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Comparison between Interleukin-2 Serum Levels and Positive and Negative Syndrome Scale Scores of Schizophrenia Patients that Received Haloperidol with Risperidone Therapy

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Abstract

BACKGROUND: There is a possibility of interleukin-2 (IL-2) being involved in the pathophysiology of Schizophrenia. The increase of IL-2 levels has been discovered in the serum of schizophrenic patients in earlier studies. An amount of antipsychotic has been associated with the decrease of IL-2.

AIM: Therefore, this study was intended to compare the serum IL-2 levels of schizophrenic patients who received Haloperidol therapy with patients who received Risperidone as well as examine the relationship between serum IL-2 levels with the positive and negative syndrome scale (PANSS) score of schizophrenic patients receiving Haloperidol and Risperidone therapy.

METHODS: This study is an observational study with a prospective cohort design consisting of 36 patients who have met the Diagnostic and Statistical Manual of Mental Disorders 5th Edition criteria for Schizophrenic patients who did not take antipsychotic drugs for 2 weeks and were hospitalized at the Special Hospital of South Sulawesi Province. Afterwards, the patients were grouped into two groups, where each group consisted of 18 people, namely, the group of patients who received Haloperidol and the group of patients who received Risperidone, and then were furtherly evaluated until the 4th week. The sample examination method used was enzyme-linked immunosorbent assay to see the blood serum IL-2 levels. Clinical symptoms of Schizophrenia were assessed using the PANSS score.

RESULTS: The study showed that serum IL-2 levels decreased at the 4th week after conducting antipsychotic therapy among both groups. The decrease in PANSS scores in the Risperidone group was greater compared to the Haloperidol group at week 3 and week 4. In the serum IL-2 levels difference of the group who received Risperidone therapy, the decrease was greater than those receiving Haloperidol therapy (3.72 ± 1.30 ng/ml vs. 2.43 ± 1.39 ng/ml, p = 0.008). In addition, based on the correlation test, no significant correlation was present between the difference in the total PANSS score and the difference in the serum IL-2 levels within the Haloperidol group (p = 0.059, r = 0.453) and the Risperidone group (p = 0.518, r = 0.113). Schizophrenic patients have higher serum IL-2 levels than healthy people. Schizophrenic patients who received antipsychotics for 4 weeks experienced a decrease in serum IL-2 levels. Risperidone administration had a higher decrease in serum IL-2 levels than Haloperidol.

CONCLUSION: Changes in serum IL-2 levels as a consideration of one of the Biomarkers are still needed for further evaluation. The therapeutic role of Haloperidol and Risperidone can be attributed as anti-inflammatory in Schizophrenia but cannot be attributed to improvement in the psychopathological status of Schizophrenic patients.

Introduction

The World Health Organization has reported that 20 million people worldwide suffer schizophrenia [1]. Ministry of the Health Republic of Indonesia indicated that the prevalence of schizophrenia/psychosis in Indonesia was 7% per 1000 households. This implies that out of 1000 households, there are 70 households that have household members with schizophrenia/severe psychosis [2].

Schizophrenia is a multifactorial disease, with contributions from multiple genetic, epigenetic, and environmental susceptibility factors. Although the exact cause of schizophrenia is still unknown, the possible involvement of the immune response system in the pathogenesis of schizophrenia has now been identified [3]. Immunology dysfunction has been reported by several authors in schizophrenic patients and despite conflicting results, most independent studies have focused on plasma levels or the production of mitogen-stimulated cytokines, such as interferon (IFN)-ɣ, interleukin (IL)-2, IL-6, and tumor necrosis factor (TNF)-α in peripheral blood mononuclear cells and Th1/Th2 imbalance [4]. Several studies have demonstrated a potential role for IL-2 in schizophrenia, with most studies reporting altered peripheral IL-2 levels when compared to healthy controls [5], [6].

Based on studies, Quetiapine, risperidone, clozapine, and haloperidol have been associated

with decreased IL-2 production [7], [8]. One study in Iran discovered that IFN-γ and IL-2 levels were significantly lower in participants after treatment compared to participants before treatment and healthy controls [9]. Based on the research of Zhang *et al*. [7] in Beijing, 78 patients were randomized to the risperidone group with the haloperidol group. Results that were acquired indicated a significant difference in serum IL-2 concentrations of healthy controls and schizophrenic patients before and after treatment. In addition, a significant correlation was found between the rate of reduction in the total score of positive and negative syndrome scale (PANSS) and changes in IL-2 concentrations before and after treatment [7].

The findings from the study of Zhang *et al*. [7] showed that risperidone and haloperidol are able to reduce the increase of the serum IL-2 in schizophrenia, with no significant difference between the two medicines after 12 weeks of treatment. Meanwhile, there is recent research about the ability of antipsychotic medicines in affecting activated microglia. That study identified that several studies showed that antipsychotic medicines significantly decrease the secretion TNF-α, nitric oxide, IL-1β, and IL-2 from activated microglia. In addition, several medicines were discovered to have a stronger inhibitory effect, for example, risperidone, which inhibits the secretion of some cytokines from activated microglia more than haloperidol, and indication of a specific effect of clozapine have also been reported [10].

Based on the above explanation, the researcher was interested in conducting further research on changes in inflammatory cytokines, such as IL-2 that are associated with PANSS score in schizophrenic patients, who received typical antipsychotic treatment (haloperidol) compared to atypical antipsychotics (risperidone) in Indonesia.

Materials and Methods

Research design

An observational analytical research using a prospective cohort design was utilized in this study. From June to August 2021, the research was conducted at the Special Hospital of South Sulawesi Province (Indonesia). It was approved by the Ethics Committee of Universitas Hasanuddin (442/UN4.6.4.5.31/PP36/2021).

Subject

The subjects were patients diagnosed with schizophrenia according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders 5th Edition. In addition, patients with treatment for the first time were chosen or at least 2 weeks without taking antipsychotics, aged between 20 and 50 years, and had an illness duration of ≤5 years. Subjects were excluded from the study if they met one or more of the following criteria: alcohol and substance abuse or dependence, chronic disease (infectious disease, hypertension, diabetes mellitus, and autoimmune disease) other than schizophrenia, heavy smoker (15 cigarettes per day), obesity (mass index 30 kg/m^2), and treatment with anti-inflammatory or immunosuppressive drugs that could interfere with serum IL-2 levels were excluded from the study. A total of 36 patients who met the criteria were recruited in the study. They were divided into two groups, in particular, the group who received treatment with Haloperidol therapy 15 mg/day (18 people) and the group who received Risperidone therapy 4 mg/day (18 people). Patients after calming down PANSS EC 15 can be given oral therapy according to the Treatment of Schizophrenia Patients at the Special Regional Hospital of South Sulawesi Province. Patients who are usually admitted for the first time and are young are given Risperidone therapy while patients who have been hospitalized and with a history of previous Haloperidol treatment are still given Haloperidol. Meanwhile, the healthy group was consisted of 10 people. The participants were assessed through semi-structured psychiatric interviews by experienced psychiatrists to rule out psychiatric disorders. Informed consent was obtained from all participants.

Procedure

The procedure for drawing blood was conducted for the Haloperidol group and Risperidone group that each consisted of 18 people. Afterwards the approval of the study was requested, then a physical examination was performed, as well as vital signs and body mass index examination by measuring the height and weight in each group. In the case of patients with restless conditions, the patients were first injected with 5 mg of Haloperidol (IM) and the patients had to be under the supervision of medical personnel and then grouped into two groups, namely who received Haloperidol therapy and the group who received Risperidone. Furthermore, blood draw was carried out in the ER of the Regional Specialty Hospital of South Sulawesi Province. Afterwards, the assessment of the PANSS score was carried out in the 1st, 2nd, 3rd, and 4th week. After the 4th week, blood was drawn again. The steps for taking blood serum began with the patient of fasting for 10–12 h before blood collection. A blood specimen was taken as much as 3 cc in the median cubital vein using a phlebotomy technique with a vacuum and inserted into a closed tube. The blood specimen was centrifuged to obtain blood plasma and then stored in frozen conditions at -70°C until enzyme-linked immunosorbent assay (ELISA) examination was performed. IL-2 levels were measured in the form of serum which was duplicated using the ELISA method from the “Human IL-2 ELISA Kit. Size 96 Wells

Brand Bioassay TL." Measurement of the severity of psychopathology in schizophrenia was performed using the PANSS developed by Kay [11]. Assessments were carried out by experienced psychiatrists.

Statistical analysis

Statistical Package for Social Sciences Version 20.0. Descriptive statistics were performed to show the demographic characteristics of the subjects. The Kolmogorov-Smirnov or the Shapiro-Wilk test was used to test the homogeneity of the normality of the data. Then, the significance test was carried out with Paired t-test, independent t-test, and Mann-Whitney Test. While the Spearman correlation test was used to evaluate the relationship between the difference in serum IL-2 levels and the difference in the PANSS scores. The correlation coefficient (r) was said to be "weak" if it was between 0 and 0.25, "moderate" if it was between 0.26 and 0.50, "strong" if it was between 0.51 and 0.75 and "very strong" if it was between 0.76 and 1.00. The level of statistical significance was accepted as $p < 0.05$.

Results

This study attained a group with 18 people who received Haloperidol therapy and a group with 18 people who received Risperidone therapy. These subjects followed the study for up to 4 weeks. Characteristics of research subjects obtained from the questionnaire can be seen in Table 1.

Table 1: Sociodemographic characteristics

Variable	Haloperidol therapy schizophrenia n = 18 (%)	Risperidone therapy schizophrenia n = 18 (%)	p
Age (mean ± SD)	37.44 ± 5.8	33.17 ± 7.4	0.063
Gender			0.121
Male	16 (88.9)	11 (61.1)	
Female	2 (11.1)	7 (38.9)	
Education			0.291
No education	2 (11.1)	3 (16.7)	
Elementary	6 (33.3)	8 (44.4)	
Middle School	4 (22.2)	2 (11.1)	
High School	6 (33.3)	3 (16.7)	
Undergraduate	0 (0)	2 (11.1)	
Job			0.516
Unemployed	10 (55.6)	13 (72.2)	
Farmer	5 (27.8)	3 (16.7)	
Trader	2 (11.1)	2 (11.1)	
Laborer	1 (5.6)	0 (0)	
Marital status			0.147
Not married	9 (50)	13 (72.2)	
Widow/Widower	2 (11.1)	0 (0)	
Illness duration (mean ± SD)	4.28 ± 1.44	3.67 ± 1.84	0.277

*Significant p < 0.05 (Chi-square test, Independent t-test).

Table 1 showed the characteristics of schizophrenia and healthy subjects. Data are expressed as amount and the percentage. Serum IL-2 levels in the healthy control group and Baseline IL-2 levels in the group that received Haloperidol therapy and the group that received Risperidone therapy can be seen in Figure 1. Research subjects who received treatment with Haloperidol as much as 15 mg/day and Risperidone as much as 4 mg/day were measured for serum IL-2 levels in the initial week of hospitalization (baseline) and at week 4. The measurement results are shown in Table 2.

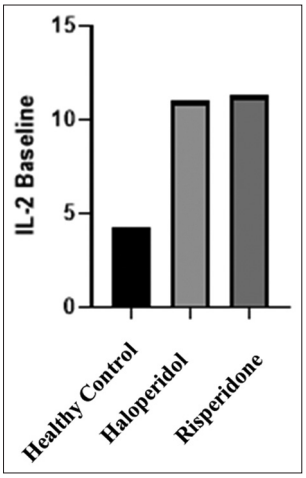

Figure 1: Baseline interleukin-2 serum levels of the healthy control group, Haloperidol group and Risperidone group with unit value ng/ml

Table 2: Comparison of serum levels of baseline IL-2 and Week 4 in the schizophrenia group treated with haloperidol and the schizophrenia group tested with risperidone

Treatment	Il-2 Serum (Baseline) Mean ± SD (ng/ml)	Il-2 Serum, p (Week-4) Mean±SD (ng/ml)	p
Haloperidol Therapy Schizophrenia	11.01 ± 2.33	8.57 ± 1.93	0.001*
Risperidone Therapy Schizophrenia	11.29 ± 1.51	7.57 ± 1.19	0.001*

*Significant p < 0.05 (Paired t-test), IL: Interleukin.

Table 2 showed the comparison of serum levels baseline IL-2 and week 4 for the schizophrenic patients that received Haloperidol therapy and schizophrenic patients that received Risperidone using the Paired t-test. The data are expressed as mean ± SD. The comparison of serum IL-2 levels for the Schizophrenia group who received Haloperidol therapy and the group who received Risperidone can be seen in Figure 2.

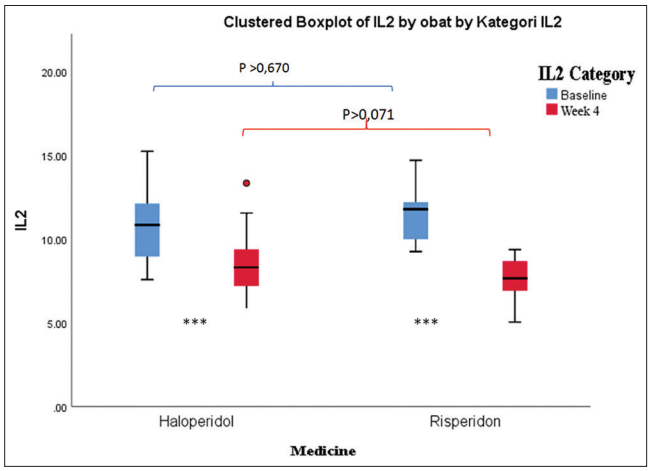

Figure 2: Comparison of serum interleukin-2 levels for the schizophrenia group who received Haloperidol therapy and the group who received risperidone

Figure 2 displays the comparison of serum IL-2 levels in the Schizophrenia group treated with Haloperidol and the Schizophrenia group treated with Risperidone. Both groups for Baseline and week 4 experienced a significant decrease using the Paired t-test ***p ≤ 0.001. In the baseline comparison between the Haloperidol group and the Risperidone group, it was not significant where p ≥ 0.670. The comparison in week 4 of the Haloperidol group with Risperidone group was also not significant (p ≥ 0.071). This study compared the value of the difference in the serum IL-2 levels at baseline and week 4, which can be seen in Table 3.

Table 3: Comparison of differences in serum IL-2 levels in the schizophrenia group with haloperidol therapy and the schizophrenia group with risperidone therapy

Schizoprhenia with haloperidol therapy	Schizophrenia with risperidone therapy
n = 18	n = 18
(ng/ml)	(ng/ml)
Mean ± SD	Mean ± SDp
Difference of serum IL-2 (Baseline and Week 4)	2.43 ± 1,39 3.72 ± 1.30 0.008*

*Significant p < 0.05 (Independent t-test), IL: Interleukin.

Table 3 showed the comparison of the value of the difference in serum IL-2 levels at baseline and week 4 in schizophrenic patients receiving Haloperidol therapy and those receiving Risperidone using the Independent t-test. Data are expressed as mean ± SD. The comparison of the PANSS scores in the group of subjects who received Haloperidol and the group who received Risperidone was measured during baseline, week 1, week 2, week 3, and week 4. The results can be shown in Table 4.

Table 4: Comparison of PANSS scores in the Schizophrenia group with haloperidol therapy and the schizophrenia group with risperidone therapy

Variable	Schizophrenia with haloperidol therapy n = 18		Schizophrenia with risperidone therapy n = 18		p
	Median	Mean ± SD	Median	Mean ± SD	
PANSS baseline	107.50	106.56 ± 8.169	110.50	108.06 ± 7.658	0.523
PANSS week 1	89.00	88.72 ± 6.424	88.50	87.61 ± 9.243	0.678
PANSS week 2	74.50	72.06 ± 7.360	70	71.39 ± 8.346	0.801
PANSS week 3	61	61.17 ± 6.600	55	56.72 ± 5.778	0.037*
PANSS week 4	51	51.22 ± 5.776	44	46.26 ± 4.561	0.004*

*Significant p < 0.05 (Independent t-test, Mann Whitney test), PANSS: Positive and negative syndrome scale

Table 4 showed the comparison of PANNS scores using the Independent T statistical test on the PANNS scores for baseline, week 1, and week 2. Meanwhile, the PANSS score for week 3 and week 4 was not homogenously distributed, thus the Mann-Whitney test was utilized. Data are expressed as Median and Mean ± SD. The relationship between the difference in serum IL-2 levels with the difference value in the total PANSS scores of the groups can be shown in Table 5.

Table 5: Correlation between the difference value in serum IL-2 levels and the difference value in PANSS scores

Variable	Schizophrenia group with haloperidol therapy n = 18		Schizophrenia group with risperidone therapy n = 18	
	Difference value of PANSS			
	R	p	R	p
IL-2 Difference	0.453	0.059	0.113	0.518

Significant *p < 0.05; **p < 0.01; ***p < 0.001 (spearman's test), r=correlation strength 0.1–0.3 weak; 0.4–0.6 moderate; 0.7–0.9 strong, PANSS: Positive and negative syndrome scale, IL: Interleukin.

Table 4 showed the relationship between the difference in serum IL-2 levels and the difference in PANSS scores in the Haloperidol group and the Risperidone group. Spearman correlation test was used to determine the strength of the correlation (r) and p-value.

Discussion

The results of this study showed that the serum IL-2 level (baseline) of patients with acute-phase schizophrenia and acute exacerbations in the Haloperidol group was 11.01 ng/ml, while the risperidone group was 11.29 ng/ml. When compared to the healthy control blood levels of 4.26 ng/ml, both groups showed an increase. After receiving treatment for 4 weeks with a dosage of Haloperidol 15 mg/day and Risperidone 4 mg/day, there was a decrease in serum IL-2 levels in both the Haloperidol group as much as 8.57 ng/ml and the Risperidone group had a total of 7.57 ng/ml. In both groups, a significant decrease was present, where p ≤ 0.001. This study is in line with previous studies about Quetiapine, risperidone, clozapine, and haloperidol that have been associated with the decreased production of IL-2 [7], [8]. Based on the Iranian study, the groups of the study were consisted of 24 schizophrenic patients and 24 healthy controls. Symptoms of schizophrenia were assessed on the PANSS and treated with risperidone. IFN-γ and IL-2 levels were significantly lower in participants after treatment compared to participants before treatment and healthy controls [9]. In Indonesia, the results are also in line with this study where there is a significant difference in serum IL-2 levels in untreated and treated Batak people with schizophrenia and healthy controls with the mean and standard deviation of each group being 10.34 ± 2.24 ng/ml, 5.53 ± 1.05 ng/ml and 3.48 ± 0.61 ng/ml [12].

There was a decrease in serum IL-2 levels in the fourth week after treatment with Haloperidol and Risperidone antipsychotics; however, no significant difference was present between the two groups, where p ≥ 0.071. This study is in accordance to the research of Zhang *et al*. [7] conducted in Beijing, where 78 patients were randomized to either the risperidone group (n = 41) or to the haloperidol group (n = 37). As a result, no significant difference was found in the reduction of serum IL-2 concentrations between risperidone and haloperidol treatment. However, there was a tendency in the decrease of IL-2 levels for the Risperidone therapy group, thus the difference in serum IL-2 levels in the initial week and fourth week were also examined, with the mean value of 2.43 ng/ml for the Haloperidol group and the 3.72 ng/ml for the Risperidone group (there was a statistically significant difference between

the two groups with p ≤ 0.008). This is in accordance with research on the ability of antipsychotic medicines to affect activated microglia. The review identified several studies showing that antipsychotic medicines significantly reduce the secretion of TNF-, nitric oxide, IL-1β, and IL-2 from activated microglia. In addition, several medicines were found to have a stronger inhibitory effect, for example, risperidone, which inhibits the secretion of some cytokines from activated microglia more than haloperidol, and indications of a specific effect of clozapine have also been reported [10]. It is possible that there are differences from previous research in terms of methods, such as in the study of Zang *et al*. [13], samples were from chronic Schizophrenia patients, whereas the samples from this study were from patients with acute schizophrenia and acute exacerbations.

According to a certain theory, there is a possibility of this effect on different medicine receptors in the two antipsychotics. Typical antipsychotics, such as haloperidol, have strong antagonism of dopamine D2 receptors, whereas atypical antipsychotics, such as risperidone, have weaker affinity and shorter antagonism than D2 receptors. However, advances in this area have shown that serotonin 5-HT2A and 5-HT2C receptors are also major targets for antipsychotics, along with muscarinic receptors, H1 serotonin receptor antagonism, D3 dopamine receptor antagonism. Microglia have receptors that are classic targets for antipsychotics, such as D2, glutamate, or 5-HT2A receptors. For example, it is known that metabotropic glutamate receptors (mGluRs) have group-dependent functions, where group 2 mGluRs mediate neurotoxicity and group 3 mGluRs mediate neuroprotective actions of microglia. Likewise, stimulating microglia with serotonin causes exosome secretion, a reaction that can impact functional signaling between neurons and microglia. These two examples prove that neurotransmitters can have a profound impact on microglia and that any medicine that affects this system does it in complex ways that affect neurons and glial cells [14].

PANSS is commonly used in clinical practice to measure the severity of psychopathological symptoms in patients with schizophrenia [11]. In this study, the initial PANSS score of Schizophrenic patients in the haloperidol group amounted to a mean of 106.56 and the Risperidone group with a mean of 108.06. After the third and fourth weeks, there was a decrease (there was a statistically significant difference with p < 0.05). According to a previous study [15], the median time to respond in this group of patients was nearly 3 weeks. Kaplan–Meier estimated the median time to respond was 41.0 days with risperidone and 38.6 days with haloperidol [16]. The significant decrease in both groups was probably due to the ability of Risperidone therapy reducing negative symptoms. This is in accordance with a study conducted by Tamnakar *et al*. in Nepal, who found that there was a significant difference in the benefits between risperidone and haloperidol in total, negative, and the General Psychopathology score subscale. Thus, it can be concluded that risperidone has a faster onset of action than haloperidol and a greater tendency to weaken negative symptoms early on. This makes psychosocial rehabilitation achievable from the start [17].

A correlation between the improvement in clinical symptoms of Schizophrenia using the PANSS score was also examined by looking at the difference in the PANSS scores at the beginning and the fourth week with the difference in serum IL-2 levels at the beginning and the fourth week in the two groups. With the Spearman correlation test in the Haloperidol group, it was revealed that there was no correlation (p > 0.059), similar to the Risperidone therapy group (p > 0.518). However, there are several studies that have found a correlation between IL-2 and PANSS scores [13], [18], [19]. Nonetheless, this study is in line with previous studies that showed no significant relationship between psychopathology scores (total, positive, and negative scores) and serum IL-2 concentrations before and after treatment [9]. Cytokine expression can be influenced by environmental factors and interactions between cytokine genes [20]. The role of genetic polymorphisms can assist in the production of cytokines. In addition, other variables were examined, such as duration of illness, weight gain, metabolic disorders, obesity, age, sex, smoking, alcohol, and drug use, which could potentially be involved in cytokine changes [21], [22], [23]. The possibility of many other factors that influence the decrease in serum IL-2 levels of Schizophrenic patients, especially for those who received antipsychotic treatment, were also considered, such as in the terms of the side effects of antipsychotics, where anemia can be one of the effects. A previous study conducted by Wasti *et al*. [24] regarding the morphological and biochemical assessments clearly described the presence of iron deficiency anemia in schizophrenic patients treated with antipsychotic medicines (haloperidol/clozapine). Schizophrenic patients after antipsychotic treatment can be explained by the following two hypotheses: First, antipsychotic administration may modulate anemia in schizophrenia. Second, the iron levels observed in schizophrenia may be affected by antipsychotic treatment [24]. The association of iron with the immune system according to previous studies has been associated with a decrease in IL-2 levels. It is explained that the process of the decreasing Protein Kinase C (PKC) activity and or its translocation is one of the mechanisms due to iron deficiency in the process of T cell function and activation. Decreased PKC activation also reduces the rate of phosphorylation of various growth factors, including the IL-2 receptor [25]. The mechanism of impaired immune function in iron deficiency is thought to be multifactorial, including impaired DNA synthesis due to impaired ribonucleotide reductase enzyme activity,

decreased production of ILs such as IL-2. IL-2 is an IL that is important for communication between a subset of lymphocytes and natural killer cells [26], [27]. This may be further investigated regarding the anemia side effect by conducting blood tests. Giving antipsychotics can also affect the side effects of tardive dyskinesia, which can affect the decrease in IL-2 levels [28]. It is essential to examine this possible side effect profile that affects the production of cytokines, especially IL-2.

The results of this study also displayed a positive correlation with moderate strength between the difference in serum IL-2 levels and the difference in PANSS scores in the Haloperidol group, although not significantly with $p \geq 0.05$ there was no correlation. However, we believe that Haloperidol's correlation strength is better because the sample of this study had many Schizophrenic patients with positive subscale PANSS scores, in which IL-2 may contribute to the pathophysiology of schizophrenia, especially to positive symptoms. Several studies have shown that both risperidone and haloperidol have an effect in reducing positive symptoms [13], due to the strong D2 receptor antagonism receptor affinity for Haloperidol compared to Risperidone [29], thus it is considered that the possibility is better on the reduction in positive symptoms which may be related to the effect of the medicine at the same serum IL-2 concentration.

Thus, we believe that there is a possibility that the decrease in IL-2 levels in Schizophrenic patients after antipsychotic treatment does not directly correlate with the PANSS score, related to side effects and other confounding variables that we did not examine further in our study. Due to the limitations of this study, it may be necessary to conduct further research related to the association between antipsychotic side effects and the inflammatory process and with a larger sample size, longer duration by looking at the confounding variables of this study.

Therefore, the writers of this study believe that there is a possibility that the decrease in IL-2 levels in Schizophrenic patients after antipsychotic treatment does not directly correlate with the PANSS score, related to side effects and other confounding variables that were not examined further in this study. Due to the limitations of this study, it may be necessary to conduct further research related to the association between antipsychotic side effects and the inflammatory process and with a larger sample size as well as a longer duration by looking at the confounding variables of this study.

Conclusion

Schizophrenia to changes in the immune response cannot be determined as a cause-and-effect relationship, because schizophrenia is a mental disorder with various causes. Changes in serum IL-2 levels as a consideration of one of the Biomarkers are still needed for further evaluation. The therapeutic role of Haloperidol and Risperidone can be attributed as anti-inflammatory in Schizophrenia but cannot be attributed to improvement in the psychopathological status of Schizophrenic patients.

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