

# Differences in Total Score of Positive and Negative Syndrome Scale between Bataknese and Javanese Men with Schizophrenia Receiving Risperidone Treatment

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## Abstract

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**BACKGROUND:** Schizophrenia is a psychopathological syndrome clinic involving cognition, emotion, perception and other aspects from the individual which interferences. This interference is normally started before age 25, and it can affect all social classes.

**AIM:** To find out the difference in total positive and negative syndrome scale (PANSS) scores in schizophrenia between Bataknese and Javanese who have received treatment with risperidone.

**METHODS:** This study is a prospective study. This study used numeric comparative analytic two unpaired groups to observe the differences of PANSS score of the man with schizophrenia between Bataknese and Javanese who had received risperidone treatment.

**RESULTS:** Our study found that the average score of PANSS for Bataknese was  $49.76 \pm 12.65$  and Javanese was  $42.43 \pm 9.05$ .

**CONCLUSION:** There was a difference score of PANSS for the man with schizophrenia between Bataknese and Javanese who had received risperidone treatment for 6 weeks ( $p = 0.037$ ).

## Introduction

Schizophrenia is a disturbing clinical syndrome of psychopathology that involves cognition, emotions, perceptions, and other aspects of behaviour. This disorder usually starts before the age of 25 and can attack people from various social groups [1]. According to Burroughs, race and ethnicity have different responses to treatment. The differences of response in race and ethnicity to the treatment are influenced by several factors including biological factors (age, gender, genetics, illness), cultural factors (attitudes, beliefs, family influences), and environmental factors (climate, parasites, pollutants, smoking, alcohol, medicines) [2].

Clinical studies and multicentre trials carried out by Buckley in Cleveland conclude that risperidone

is an antipsychotic that effectively improves positive and negative symptoms in schizophrenia globally. The study compared risperidone and conventional antipsychotics (chlorpromazine) at the mean  $\pm$  SD dose of risperidone at  $6.8 \pm 2.0$  mg and equivalent dose of chlorpromazine at  $1.295 \pm 789$  mg to improve positive and negative symptoms in schizophrenia [3]. Genetics has been known to affect the pharmacokinetics and pharmacodynamics of antipsychotic drugs. This is based on the time separation in the evolutionary trends in Africa. For example, genetics in Orientals and Caucasians are related to the cytochrome P450 enzymes (CYP 450), which have a relationship in the metabolism of psychotropic drugs in humans.

Recent studies on the pharmacokinetics and pharmacodynamics of antipsychotic drugs and sociocultural factors that influence the response of

antipsychotic drugs consistently provide racial differences in response to antipsychotic drugs [4]. Ethnicity also plays a role in responding to risperidone treatment among children and adolescents with the schizophrenic disorder [5]. In an experimental study by Sianturi [6] in Indonesia, there was a difference in the effectiveness of risperidone and haloperidol on the positive symptoms of schizophrenic patients in the Positive and Negative Syndrome Scale (PANSS) at the fourth week. The results showed that the mean difference of the PANSS positive scores for the risperidone therapy group was 13.1 (SD  $\pm$  3.4) whereas the mean difference of the PANSS positive scores for the haloperidol therapy group was 10.4 (SD  $\pm$  1.9),  $P = 0.005$  ( $P < 0.05$ ). There was also a difference in the PANSS positive delta scores based on the intervention groups [6]. Furthermore, a pilot study conducted by Frackiewicz *et al.*, [7] found that there was a significant difference in the PANSS scores between 10 Hispanic schizophrenic in-patients and 8 non-Hispanic schizophrenic in-patients who received risperidone ( $p < 0.02$ ).

Men with schizophrenia usually experience a much earlier age onset. They tend to have primary negative symptoms associated with the occurrence of chronicity which is a large clinical case [8]. Schizophrenia is defined as a disorder that lasts for six months or more, in which the person has the notion, hallucinations, irregular speech, catatonic behaviour, or negative symptoms for at least one month [9]. Recent studies estimate that socioeconomic status might influence health risk factors of schizophrenic people to obesity and diabetes because lower middle class tend to consume excess calories [10]. The PANSS has become a standard tool for assessing clinical outcomes in the treatment studies of schizophrenia and other psychotic disorders and has been proven to be easily administered, reliable, and sensitive to changes with treatment. The PANSS scores of in-patients rarely exceed 80-150 [11].

Based on the information obtained from the first century AD, the Batakese tribe originated from Greece and Chinese [12]. Indonesia has various ethnic groups, and the distribution of the ethnic groups is Sundanese with 36.7 million people (15.5%), Batakese with 8.5 million people (3.6%), and other ethnic groups from Sulawesi with 7.6 million people (3.2%), and others [13]. The Batakese people are known for their openness, spontaneity, and aggressiveness both physically and verbally. Previous research found that Batakese people often choose to express their anger when they are angry while Javanese people tend to hide their anger [14]. Thus, Batakese people mostly have low emotional regulation whereas Javanese people have polite behaviour in their speech and self-presentation by showing respect for others [15], [16]. Risperidone is effective for various psychopathology of schizophrenia and will be more effective than the First-Generation

Antipsychotics (FGA).

Risperidone has been widely used and becomes the highest number of antipsychotics in the world. Risperidone has a high affinity for dopamine 2 (D2) and serotonin 2A (5-HT2A) receptors [17]. Differences between ethnic groups in drug metabolic enzymes and transporters have the potential to cause variability in the dose choice [18]. Allele gene polymorphisms that highly depend on ethnicity have a major role in the functions of 2D6, 2C19, 2C9, 2B6, 3A5, and 2A6 CYPs and lead to different pharmacogenetics phenotypes [19].

Bakare stated that genetics influence the pharmacokinetics and pharmacodynamics of antipsychotic drugs, but Patel reported that there were significant CBCL differences between African-American, Hispanic, but not Caucasian races. Also, Frackiewicz stated that racial factors affect the improvement of PANSS symptoms. However, there have been no previous studies in Indonesia that examined the relationship between ethnicity and risperidone effectiveness in men with schizophrenia. Therefore, the researchers were interested in conducting this research.

The present study was the first study conducted in Indonesia, especially in North Sumatra, which examined PANSS total score differences in men with schizophrenia between Batakese and Javanese ethnic groups. To find out the sample size, therefore, a preliminary study was carried out from July to September 2017 by recruiting 20 subjects with 10 Batakese and Javanese, respectively.

## Methods

The present study was an observational study through a prospective cohort approach. This study was an unpaired numerical comparative analytical study of two groups to determine the difference in the PANSS total scores between Batakese and Javanese men with schizophrenia who had received 6 mg of risperidone for 6 weeks. Subjects in this study were determined by consecutive sampling, which is a non-probability sampling type. The inclusion criteria in this study were male patients who had been diagnosed with schizophrenia at the Inpatient Installation in Prof. Moh. Ildrem Mental Hospital Medan North Sumatra. The patients with age 15-40 years received a fixed dose of 6 mg of risperidone per day and had the PANSS total score of 80-120. Also, the subjects had an inappropriate affect and dysphoric mood, cooperative (willing to be the research subject), normal body mass index, no history of liver disease and had a good liver function, had insight I or II when patients received 6 mg of risperidone per day. The exclusion criteria were having a history of general

medical illness and the use of prohibited substances except for nicotine and caffeine, having a family history of schizophrenia, and having a disease and history of kidney disorders.

The calculation of the sample size giving the highest number was 21 subjects for the Javanese ethnic group and 21 subjects for the Batakese ethnic group. Data collection was preceded by finding patients from Batakese and Javanese ethnicity who were diagnosed with schizophrenia in Prof. Ildrem Mental Hospital and received a fixed-dose at 6 mg of risperidone (in the first week of treatment). Structured interviews using MINI ICD-10 was performed to find people with schizophrenia determined by diagnostic guidelines based on PPDGJI-III. Screening using inclusion and exclusion criteria was done to determine the research subjects. In the interviews, several information was also collected from the patients including the age of the first attack, duration of attack, number of attacks, insight, education level, socioeconomic level, personality of the patients before diagnosed with schizophrenia, family history, and history of liver disease and liver function of patients from laboratory tests. Men with schizophrenia from Batakese and Javanese ethnicity who fulfilled the inclusion criteria filled out written approval after getting detailed and clear explanations to participate in the study until the number of subjects in each Javanese and Batakese group was 21 patients. Then, the PANSS total score of both Batakese and Javanese patients who fulfilled the inclusion criteria and had received 6 mg of risperidone (first week of treatment) was measured. The patients were observed until the sixth week. After the sixth week of treatment, the PANSS total score was measured again. The PANSS total scores of Batakese and Javanese male patients with schizophrenia in the sixth week were analysed to see if there were differences between the Batakese and Javanese subjects. The research results were reported and presented in a table. Test analysis was performed on the PANSS total scores of the Batakese and Javanese subjects. Data normality was tested using the Shapiro-Wilk test because the number of samples was 21 subjects for each Batakese and Javanese group (less 50). The PANSS total score of the Batakese and Javanese subjects after receiving 6 mg of risperidone for 6 weeks was normally distributed so that the analysis was continued with an unpaired t-test. The PANSS total scores of the Batakese and Javanese subjects are shown in the mean and standard deviation.

## Results

The difference in the PANSS total scores between the Batakese and Javanese subjects is shown in Table 1.

**Table 1: Difference in the Total PANSS Score between the Batakese and Javanese subjects in the sixth week**

PANSS total score of Javanese subjects	PANSS total score of Batakese subjects
50	44
34	58
41	62
40	41
57	58
60	66
48	62
44	68
54	53
57	63

Mean ± Standard Deviation = 48.50 ± 8.618    Mean ± Standard Deviation = 57.50 ± 8.997

The characteristics of the research subjects can be seen in Table 2. Based on the age, the median (minimum-maximum) age of the Javanese subjects was 37.00 (26-40) years, whereas the median (minimum-maximum) age of the Batakese subjects was 36.00 (24-40) years. Based on the education level, 7 Javanese subjects (33.3%) graduated middle school, 13 Javanese subjects (61.9%) graduated high school, and 1 Javanese subject (4.8%) graduated university. Similarly, 8 Batakese subjects (38.1%) graduated middle school, 12 Batakese subjects (57.1%) graduated high school, and 1 Batakese subject (4.8%) graduated university. Regarding the employment status, 37 subjects (88.09%) were unemployed, and 5 subjects (11.91%) were employed from both groups. In the Javanese ethnic group, 1 subject (4.8%) was employed, and 20 subjects (95.2%) were unemployed. Similarly, in the Batakese ethnic group, 4 subjects (19%) were employed, and 17 subjects (81%) were unemployed. The median (minimum-maximum) duration of illness of the Javanese subjects was 4.00 (1-5) years whereas the median duration of illness of the Batakese subjects was 3.00 (1-5) years. Regarding the marital status, there were 9 married subjects (42.9%) and 12 unmarried subjects (57.1%) in the Batakese ethnic group whereas there were 5 married subjects (23.8%) and 16 unmarried subjects (76.2%) in the Javanese ethnic group. The mean body mass index of the Javanese subjects was  $22.50 \pm 1.30 \text{ Kg/m}^2$  while the mean body mass index of the Batakese subjects was  $21.64 \pm 1.57 \text{ Kg/m}^2$ .

The median (minimum-maximum) onset of an attack of the Javanese and Batakese subjects was 33.00 (24-35) years and 33.00 (23-35) years, respectively. Based on the frequency of attack, 21 Javanese subjects (100%) experienced attacks two times or less. Similarly, 18 Batakese subjects (85.71%) experienced attacks two times or less, and 3 Batakese subjects (14.29%) experienced attacks two to five times. In terms of insight, 2 Javanese subjects (9.52%) had insight I and 19 Javanese subjects (90.48%) had insight II whereas Batakese subjects (52.38%) had insight I and 10 Batakese subjects (47.62%) had insight II. Regarding the socioeconomic level, 11 subjects (80.95%) Javanese subjects were in the lower class, and 4 Javanese subjects (14.51%) were in the middle class while 16 Batakese subjects (76.19%) were in the lower class, and 5 Batakese subjects (23.81%) were in the middle class. The mean

PANSS total scores of the Javanese and Batakese ethnic groups in the first week receiving a fixed dose of 6 mg of risperidone were  $99.10 \pm 9.88$  and  $104.19 \pm 12.38$ , respectively.

**Table 2: Distribution of Samples Based on Demographic Characteristics**

	Javanese Men with Schizophrenia N (%)	Batakese Men with Schizophrenia N (%)	p
Age {Median (Minimum-Maximum)}	37.00(26-40)	36.00(24-40)	0.559 <sup>b</sup>
Education Level			
Middle school	7 (33.3%)	8 (38.1%)	0.747 <sup>c</sup>
High school	13 (61.9%)	12 (57.1%)	
University	1 (4.8%)	1 (4.8%)	
Employment Status			
Employed	1 (4.8%)	4 (19.0%)	0.343 <sup>d</sup>
Unemployed	20 (95.2%)	17 (81.0%)	
Marital Status			
Married	5 (23.8%)	9 (42.9%)	0.190 <sup>c</sup>
Not married	16 (76.2%)	12 (57.1%)	
Duration of Illness (Median (Minimum-Maximum))	4,00(1-5)	3,00(1-5)	0.078 <sup>b</sup>
Body Mass Index in the first week receiving risperidone with a fixed dose of 6 mg (Mean $\pm$ SD)	22.50 $\pm$ 1.30	21.64 $\pm$ 1.57	0.061 <sup>a</sup>
Onset of Illness {Median(Minimum-Maximum)}	33.00(24-35)	33.00(23-35)	0.759 <sup>b</sup>
Frequency of Illness			
$\leq 2$ times of Illness	21 (100%)	18 (85,71%)	0.232 <sup>d</sup>
3-5 times of Illness	-	3 (14,29%)	
$> 5$ times of Illness	-	-	
Socioeconomic Level			
Lower class	17 (80,95%)	16 (76,19%)	1.000 <sup>d</sup>
Middle class	4 (14,51%)	5 (23,81%)	
High class	-	-	
Insight			
Insight I	2 (9,5%)	11 (52,4%)	0.003 <sup>c</sup>
Insight II	19 (90,5%)	10 (47,6%)	
PANSS Total Score in the first week receiving risperidone with a fixed dose of 6 mg	99.10 $\pm$ 9.88	104.19 $\pm$ 12.38	0.148 <sup>a</sup>

<sup>a</sup>Independent T-Test; <sup>b</sup>Mann-Whitney U; <sup>c</sup>Chi Square Test with Yates correction; <sup>d</sup>Fisher Test.

As seen in Table 3, the mean PANSS total score in the Javanese subjects was  $42.43 \pm 9.05$ , whereas the mean PANSS total score in the Batakese subjects was  $49.76 \pm 12.65$ . Based on the study results, there was a difference in the PANSS total scores of men with schizophrenia between the Batakese and Javanese ethnic groups who had received 6 mg of risperidone treatment for 6 weeks ( $p = 0.037$ ).

**Table 3: The PANSS Total Score of Men with Schizophrenia from Batakese and Javanese Ethnic Groups**

	Javanese Men with Schizophrenia (n = 21)	Batakese Men with Schizophrenia (n = 21)	P
PANSS total score in the sixth week after receiving 6 mg of risperidone (mean $\pm$ SD)	42.43 $\pm$ 9.05	49.76 $\pm$ 12.65	0.037*

\*Independent T-Test.

## Discussion

In this study, the median (minimum-maximum) onset of the attack of the Javanese and Batakese subjects was 33.00 (24-35) and 33.00 (23-

35) years, respectively. This is consistent with the statement of the American Psychiatric Association that the psychotic picture of schizophrenia usually appears between the late teens and middle thirties; the onset before adolescence is rare. The peak age during onset for the first psychotic episode was in the early to middle twenties for men and in the late twenties for women. The onset may be sudden or dangerous, but most individuals show a slow and gradual development of various clinically significant signs and symptoms. In a cohort study conducted in Melbourne by Gogtay in subjects at high risk for schizophrenia, the average age of onset was  $19 \pm 3.5$  years and occurred in 58% of men. In the Buoli study, it was stated that the mean onset age of schizophrenia was  $23.22 \pm 5.97$  years [20], [21].

Based on the education level of the Javanese subjects, 7 subjects (33.3%) graduated middle school, 13 subjects (61.9%) graduated high school, and 1 subject (4.8%) graduated university. Similarly, the education level in the Batakese subjects showed that 8 subjects (38.1%) graduated middle school, 12 subjects (57.1%) graduated high school, and 1 subject (4.8%) graduated university. Most of the subjects for both ethnic groups in this study were at the high school level. This is consistent with the findings of the Arnold study. Similarly, Huang found that most of the schizophrenic patients were in the high school level with 39.5% ( $n = 43$ ) while 34.7% ( $n = 38$ ) was in the university level and 25.7% ( $n = 28$ ) was in the middle school level [22], [23].

In this study, the median (minimum-maximum) duration of illness of the Javanese and Batakese subjects was 4.00 (1-5) years and 3.00 (1-5) years, respectively. The mean body mass index of the Javanese subjects was  $22.50 \pm 1.30$  Kg/m<sup>2</sup> while the mean body mass index of the Batakese subjects was  $21.64 \pm 1.57$  Kg/m<sup>2</sup>. Regarding the employment status, 1 Javanese subject (4.8%) was employed and 20 Javanese subjects (95.2%) were unemployed whereas 4 Batakese subjects (19%) were employed and 17 Batakese subjects (81%) were unemployed. This is by the literature [22]. Furthermore, a study by Huang and colleagues showed that there were 46 unemployed schizophrenic patients (42.2%) and 37 employed schizophrenic patients (33.9%) [22].

Based on the marital status, 9 subjects (42.9%) were married, and 12 subjects (57.1%) were not married in the Batakese ethnic group whereas 5 subjects (23.8%) were married, and 16 subjects (76.2%) were not married in the Javanese ethnic group. This is also by the findings of Arnold and colleagues regarding patients who received antipsychotics [23]. Similarly, Huang and colleagues in China reported that 61 schizophrenic patients (56%) were not married, and 23 schizophrenic patients were married (21.1%) [22].

Regarding the socioeconomic level, 17 Javanese subjects (80.95%) were in the lower class,

and 4 Javanese subjects (14.51%) were in the middle class while 16 Batakese subjects (76.19%) were in the lower class, and 5 Batakese subjects (23.81%) were in the middle class. Huang and colleagues in China found that 29 subjects (26.6%) were in the lower class, 62 subjects (56.9%) were in the middle class, and 18 subjects (16.5%) were in the high class among schizophrenic patients [22]. The present study also found that the mean PANSS total score of Javanese subjects was  $42.43 \pm 9.05$  while the mean PANSS total score of Batakese subjects was  $49.76 \pm 12.65$ . Thus, there was a significant difference in the PANSS total score of men with schizophrenia receiving 6 mg of risperidone for 6 weeks between the Javanese and Batakese ethnic groups ( $p = 0.037$ ). This is consistent with a pilot study conducted by Frackiewicz and colleagues in the United States which found that there was a significant difference in the PANSS score between 10 Hispanic schizophrenic in-patients and 8 non-Hispanic schizophrenic in-patients who received risperidone ( $p < 0.02$ ) [7].

One of the limitations in the current study was that this study did not examine the Batakese ethnicity more specifically because this ethnicity consists of five sub-ethnicities. In addition, the study also did not explore the cause of the difference in the PANSS total scores between the Javanese and Batakese subjects in the sixth week after receiving a fixed dose of 6 mg of risperidone, whether it was due to biological factors such as genetic influencing drug pharmacokinetics and pharmacodynamics, environmental factors, or cultural factors. The subjects in this study did not have the same belief because belief is a cultural factor that might influence the effectiveness or adherence to drug therapy [19].

In conclusion, the mean PANSS total score of the Javanese men with schizophrenia was  $42.43 \pm 9.05$  while the mean PANSS total score of the Batakese men with schizophrenia was  $49.76 \pm 12.65$ . Thus, there was a difference in the PANSS total score between Batakese and Javanese men with schizophrenia in which Javanese patients were more responsive to the 6 mg of risperidone treatment for 6 weeks ( $p = 0.037$ ), so the research hypothesis was accepted.

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