

# The Comparison of Olanzapine and Risperidone Treatment in Male Schizophrenic Patients using Positive and Negative Syndromes Scale (PANSS)

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## Abstract

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**INTRODUCTION:** The most common method to compare olanzapine and risperidone is by calculating the score of positive and negative syndromes scale (PANSS). However, there were some conflicting results mentioned from previous studies.

**AIM:** This study aimed to compare the treatment of olanzapine and risperidone using PANSS, limited to only male patients receiving inpatient treatment to obtain more significant results.

**METHODS:** The subjects of this study were male schizophrenic patients in the acute phase of treatment (N = 68) who were hospitalised at the Mental Hospital Prof. Dr M. Ildrem, Indonesia. These participants were divided into two groups and treated with different atypical antipsychotics (olanzapine, 20 mg/day [n = 34]; risperidone, 6 mg/day [n = 34]). The scores of PANSS from both groups were collected from pre-test and post-test after 6-week treatment.

**RESULTS:** The improvement of the schizophrenia symptoms measured by PANSS after 6 weeks showed significant differences in the scores of PANSS between the male patient groups treated with olanzapine and risperidone (p-value < 0.001).

**CONCLUSION:** The group of olanzapine shows a higher improvement of the scores of PANSS than that the group of risperidone.

## Introduction

Schizophrenia is a psychotic disorder characterised by a disorder of mind, mood, and behaviour. Schizophrenia accounts for around 1% of the population. This disorder usually starts before the age of 25, survives throughout life, and may affect people from all social classes. Schizophrenia consists of positive symptoms, negative symptoms, cognitive symptoms, aggressive symptoms, and affective symptoms. The positive symptoms include delusions, hallucinations, disorganised speech or behaviour, catatonic behaviour, and agitation. The negative symptoms include blunted or flat affect, emotional withdrawal, poor rapport, indifference, withdrawal from social life, abstract-thought disorder, alogia, avolition, anhedonia, and concentration disorder [1].

Among atypical antipsychotics, risperidone and olanzapine have been shown to reduce both the positive and the negative symptoms significantly of schizophrenia [2], and are also more effective than conventional antipsychotic drugs [3]. Risperidone and olanzapine exploit multiple actions on serotonin and dopamine which resulted in improved adherence by minimising the side effects of extrapyramidal [4] [5].

One way of measuring the positive symptoms, the negative symptoms, and the general symptoms in schizophrenic patients is by using Positive and Negative Syndrome Scale (PANSS). The measurement of the scores of PANSS has been proven to be sensitive and specific about the use of pharmacology from the assessment of the positive symptoms and the negative symptoms in schizophrenic patients [6]. Several studies have been

conducted to compare the effectiveness of olanzapine and risperidone using the scores of PANSS. Conley et al. (2001) found that olanzapine leads to better improvement in both positive and negative symptoms, better overall response rates, and less severe side effects than risperidone. In addition, patients treated with olanzapine appear to maintain a better response than patients treated with risperidone [7]. This contrasts with previous findings by Tran et al. (1997) which showed differences only in the negative scale, in which the group treated with olanzapine had a higher score than the group treated with risperidone. On the other hand, the positive scale and the total score between the two groups were found to be comparable [8]. Similarly, Shah et al. (2011) and Kumar et al. (2016) reported that although the improvement in the negative scale was significantly higher in the group treated with olanzapine, there were no significant differences for the positive scale and the total score of PANSS in both groups [9] [10].

Some factors which might influence different results in previous studies mentioned above are the methods of the patient's treatment (inpatient or outpatient care), the dose of drugs used by the patient during the assessment (flexible dose or fixed dose), and gender of the patient (male or female). To our best knowledge, there is no previous study which limits participants only to patients with a specific gender. Therefore, this study aimed to measure differences in the scores of PANSS on the use of olanzapine and risperidone limited to male with schizophrenia who were hospitalised with a fixed dose. The inpatient method was chosen because this method could easily control the physical activity and lifestyle of the participants so that the results would have a more valid value. The reason for selecting male participants was because male schizophrenic patients tend to have negative symptoms, a worse pre-morbid history, and a greater likelihood of having deficit syndromes and worse prognosis than female schizophrenic patients [11].

## Methods

The research design was a quasi-experiment with pre-test and post-test, between the olanzapine group and the risperidone group in the period of June-September 2017. The drop-out criteria used was an intention to treat analysis in which if there was a drop-out subject, the subject would still be included for the analysis in the last week with the data used was the data recorded in the last week before the subject dropped-out [12].

The subject used was determined by non-probability sampling known as the consecutive sampling [13]. Subjects who met the criteria were required to sign an informed consent after being

briefed about the study. According to that, this study recruited subjects of 68 male patients with schizophrenia who were hospitalised in the acute phase of treatment at the Mental Hospital Prof. dr. M. Ildrem, North Sumatra, Indonesia. These participants were divided into two groups based on simple randomisation consisting of 34 patients treated with olanzapine treatment and 34 patients treated with risperidone treatment. If the subject encountered the side effects of extrapyramidal symptoms during the treatment, the subject would be given anticholinergic (i.e. triheksilpenidil) with a dose range of 2-5 mg for 2-4 times of administration during 1-2 weeks [14] [15].

The inclusion criteria were including male patients with schizophrenia which corresponded to the Guidelines of Diagnostic Classification for Mental Disorders III prevailed in Indonesia with semi-structured interviews mini ICD – 10 [11], in the acute phase of treatment (total score of PANSS 80-150) [16], between the age of 20 and 45 years, duration of illness  $\leq$  5 years, normal body mass index (BMI = 18.5-24.99), PANSS excited component (PANSS-EC)  $<$  20. The PANSS-EC consisted of 5 items: excitement, tension, hostility, uncooperativeness, and poor impulse control. It was rated from 1 (not present) to 7 (extremely severe) with the score ranged from 5 to 35 [17]. The exclusion criteria consisted of having general medical disorders or other comorbidities, history of substance use (except caffeine and nicotine), and hypersensitivity or unresponsive to olanzapine dan risperidone.

The administration of olanzapine was carried out with an initial dose of 10 mg/day. Then, this dose was increased to 15 mg/day on the 7<sup>th</sup> day while the dose at night was increased to 20 mg/day on the 14<sup>th</sup> day. The last dose was used for 6 weeks. The initial dose of risperidone was 2 mg/day; then this dose was increased to 4 mg/day on the 4<sup>th</sup> day. Finally, the dose was increased to 6 mg/day at the 8<sup>th</sup> day. The last dose was used in the morning and at night for 6 weeks. The measurement of PANSS began in the first week with the fixed dose. At the end of the research or the 6<sup>th</sup> week, the total score of PANSS was measured.

The results measured in each symptom were the change in the mean value from the baseline to the end-point in the score of PANSS. Before the intervention, the baseline was assessed through interviews using a questionnaire of PANSS which consisted of 30 items with 3 subscales: 7 items were the positive symptoms scale (P1-P7), 7 items were the negative symptoms scale (N1-N7), and 16 items were general psychopathology symptoms scale (G1-G16). Each item was scored on a 7-point Likert scale ranging from 1 to 7. Thus, the range of the positive and the negative sub-scales were 7 to 49 while the range of the general psychopathology scale was 16 to 112 [18]. The agreement test was obtained with a numerical agreement comparative test (Bland Altman) performed by an independent, professional, and trained psychiatrist. Furthermore, the scores of

PANSS of subjects were evaluated on a weekly basis using the same questionnaire with the previous questionnaire until the endpoint, the 6<sup>th</sup> week.

The data processing and the statistical analysis were performed with the use of IBM SPSS statistical software version 22. The baseline comparison for the demographic characteristics of the subjects was performed using an independent t-test (normal distribution) or Mann-Whitney U test (non-normal distribution), and Chi-Square test. The mean score in each group before and after the intervention was obtained using paired t-test (normal distribution) or Wilcoxon test (non-normal distribution). The mean score at the end-point of the 6<sup>th</sup> week was obtained using an independent t-test or Mann-Whitney U test [19].

## Results

Table 1 shows the demographic characteristics of the olanzapine group (n = 34) and the risperidone group (n = 34). Most participants were from the primary education level (64.7% for both groups) and unmarried status (76.5% for the olanzapine group and 85.3% for the risperidone group). The mean age of the olanzapine group was 30.29 years (SD = 6.89), and the mean age of the risperidone group was 30.24 years (SD = 6.40).

**Table 1: Demographic characteristics of research subjects**

Variable	Group of Olanzapine Treatment (n = 34)		Group of Risperidone Treatment (n = 34)		p
	Mean	SD	Mean	SD	
Age (years)	30.29	6.89	30.24	6.40	0.971*
Body mass index	22.08	1.45	21.78	1.31	0.386*
Duration of illness (years)	2.67	1.09	2.50	1.08	0.397**
Education level	N	%	N	%	
Primary	22	64.7	22	64.7	
Middle	12	35.3	12	35.3	1.000**
Marriage status					
Married	8	23.5	5	14.7	0.537**
Unmarried	26	76.5	29	85.3	

\*Independent T-test, \*\*Chi-square Test.

The mean duration of illness experienced by the subjects was 2.67 years (SD = 1.09) for the olanzapine group and 2.50 years (SD = 1.08) for the risperidone group. As shown in Table 1, the two groups had insignificant differences for all variables indicated by the p-value > 0.05. These results indicate that the overall results of this study are unbiased.

**Table 2: Baseline of the scores of PANSS (0-week)**

PANSS	Group of Olanzapine Treatment (n = 34)		Group of Risperidone Treatment (n = 34)		P*
	Mean	SD	Mean	SD	
Positive scale	32.26	2.16	32.62	2.23	0.510
Negative scale	24.41	2.45	24.35	2.42	0.892
General psychopathology scale	38.65	3.60	37.91	3.46	0.394
Total Score	95.26	4.57	94.94	4.33	0.765

\*Independent T-test.

Table 2 shows the baseline for the scores of PANSS at the 0-week. According to the table, there was no significant difference between the two groups.

**Table 3: The differences in the PANSS scores before and after 6 weeks of treatment with olanzapine**

PANSS	Before treatment		After 6 weeks of treatment		P*
	Mean	SD	Mean	SD	
Positive scale	32.62	2.23	12.00	1.02	<0.001
Negative scale	24.41	2.45	9.03	1.34	<0.001
General psychopathology scale	37.91	3.46	14.00	1.39	<0.001
Total Score	94.94	4.33	34.97	2.98	<0.001

\*Paired T-test.

Table 3 and Table 4 show the mean score of PANSS in the olanzapine group and the risperidone group before and after the treatment. As shown in the table, there was a significant change in the positive scale, the negative scale, the general psychopathology scale, and the total score of PANSS of the subjects before and after the treatment in both groups.

**Table 4: The differences in the PANSS scores before and after 6 weeks of treatment with risperidone**

PANSS	Before treatment		After 6 weeks of treatment		P*
	Mean	SD	Mean	SD	
Positive scale	32.26	2.16	16.18	1.40	<0.001
Negative scale	24.35	2.42	12.38	1.30	<0.001
General psychopathology scale	38.65	3.60	19.59	1.39	<0.001
Total Score	95.26	4.57	47.71	2.69	<0.001

\*Paired T-test.

Table 5 shows the differences in the score of PANSS after 6 weeks of treatment between the olanzapine group and the risperidone group. According to the table, the mean of the PANSS score in a male with schizophrenia at the end-point of the 6<sup>th</sup> week for the positive scale in the olanzapine group was 12.00 (SD = 1.01) whereas the risperidone group showed the mean score of 16.18 (SD = 1.40). The mean of the negative scale for the olanzapine group was 9.03 (SD = 1.34) while the mean of the negative scale for the risperidone group was 12.38 (SD = 1.30). The mean of the general psychopathology scale for the olanzapine group was 14.1 (SD = 1.39) while the mean of the general psychopathology scale for the risperidone group was 19.59 (SD = 2.19).

**Table 5: The differences in the PANSS scores after 6 weeks of treatment between the olanzapine group and the risperidone group**

PANSS	Group of Olanzapine Treatment (n = 34)		Group of Risperidone Treatment (n = 34)		P
	Mean	SD	Mean	SD	
Positive scale	12.00	1.01	16.18	1.40	<0.001
Negative scale	9.03	1.34	12.38	1.30	<0.001
General psychopathology scale	14.00	1.39	19.59	2.19	<0.001
Total Score	34.97	2.98	47.71	2.69	<0.001

\*Independent T-test.

Thus, the mean of the total score of PANSS obtained was 34.97 (SD = 2.98) for the olanzapine group and 47.71 (SD = 2.69) for the risperidone group. Based on these results, there was a very

significant difference between the two groups at the end-point of the 6<sup>th</sup> week ( $p$ -value < 0.001). The scores of PANSS obtained from olanzapine group showed a higher improvement than that of risperidone group.

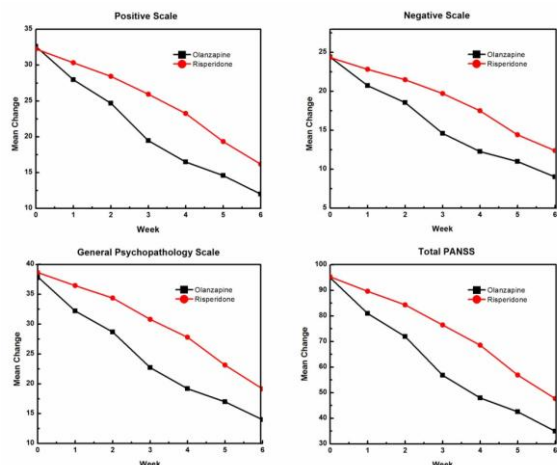


Figure 1: Mean change from baseline in weekly for positive scale, negative scale, general psychopathology scale, and a total score of PANSS of male schizophrenic patients treated with olanzapine or risperidone ( $p$ -value < 0.001)

Figure 1 shows the mean change from baseline in weekly scores of PANSS. The decreases in the scores of PANSS from baseline to each visit were significantly greater in the olanzapine group than that in the risperidone group from week 1 through week 6.

## Discussion

This study has provided very clear boundaries in recruiting participants as the research subjects. The selected participants were male patients aged 20-45 years. As previously mentioned, the male participants were recruited because male patients tend to have worse symptoms than female patients. The age selection is also because the most frequent onset of schizophrenia is the age of 15-30 years whereas the peak of the attack in men is between the ages of 10-25 years. Also, 90% of patients receiving schizophrenic treatment are between the ages of 15-55 years [1]. Patients under the age of 18 were excluded from this study as a consideration of their long-term safety, including cardiometabolic effects and effects on their growth, maturity, and behavioural development. In addition, geriatric patients were also excluded because these patients experience the decreased function of kidney, liver, and heart, and increased tendency of postural hypotension [20].

As previously explained, the use of risperidone and olanzapine in this study was because

both have been shown to significantly reduce the positive symptoms and the negative symptoms of schizophrenia [21]. The determination of dose for both was based on several studies on olanzapine and risperidone in people with schizophrenia. Based on monograph products, the daily dose target for people with schizophrenia is 10 mg for olanzapine and 6 mg for risperidone. However, in clinical practice, the average dose of olanzapine and risperidone is recommended to be higher than the target dose recommended in the monograph [22]. Marder et al. (2017) [23] found that olanzapine was effective if given in the dose of 10-20 mg/day in the acute phase of schizophrenia [23] although a higher dose up to 60 mg/day was reportedly used for people with schizophrenia resistant to treatment. Also, the administration of olanzapine at night can improve general sedation tolerance in early treatment [24]. On the other hand, risperidone has a target dose of 3-6 mg in a day. Risperidone at a dose of 6 mg is as effective as the higher dose, but risperidone at a medium dose (4-6 mg/day) suggests a lower risk of extrapyramidal symptoms (EPS) than the first generation of antipsychotics [21]. Based on the above description, it has been determined that the dose of olanzapine administered was 20 mg/day and the dose of risperidone administered was 6 mg/day because this dose would be well tolerated without adverse events.

The calculation results of the scores of PANSS in this study showed significant differences in the scores of PANSS for the positive scale, the negative scale, general psychopathology scale, and the total score of PANSS in male schizophrenic patients. This is similar to a study conducted by Conley et al. (2001) in Los Angeles which compared the treatments of olanzapine and risperidone to 134 patients who were hospitalised. The patients were treated with risperidone and olanzapine with flexible dose for 8 weeks. In both groups, there was also a significant difference in the scores of PANSS for the positive scale, the negative scale, general psychopathology scale, and the total score of PANSS at the end of the 6<sup>th</sup> week ( $p$  < 0.01) [7]. In contrast, a study by Shah et al. (2011) [11] in Nepal found that both groups showed significant improvement at the end of the 6<sup>th</sup> week. More specifically, the negative scale was higher in the group treated with olanzapine than risperidone while the positive scale and the total score of PANSS had improvement, but there was no significant difference in the two groups ( $p$  = 0.498) [8]. This difference was because Shah et al. (2011) used participants with the outpatient method, so the physical activity and the dose of drugs could not be fully controlled while the study by Conley et al. (2001) used participants who were hospitalised. Nevertheless, Tran et al. (1997) [9] and Kumar et al. (2016) [10] who recruited participants who were hospitalised also found similar results to the results of Shah et al. (2011) [8].

The results of this study were not biased because the comparative test results between the variables on the demographic characteristics indicated that there was no significant difference in terms of age, education level, marital status, duration of illness, body mass index, positive scale, negative scale, general psychopathology scale, and total score of PANSS in both groups.

The limitations of this study were that this study did not analyse changes in people's lifestyle and other behaviour patterns, such as smoking.

In conclusion, the results of this study showed that there were significant differences in the scores of PANSS including the positive scale, the negative scale, general psychopathology scale, and the total score of PANSS in male schizophrenic patients between the group of olanzapine treatment with the fixed dose of 20 mg/day and the group of risperidone treatment with the fixed dose of 6 mg/day at the end of the 6<sup>th</sup> week with the  $p$ -value < 0.001. This is in accordance with the results obtained by Conley et al. (2001) who studied men and women as subjects using a flexible dose. Based on these different scores, it can also be concluded that olanzapine provides a higher improvement in the positive symptoms and the negative symptoms than risperidone.

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