



EFFECT OF VOCATIONAL THERAPY ON THE IMPROVEMENT OF COGNITIVE FUNCTION AND INTERLEUKIN LEVELS 17 IN SCHIZOPHRENIC PATIENTS RECEIVING RISPERIDONE

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Abstract

Background – Schizophrenia is a severe mental disorder in which chronic inflammation is one of the causes. Schizophrenia can affect the cognitive function of sufferers, therefore the management must be comprehensive by combining pharmacological and non-pharmacological therapies. Risperidone therapy combined with vocational therapy was thought could improve cognitive function in schizophrenic patients and was associated with changes in IL-17 levels. **Aim** – To determine the effect of vocational therapy in improving cognitive function and IL-17 levels in schizophrenic patients receiving risperidone.

Method – Pre and post-test experimental analysis with non-random group selection. The number of subjects were 28 schizophrenic patients who were evenly divided into 2 groups, namely the treatment group receiving risperidone 2-6 mg/day with 8 weeks vocational therapy and the control group receiving only 2-6 mg risperidone/day. MoCA-Ina was used to measure the cognitive function and the levels of IL-17. Comparison and correlation tests were performed between groups.

Results – Vocational therapy had an effect on improving cognitive function in both groups ($p < 0.000$). However, in the treatment group who received a combination of risperidone 2-6 mg/day and 8 weeks of vocational therapy had a better result.

Conclusion – Vocational therapy for 8 weeks with by risperidone therapy 2-6 mg/day could improve cognitive function in schizophrenic patients. Vocational therapy for 8 weeks did not affect IL-17 levels. There is no correlation between the improvement of cognitive function in schizophrenic object with changes in IL-17 levels experienced.

Keywords Schizophrenia, Vocational Therapy, Cognitive Function, IL-17 and Risperidone.

Introduction

World Health Organization (WHO) in 2018 stated that around 23 million people worldwide suffer from schizophrenia. The prevalence of schizophrenia in Indonesia is increasing every year. Based on the 2018 Basic Health Research data, 6.7 per 1000 households suffered from schizophrenia, which previously was 1.3 per 1000 households in 2013.

In terminology, schizophrenia is a severe mental disorder that is chronic in nature, characterized by distortion of reality (delusions and hallucinations), disorganization (speech or behavior), psychomotor poverty, impaired cognitive function and affective disorders [1]. The etiology is multifactorial, such as; genetic, fetomaternal events, environmental stressors, inflammation, immune system disorders and their complex interactions with the central nervous system, imbalance between helper T cells and the cytokines they produce [2 - 7]. The etiology of schizophrenia is complex, so its treatment must be comprehensive. Therefore, the treatment of this disorder must be comprehensive in nature that combines pharmacotherapy and non-pharmacotherapeutic approaches (psychosocial interventions) [8]. One of the psychosocial interventions is vocational therapy [9]. Vocational therapy showed significant improvement in cognitive function and negative symptoms [10]

Research on the effect of vocational therapy on cognitive function in schizophrenic patients and its relationship to levels of the blood inflammatory marker IL-17 has never been done. Because on literature review by research, studies that has been done was only related to the effect of vocational therapy on improving cognitive function in schizophrenic patients. This study has several novelist values, such as the type of vocational therapy given which was different from previous studies [11 – 13]. In this study, the vocational therapy was carried in the psychosocial rehabilitation installation of the Dadi Hospital in South Sulawesi Province such as hydroponic plantations, making salted eggs, carpentry (making wooden chairs), fashion, catering and sewing where this type of therapy is adjusted to the patient's interests so that the patient undergoes a therapy session without a burden. Another novelist value is that the subjects in this study were stable patients, while in others study, the first episode of schizophrenia and chronic patients. The antipsychotics consumed by the subjects in this study were also different from other studies. In other, they used typical antipsychotics, atypical and even both, while in this study all research subjects used atypical antipsychotics (risperidone 26 mg/day). The measuring instrument used in assessing cognitive function is also different from previous studies. In this study, Montreal Cognitive Assessment (MoCA-Ina) was used while the previous study used the Positive and Negative Syndrome Scale (PANSS) and Brief Psychiatry Rating Scale/BPRS. The measured schizophrenia biomarkers are also different from the biomarkers in other studies. In other studies, several biomarkers such as IL-6, TNF- and IL-10 [14 – 16]. Based on these novelist values, the researcher conducted this research in Indonesia, especially Makassar.

Material and Methods

Subjects

The subjects in this study were all schizophrenic male patients treated at the Dadi Regional Special Hospital, South Sulawesi Province who met the inclusion criteria. Inclusion criteria were male patients diagnosed with schizophrenia according to DSM-V and PPDGJ III, patients aged 20-45 years, able and willing to participate in vocational therapy sessions, ineated with risperidone 2-6 mg/day, the family agreed to join the vocational therapy session. Exclusion criteria: having organic comorbidities, history of drug atured and using anti-inflammatory drugs and antibiotics. Samples were dropped out when not regularly attending vocational therapy sessions, irregularly taking risperidone, research subjects and families refused to continue the study and the research subject died. Blood samples were obtained from subjects in the morning (around 08.00 AM). Serum was separated, collected and stored at -80°C before use. The concentration of IL-17 was measured in the serum of 1subjects using the EnzymeLinked Immunosorbent Assay (ELISA) method, according to the manufacturer's instructions. Values are expressed as pg/mL.

Procedure

Every patient who met the criteria for schizophrenia according to DSM-V and PPDGJ III, and met the inclusion criteria in the study group was recorded and a history of past illness was taken. The researcher then explained to the family and research subjects about the aims and objectives of the study. If agreed, the subject will be included in the study (informed consent). The research subjects were divided into two groups (treatment group treated risperidone with vocational therapy and the control group treated with risperidone without vocational therapy). The MoCA-Ina scores were ineamered for the two groups at the beginning of the study, at week 4 and week 8. The blood levels of IL-17 in both groups were checked at the beginning of the study, at week 4 and week 8. Blood specimens were taken as 3 ml in the median cubital vein. Blood specimens were centrifuged to obtain blood serum. Serum IL-17 levels was the human IL-17 ELISA essay kit.

Statistical Analyzes

Data was analyzed instruments using the SPSS 24.0 computer program and Microsoft Excel to obtain the expected statistical results with Chi Square, Shapiro-Wilk test, homogeneity test, independent t test, Mann Whitney test, Friedman test and Spearman's test.

Research Ethics

This research, was approved by the Ethics Committee for Biomedical Research in Humans, Faculty of Medicine, Hasanuddin University. Informed consent was improvised from the subject the confidentiality was kept.

Result

Characteristics of Patients

This research was carried out in the Psychosocial Rehabilitation Room at Dadi Hospital, South Sulawesi Province in December 2021-January 2022 and the blood serum was processed at the Hasanuddin University Medical Research Center (HUMRC). The 45 research subjects who were referred to the Psychosocial Rehabilitation Room at Dadi Hospital, South Sulawesi Province for screening and assessing the subject's interest in the types of vocational therapy available. Five patients did not meet the requirements so that 40 subjects participated in the study.

There were 40 subjects in this study which were divided into 2 groups (20 from treatment group and 20 from control group). In the treatment group consisted of 7 subject who were interested in the hydroponic plantation class, 4 subject in the carpentry class and 9 subject in the salted egg class. The treatment group attended vocational therapy sessions 2 times per week according to its class for 8 weeks, while the control group did not attend vocational therapy sessions. At the end of the study, 12 subjects dropped out because the patient went home and was no longer willing to continue vocational therapy sessions so only 28 subjects remain (14 subjects in the treatment group and 14 subjects in the control group).

The demographic characteristics of the research subjects (N=28) were all male (100%). Most by aged 36-45 years (57.1%) eithen in the treatment group or the control group. Most of the research subjects came from outside the city of Makassar (85.7%) both in the treatment group and the control group. The level of education, most by junior high school (92.9% for the treatment group, 85.7% for the control group). The onset of disease variable <5 years of 57.1% in the group treatment, 78.6% in the control group and. For occupation variable almost the same between those who had occupation (53.6%) and who did not have occupation (46.4%). Likewise, the frequency of hospitalization and marital status were almost the same between 1st hospitalization (53.6%) and for 2-10 years hospitalization (46.4%) and married (46.4%) and unmarried. (53.6%). The mean age of the subjects at the time of the study were 33.21 ± 7.28 years with a p 0.097 (Mean SD, Independent t Test).

Table 1. Sociodemographic Characteristics by Frequency (N=28)

Variables	Treatment		Control		Total N		p
	N = 14	%	N = 14	%	= 28	%	
Gender Male	14	100%	14	100%	28	100%	
<i>Age (Years)</i>							
17-25	2	14,3%	3	21,4%	5	17,8%	0,309
26-35	4	28,6%	7	50,0%	11	39,3%	
36-45	8	57,1%	4	28,6%	12	42,9%	
<i>From</i>							
Makassar	2	14,3%	2	14,3%	4	14,3%	1,000
Outside Makassar	12	85,7%	12	85,7%	24	85,7%	
<i>Occupation</i>							
Working	7	50,0%	8	57,1%	15	53,6%	1,000
Not Working	7	50,0%	6	42,9%	13	46,4%	
<i>Marital Status</i>							
Married	6	42,9%	7	50,0%	13	46,4%	1,000
Not Married	8	57,1%	7	50,0%	15	53,6%	
<i>Education Level</i>							
Elementary	1	7,1%	2	14,3%	3	10,7%	1,000
Secondary	13	92,9%	12	85,7%	25	89,3%	
<i>Disease Onset</i>							
< 5 Years	8	57,1%	11	78,6%	19	67,9%	0,420
5-10 Years	6	42,9%	3	21,4%	9	32,1%	
<i>Hospital Admission</i>							
1 st Time	6	42,9%	9	64,3%	19	67,9%	0,449
2-10 Times	8	57,1%	5	35,7%	9	32,1%	

Chi Square test

Comparison The Mean Values of MoCA-Ina

Comparison the mean MoCA-Ina values in both the treatment group and the control group at baseline, week 4 and week 8.

Table 2. Comparison the Mean Values of MoCA-Ina

Group	MoCA-Ina Value			p
	Baseline	Week 4	Week 8	
Treatment	15 ± 4	19 ± 5	24 ± 5	0.000
Control	16 ± 3	18 ± 3	20 ± 3	0.000

Mean ± SD

Significant $p < 0.05$ (Friedman test)

Table 3. Comparison of Mean Values Week 8 Both Groups

Variables	Group		p
	Treatment	Control	
MoCA-Ina Baseline	15 ± 4	16 ± 3	0.462*
MoCA-Ina Week 4	19 ± 5	18 ± 3	0.221**
MoCA-Ina Week 8	24 ± 5	20 ± 3	0.026*

Mean ± SD

* Independent t test

** Mann Whitney test

Significant $p < 0.05$ (Friedman test)

In this study, the MoCA-Ina values at baseline, weeks 4 and weeks 8 both treatment and control group were normally distributed with $p = 0.000$ in both groups. This indicates that the mean value of MoCA-Ina in both the treatment group and the control group had statistical significance. More specifically, the comparison of the mean MoCA-Ina values at baseline, week 4 and week 8 for both treatment and control group were as following:

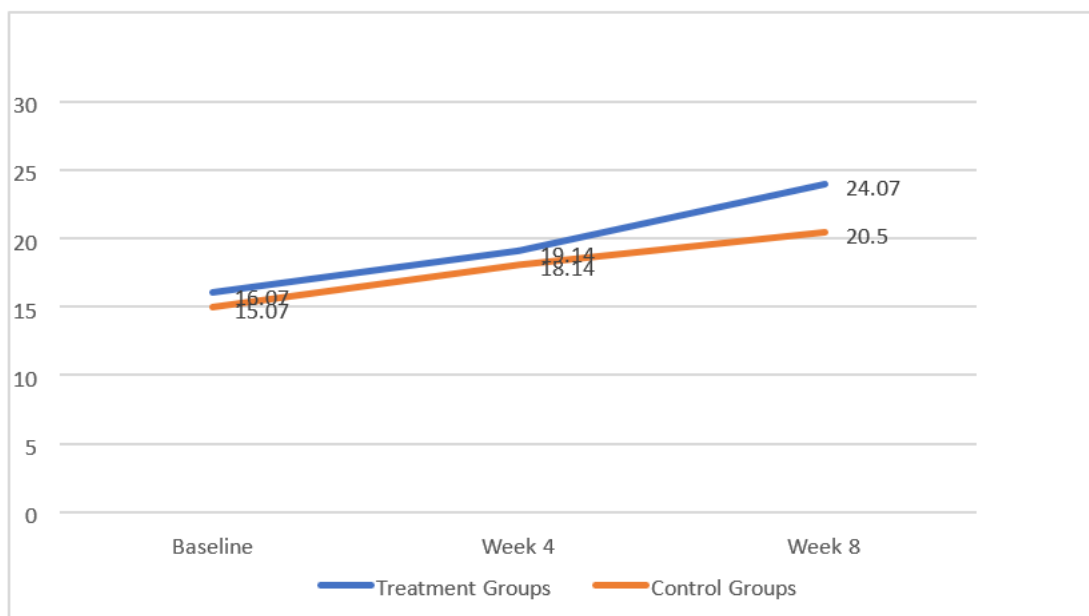


Figure 1. Comparison of Mean MoCA-Ina Values

From Figure 1, it could be seen that both the treatment of 2 group increase in the MoCAIna value from week 4 to week 8 but there was a higher increase in the treatment group with $p 0.026$ (independent t test).

Comparison The Mean Levels of Interleukin-17

Comparison the mean levels of IL-17 in both the treatment group and the control group at baseline, week 4 and week 8.

Tabel 4. Comparison the Mean Levels of Interleukin-17

Group	Blood Serum IL-17 Level			<i>p</i>
	Baseline	Week 4	Week 8	
Treatment (14)	88 ± 123	110 ± 132	99 ± 120	0.758*
Control (14)	66 ± 65	85 ± 107	77 ± 97	0.424*
Healthy Control (6)			97 ± 110	

Mean ± SD

Mann Whitney Test

*Significant $p < 0.05$ (Friedman test)

In this study, the IL-17 levels at baseline, week 4 and week 8 both treatment group and control group were normally distributed. This indicates that the mean levels of IL-17 in both the treatment group and the control group did not have statistical significance.

More specifically, the comparison of the mean levels of IL-17 at baseline, week 4 and week 8 in the study subjects, either in the treatment group or in the control group were as following:

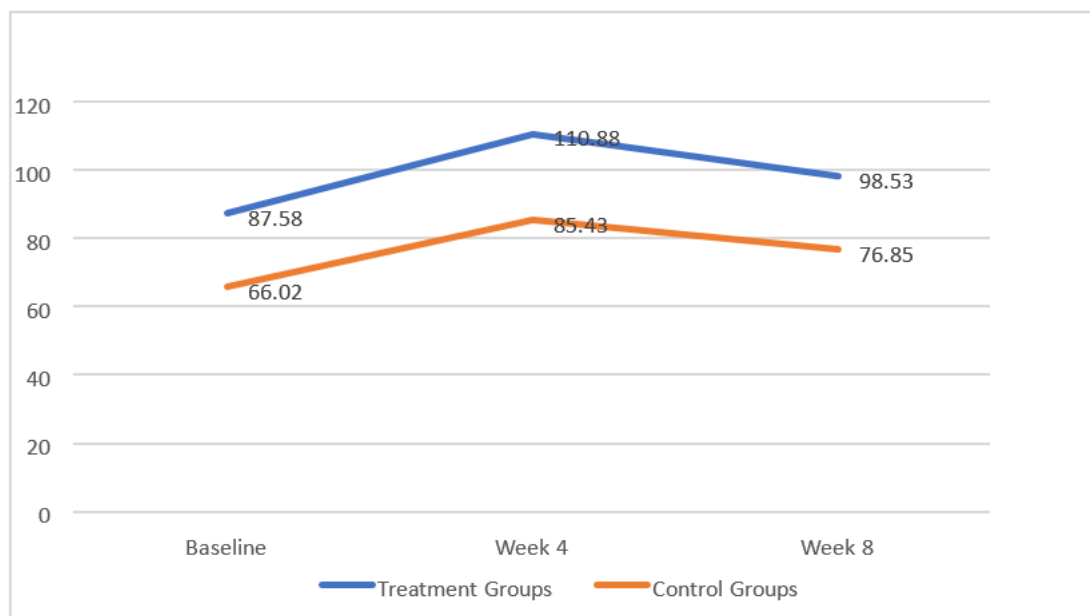


Figure 2. Comparison of the Mean Levels of Interleukin-17

From Figure 2 it could be seen that both the treatment group and the control group had on increased levels of IL-17 at 4th week but decreased at 8th week. However, the increased and the decreased of levels IL-17 in the treatment group still better then the control group.

Correlation of Cognitive Function (MoCA-Ina) and IL-17 Level

Correlation of cognitive function (MoCA-Ina) and IL-17 level in both the treatment group and the control group at baseline, week 4 and week 8.

Table 5. Correlation of Cognitive Function (MoCA-Ina) and IL-17 Level

MoCa-Ina and IL-17	Treatment		Control	
	<i>p</i> Value	<i>r</i> Value	<i>p</i> Value	<i>r</i> Value
Baseline	0,026	-0,590	0,605	0,152
Week 4	0,341	-0,275	0,808	0,071
Week 8	0,200	-0,365	0,874	0,047

Significant $p < 0.05$ (spearman test)

From Table 5 above, there was a statistically insignificant correlation between MoCAIna values and IL-17 levels with the improvement of cognitive function in schizophrenic patients after being given vocational therapy. However, by the *r* value, there were tendency of better correlation of the treatment group compered to control group (-0.365).

Discussion

The level of MoCA-Ina was given from 15 at baseline to 19 at the 4th week and to 24 at the 8th week in the treatment group. Where in the control group, the level of MoCA-Ina was given from 16 at baseline to 18 at the 4th week and to 20 at the 8th. The increase value of MoCA-Ina in both were statistically significant with $p = 0.000$ ($p < 0.05$). Although there was an increase value of MoCA-Ina in both groups, both in the treatment group was better at 8 weeks. The data above that there was an improvement of cognitive function in schizophrenia subjects who were treated used Risperidone 2-6 mg with combination of 8 week of vocational therapy.

This study was in according with studding by Sohn et al. [11], where vocational therapy in schizophrenia patients by virtual reality in 8 weeks could improvement cognitive function especially

memory and attention. Other studies throe similar result only different in length and type of vocational therapy [12, 13].

Vocational therapy in this study was proved could improve the cognitive function in schizophrenia subjects. Vocational therapy also could influence between in accordance with learning theory (class conditioning by Ivan Pavlov and social learning theory by Albert Bandura), which in town could improve cognitive function.

Improvement of cognitive function in control group was also seen where the control group only had Risperidone treatment. It was obvious, that risperidone therapy could improve cognitive function by occupancy 5HT_{2A} receptor in mesocortical pathway [17].

The study also measured IL-17 level of schizophrenic patients who the were treated with vocational therapy for 8 weeks. Type of vocational therapy which was taken by schizophrenic patients including making of malted egg, hydroponic plantation.

In this study was found the decreased of IL-17 level either in treatment group on in control group. The mean level of IL-17 at treatment group at baseline 88 pg/ml, increase to 110 pg/ml at 4th week and decrease to 99 pg/ml at 8th week. The mean level of IL-17 at control group at baseline 66 pg/ml, increase to 85 pg/ml at 4th week and decrease to 77 pg/ml at 8th week.

This finding was differing with studies by Reale et al. [18] and Xiu et al. [19]. Where the IL-17 level was increase in the first episode schizophrenia patients treated with antipsychotic and chronic hospitalized patients who were free medication for at least 4 weeks [18, 19].

This finding was not differing with studies by Borovcanin et al. [20], Dimitrov et al. [21]. Where the IL-17 level was decrease in the first episode schizophrenia patients treated with antipsychotic and chronic schizophrenia patients treated with antipsychotic.

Correlation between cognitive function which were measured by MoCA-Ina and IL-17 level in the treatment group was found not statistically significant. This finding was differing with the study by Borovcanin et al. [22]. Where there was on proritune correlation between cognitive function and IL-17 level.

In this study, the result was different which the finding of Borovcanin et al. [22], which was assessed caused by progressivity of schizophrenia disorders, the influence of antipsychotic, demographic factor, once of the disorders and length of the disorders.

The limitation of this study was only 8 weeks observation, where other studies did observation until 3 months and 6 months.

Conclusion

There was an improvement cognitive function in schizophrenic subject who received risperidone 2-6 mg/day in combination with vocational therapy for 8 weeks. Vocational therapy for 8 weeks did not affect the IL-17 levels in control group. There is no correlation between the improvement of cognitive function in schizophrenic patients with changes in IL-17 levels.

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Conflict of Interest

None

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