treated group SAPS score was reduced from 62.51 ± 3.06 to 40.5 ± 6.3 at 12 weeks of drug treatment and the reduction was significant ($p < 0.05$). Whereas in risperidone treated group BPRS score was reduced from 61.11 ± 3.45 to 45.7 ± 5.5 and the reduction was also significant ($p < 0.05$). Table-IV shows, in olanzapine treated group the score was reduced more than that of risperidone treated group and the difference was significant ($p < 0.05$).

Table-I: SAPS scores of study group at baseline

	Group		p-value
	Olanzapine(n=40)	Risperidone(n=35)	
SAPS scores	62.51 ± 3.06	61.11 ± 3.45	>0.05

• Data were presented as mean \pm SD and were analyzed by unpaired 't'test

Table-II: SAPS scores at baseline, 4 weeks, 8 weeks and 12 weeks of treatment

Groups	At Baseline	At 4th week	At 8th week	At 12 weeks
Olanzapine treated group (n=40)	62.51 ± 3.06	58.1 ± 5.5	49.5 ± 5.5	40.5 ± 6.3
Risperidone treated group (n=35)	61.11 ± 3.45	59.9 ± 4.9	51.7 ± 4.4	45.7 ± 5.5

• Data were presented as mean \pm SD

Table-III: SAPS scores at baseline and 12 weeks of treatment

Group	At Baseline	At 12 weeks	p-value
Olanzapine treated group (n=40)	62.51 ± 3.06	40.5 ± 6.3	<0.0001
Risperidone treated group (n=35)	61.11 ± 3.45	45.7 ± 5.5	<0.0001

• Data were presented as mean \pm SD and were analyzed using Paired t-Test

Table-IV: Comparison of SAPS scores between olanzapine and risperidone groups after 12 weeks of treatment

	Group		p-value
	Olanzapine (n=40)	Risperidone (n=35)	
SAPS scores	40.5 ± 6.3	45.7 ± 5.5	<0.001

• Data were presented as mean \pm SD and were analyzed using unpaired t-Test

Discussion

The prime intention of this study was to evaluate once more the safety and effectiveness of olanzapine and risperidone in treatment of schizophrenic patients. Ultimately the outcomes of both olanzapine and risperidone were appreciably effective in reducing the overall psychotic symptoms. Nevertheless, the findings are a bit comparable to a different analogous double-blind, 28 weeks study on 339 patients meeting DSM-IV criteria for schizophrenia, schizophreniform or schizoaffective disorder¹⁰. In current appraisal there was no significant variation amongst olanzapine and risperidone in respect to association of positive symptoms. There are few other clinical trials having varying outcomes; such as, in a head to head clinical trial for 8 weeks comparing olanzapine with risperidone on patients meeting DSM-IV criteria for schizophrenia or schizoaffective disorder, no significant variation found among them with respect to efficacy or side effects¹⁷, in existing consideration significant deterioration of adverse effects was apparent only by risperidone. Another study of olanzapine vs risperidone concluded that, though there was better efficacy in risperidone group, there was considerable raise in side effects as well in the same group compared to olanzapine treated group¹⁸. A study by Robinson et al¹⁹ evaluated comparison of 4 months treatment outcomes for olanzapine vs risperidone in patients with first episode schizophrenia spectrum disorders. Among one hundred twelve subjects there were with first episode schizophrenia, schizophreniform or schizoaffective disorder which were randomly assigned to treatment with olanzapine (2.5-20 mg/day) or risperidone (1-6 mg/day). At the end of the study clinical outcomes with risperidone were equal to those with olanzapine. A prospective observational

study by Ascher-Svanum et al olanzapine and risperidone treated group were compared one year for assessing rate, duration and time to hospitalization. In this study 516 patients who were newly initiated on olanzapine or risperidone were recruited, a total of 271 patients comprising the olanzapine (n=159) and risperidone (n=112) treatment groups. Compared to risperidone, olanzapine treated patients had lesser hospitalization rates (24.1% vs 14.4% respectively) and smaller number hospitalization days (14.5 days vs 9.9 days respectively).

Similarly, there are other studies that have similar statement in support of risperidone^{14,15}. Possibly, applying different efficacy measures with various psychomotor properties and different samples using distinct diagnostic criteria may elucidate these contradictory results to some extent. In addition, as weight gain rate was noticeably higher in the olanzapine group, it became an important trouble especially for women, and such metabolic side effect, should always be taken in consideration by treating clinician. Equal vigilance also should be applied regarding extrapyramidal symptoms which are more challenging with risperidone. In a Cochrane review article by Komossa et al²⁰ risperidone improved the general mental state (PANSS total score) slightly less than olanzapine but slightly more than quetiapine and ziprasidone. Whilst in comparison with the earlier studies, the result of the present study may not be shown to be more influential and free from controversy. It may put forward the requisite of more analogous trials regarding comparison between atypical antipsychotics. Instead of diagnosing whole of schizophrenia, schizoaffective and schizophreniform disorders like aforesaid trials, restriction to only schizophrenia diagnosis, could support a more accurate trial in the present assessment. Moreover, equal efficacy of these two second generation antipsychotics in progress of positive symptoms may weaken any kind of irrational clinical preference during selection one of them as first choice. The number of patients studied was not large enough to draw a definitive conclusion and short duration of assessment, gender, habitat, lack of placebo arm may have radically impact on the evaluate sensitivity to the study. Thus the discrepancy of our results with other studies could be due to those factors. Further comparable trials are expected in upcoming days to improve our knowledge in this regard.

Conclusion

Even though both of olanzapine and risperidone are similarly efficient for the treatment of schizophrenia, in present study olanzapine showed better response with respect to positive symptoms.

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