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COMPARISON OF OLANZAPINE AND RISPERIDONE IN TREATMENT OF PARANOID SCHIZOPHRENIA

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Abstract

Objective:
To compare the frequency of clinical improvement of olanzapine and risperidone in treatment of paranoid schizophrenia.

Methodology: *This randomized controlled trial consisting of 460 cases (230 in each group) was conducted at the Punjab Institute of Mental Health, Lahore (Teaching Unit-B), from Nov 24 to June 25. Paranoid Schizophrenia cases from both inpatients and outpatients fulfilling the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) criteria for schizophrenia, were included. Two groups were formed: Group R (risperidone) and Group O (olanzapine). Participants were randomly assigned using the lottery method to receive risperidone (2–8 mg/day) or olanzapine (5–20 mg/day). The primary outcome was clinical improvement, defined as a ≥20% reduction in total Positive and Negative Syndrome Scale (PANSS) scores after 3 months.*

Results: *Of 460 cases, mean % reduction in both groups showing (25.87 ± 10.06%) in risperidone group and (19.78 ± 9.32%, $p < 0.001$) in olanzapine group. Clinical response was achieved by 168 patients (73.0 %) in the risperidone group and 114 patients (49.6 %) receiving olanzapine, $p < 0.001$). Conclusion: Risperidone is found to be more effective for improved clinical outcome when compared with Olanzapine treated group cases for the management of paranoid schizophrenia after 3 months of treatment whereas no significant difference was found for overall adverse events.:*

INTRODUCTION

Mental disorders including schizophrenia spectrum and other psychotic disorders are very common these days. Developed nations are not immune to the negative impact of mental diseases. These should put a lot of money into mental health services to help with prevention (when possible), affordable treatment, care, and rehabilitation, and to try to integrate mental and physical health services because of the stigma, lack of awareness, and inadequate coverage of mental health.1-2 In its special initiative for mental health

(2019–2023), the World Health Organization pushed for mental health to be part of the universal health coverage plan. It also said that there should be policies in place for mental health that are based on human rights principles, and that mental health interventions and services should be scaled up from the primary level onward.3

Schizophrenia affects thinking, feeling, and socializing. Schizophrenia symptoms fall into three categories. Positive or psychotic symptoms alter thoughts, behavior, and worldview. Second, negative symptoms include diminished desire, interest, or pleasure in daily tasks, social retreat, difficulty expressing feelings, and difficulties functioning regularly. The third type is cognitive symptoms—attention, focus, and memory difficulties. schizophrenia has one of the highest fatality rates of all psychiatric diseases.4

Antipsychotics are the principal schizophrenia treatment. Fluphenazine, haloperidol, and chlorpromazine are common antipsychotics. However, atypical antipsychotics include quetiapine, risperidone, olanzapine, and newer ones like clozapine and ziprasidone.5 Conventional/ typical antipsychotics have demonstrated effectiveness in improving positive symptoms of psychosis but their ability to control negative symptoms is considered to be limited. In fact, these antipsychotics may cause potential exacerbation of negative symptoms. Moreover, these are associated with various side effects in particular extrapyramidal symptoms (EPS) such as parkinsonism and tardive dyskinesia.6 Olanzapine and risperidone outperform other atypical and conventional antipsychotics in controlled clinical trials.7 Various assessments are done to compare these two atypical antipsychotics revealed varied outcomes.

By week 8, PANSS positive symptom scores had decreased significantly more in the risperidone group (25.4%) than in the olanzapine group (16.0%), a difference that remained evident at the study endpoint.8 Zhang et al. in their study found that risperidone was superior to olanzapine in terms of PANSS total endpoint ($p < 0.05$). However, Cumulative response (approximately 30% reduction in PANSS total score) was similar for both drugs. Contrarily Olanzapine was associated with the largest weight gain at week 4 and 8 ($p < 0.01$ olanzapine = 49.0% vs. risperidone = 32.5%)9 Regarding treatment discontinuation, the rates were higher with risperidone (71.43%) compared to olanzapine (69.09 %).10 Also, risperidone had statistically significant higher rate of sexual dysfunction (92.9%) and amenorrhea (57.1%) than olanzapine (82.8%, 48.3% respectively).11

The efficacy of these two antipsychotics is required to be studied while managing paranoid schizophrenia. The complex responses to these drugs must be understood to improve treatment outcomes. Preliminary studies suggest paranoid patients may prefer olanzapine. A complete and systematic comparison is needed to provide strong evidence and support therapeutic decision-making. Rationale of this study is that this study will objectively examine the efficacy, tolerability, and side effects of olanzapine with risperidone in paranoid schizophrenia. We want to improve the individualized treatment of this schizophrenia subtype by undertaking a well-designed randomized controlled experiment. This research may help doctors make informed judgments based on their patients' symptoms, improving paranoid schizophrenia therapy and results.

METHODOLOGY:

In this randomized controlled trial, a total of 460 cases (230 in each group) were included. The sample size was calculated using the WHO sample size calculator, based on an expected significant reduction in Positive and Negative Syndrome Scale (PANSS) positive symptom scores (25.4% for risperidone versus 16.0% for olanzapine)[8], with a level of significance of 5% and study power of 80%. The study was conducted at the Punjab Institute of Mental Health, Lahore (Teaching Unit-B). Non-probability consecutive sampling technique was used. In this study, Paranoid Schizophrenia was defined as a type of schizophrenia meeting the following criteria:

A. Preoccupation with one or more delusions or frequent auditory hallucinations; and

B. None of the following being prominent: disorganized speech, disorganized or catatonic behavior, or flat or inappropriate affect.

Both inpatients and outpatients fulfilling the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) criteria for schizophrenia, aged 18–50 years, of either gender, and in the maintenance phase were included. Patients with any

other DSM-V axis I diagnosis, a retrospective DSM-V diagnosis of substance abuse within the last three months, documented central nervous system disease, concomitant therapy with mood stabilizers or antidepressants, or prior exposure to olanzapine or risperidone were excluded. The study commenced after approval by the Hospital Ethical Review Committee. Written informed consent was obtained from all participants.

Two groups were formed: Group R (risperidone) and Group O (olanzapine). Participants were randomly assigned using the lottery method to receive risperidone (2–8 mg/day) or olanzapine (5–20 mg/day).

Outcome Variables: The primary outcome was clinical improvement, defined as a ≥20% reduction in total Positive and Negative Syndrome Scale (PANSS) scores after 3 months.

Weekly assessments were conducted, during which extrapyramidal symptoms were documented. Symptom severity and psychopathology were measured at baseline and at clinical improvement using the Extrapyramidal Symptom Rating Scale and the PANSS. PANSS total scores and the five PANSS factor scores were used to assess changes in symptom severity. The overall severity of illness was rated based on improvement in the PANSS total score. We hypothesized that "there is a difference in the frequency of clinical improvement between olanzapine and risperidone in the treatment of paranoid schizophrenia."

Adverse events were recorded weekly. Standard laboratory tests were performed at randomization and as per standard guidelines. Age, gender, and duration of disease were recorded for all patients. Data were entered and analyzed using SPSS version 26. Mean ± SD was used for quantitative variables such as PANSS, duration of disease, and age, while frequencies and percentages were calculated for qualitative variables such as clinical improvement and gender. The outcome variable (clinical improvement) was compared between the two groups using the chi-square test.

RESULTS:

Demographics of this study are presented in the following Table 1. Where the mean age was 33.9+8.1 years of the subjects in risperidone group 33.9 ± 8.1 years whereas 34.5 ± 7.8 years in olanzapine group cases, ($p = 0.48$). Males subjects were in majority in both groups—60.0% in risperidone and 65.7% in olanzapine group cases ($p = 0.32$). The duration of illness was found as similar in both of the groups i.e. (5.26 ± 2.35 years), shows no demographic details in both groups are comparable. In Table 2 we compared PANSS outcomes in Risperidone and Olanzapine groups showing (94.35 ± 8.60) in risperidone and (93.89 ± 8.33) in olanzapine group of cases ($p = 0.560$). Whereas, 3 months after the treatment done, a significant reduction was recorded by calculating (69.91 ± 11.40) in the risperidone and (75.26 ± 10.61) in the olanzapine group ($p < 0.001$), it was significant statistically. We further computed mean % reduction in both groups showing (25.87 ± 10.06%) in risperidone group and (19.78 ± 9.32%, $p < 0.001$) in olanzapine group.

Table 1. Demographic Characteristics by Group

Variable	Risperidone (n=230)	Olanzapine (n=230)	Total (n=460)	p-value
Age (years, Mean ± SD)	33.9 ± 8.1	34.5 ± 7.8	34.2 ± 8.0	0.48
Gender Male	138 (60.0%)	151 (65.7%)	289 (62.8%)	0.32
Gender Female	92 (40.0%)	79 (34.3%)	171 (37.2%)	
Duration of illness (years, Mean ± SD)	5.26 ± 2.35	5.26 ± 2.35	5.26 ± 2.35	—

Table 2. PANSS Outcomes by Treatment Group

Outcome	Group	N	Mean	SD	p-value
PANSS Baseline	Risperidone	230	94.35	8.596	0.560
PANSS Baseline	Olanzapine	230	93.89	8.332	
PANSS at 3 months	Risperidone	230	69.91	11.400	<0.001
PANSS at 3 months	Olanzapine	230	75.26	10.605	
% Reduction (PANSS)	Risperidone	230	25.87	10.06	<0.001
% Reduction (PANSS)	Olanzapine	230	19.78	9.32	

**Independent-samples t-test comparing groups for each outcome; p-values correspond to between-group comparisons.*

Table 3. Clinical Improvement (≥20% PANSS Reduction) by Group

Clinical Improvement	Risperidone (n=230)	Olanzapine (n=230)	Total (n=460)	Chi-square p-value
Yes (≥20%)	168 (73.0%)	114 (49.6%)	282 (61.3%)	<0.001
No (<20%)	62 (27.0%)	116 (50.4%)	178 (38.7%)	

Pearson chi-square test for 2×2 table; continuity-corrected and Fisher's exact p-values were also <0.001.

Table 4. Adverse Events by Group

Adverse Event	Risperidone (n=230)	Olanzapine (n=230)	Total (n=460)	Chi-square p-value
Yes	81 (35.2%)	93 (40.4%)	174 (37.8%)	0.249
No	149 (64.8%)	137 (59.6%)	286 (62.2%)	

DISCUSSION:

In this randomized trial we found risperidone with more better clinical improvement than olanzapine among patients with paranoid schizophrenia, as our results computed and showing PANSS scores as 73% versus 49.6%, p=<0.0001. Similarly, the mean reduction in percentage in PANSS score also remarkably higher with risperidone by computing 25.87+10.6% compared to 19.78+9.32% in Olanzapine group pointing out risperidone more effective in alleviation of negative and positive symptoms. Whereas the adverse events were comparable in both groups and statistical difference did not reach on significant level(p=0.249), suggesting comparative tolerability profiles. These findings are suggestive of both agents as effective as atypical antipsychotics, while risperidone is found with more favorable symptoms for improvement without safety compromise.

Consistent with portions of Yang H and Wu H's meta-analysis, our study also indicates risperidone's stronger clinical impact relative to other agents in first-episode schizophrenia, though their data likewise pointed to increased extrapyramidal and weight-related complications.13 Supporting these observations, Yang L and Qi X found that dual therapy with risperidone and olanzapine led to improved clinical and cognitive results over risperidone alone, while the incidence of side effects remained similar.14 The pattern across studies supports the dependable performance of risperidone across varying treatment paradigms. The comparatively higher improvement noted in this investigation may owe to monotherapy advantages within paranoid schizophrenia, leveraging risperidone's balanced modulation of dopamine and serotonin transmission.

In contrast, the studies by Nazrina S and others pointed out that Olanzapine achieved more reduced in positive symptoms compared to risperidone in 12 weeks duration of schizophrenia.15 This difference may be due to the reason of difference in sample characteristics, outcome measures and intervention durations. In Nazrina S study, they emphasized improvement in positive symptoms unlike our broader three-months evaluation study which includes negative and cognitive parameters.

Another study by Barbosa et al.'s large-scale Brazilian cohort is evident and contributes an important real-world perspective. More than 16 years of follow-up, longer treatment retention was noted with Olanzapine users than with olanzapine users while fewer psychiatric hospitalizations than risperidone users.16 While it is contrary to the superior short-term efficacy of risperidone in our study, it reveals that olanzapine may promote adherence through improved tolerability. These findings remind clinicians that real-world effectiveness often hinges on persistence and patient acceptance rather than symptom reduction alone.

Cognitive recovery constitutes an essential outcome in schizophrenia care. Another study b Lungu and others experienced that second-generation antipsychotics such as risperidone and olanzapine contribute positively to cognitive domains, working memory, particularly attention, and learning.17 This echoes with the cognitive steadiness noted in our cohort, where no decline accompanied symptom improvement. In agreement with this, Yang L et al reported superior WCST performance under combined olanzapine–risperidone therapy.14 These findings indicate that both agents support cognitive stability, and tailored regimens may improve outcomes in difficult-to-treat cases.

Liu et al. offered an innovative perspective in schizophrenia genetics by exploring the impact of 5-hydroxytryptamine receptor (5-HTR) gene polymorphisms on the clinical performance of atypical antipsychotics.18 They reported that particular 5-HTR SNPs are linked to variable therapeutic responses to risperidone and olanzapine. These findings provide a plausible explanation for inter-patient differences in efficacy noted in our study and suggest that pharmacogenomic-guided treatment could improve individualization of therapy in paranoid schizophrenia.

While risperidone remains the more consistently effective antipsychotic, recent evidence underscores the potential of high-dose olanzapine in hard-to-treat schizophrenia. Aggarwal et al. detailed a case in which a 50 mg daily dose led to notable symptomatic improvement without major toxicity.19 This finding expands the therapeutic spectrum of olanzapine,

though high doses must be administered with careful monitoring due to safety concerns.

In the wider neuropsychiatric landscape, including dementia-associated psychosis, risperidone and olanzapine both demonstrate measurable benefit in mitigating behavioral disturbances, though their adverse-effect spectra remain distinct. Qasim et al. observed that risperidone effectively alleviates paranoia and aggression in older adults with psychosis, whereas olanzapine reduces hostility and hallucinations but may worsen depressive features.20 This aligns with our findings of equivalent safety yet varied efficacy, highlighting how therapeutic responses differ by symptom type and etiology.

Our study provided a remarkable comparative analysis suggestive of superiority of risperidone regarding its better clinical improvement whereas also maintaining tolerability than Olanzapine while managing paranoid schizophrenia. Larger sample size and randomization is the main strength of this study with the objective of evaluation through a measurable PANSS scoring system. However, being a single-center study and shorter follow-up limits its generalizability to other populations. Moreover, metabolic and endocrine markers were not analyzed, which could have provided further insights into drug safety. Future research should extend follow-up duration and integrate pharmacogenomic and cognitive assessments to delineate the broader implications of long-term therapy.

Owning to this, risperidone may be recognized as the first-line treatment for significant alleviation of symptoms, with olanzapine positioned for cases focusing on safety profile and treatment compliance.

CONCLUSION:

Risperidone is found to be more effective for improved clinical outcome when compared with Olanzapine treated group cases for the management of paranoid schizophrenia after 3 months of treatment whereas no significant difference was found for overall adverse events. Our results are in favour of risperidone as a preferred first-line treatment option for short-term symptom control, whereas prolonged follow-up with endocrine/metabolic monitoring is warranted to inform long-term treatment choices.

CONFLICT OFF INTEREST:

Nil

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