Cognitive Function and Vitamin D Serum Level in Schizophrenia

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Abstract

Background

Cognitive dysfunction is a core feature of schizophrenia that interferes with daily function and quality of life. Vitamin D has long been hypothesized related to Schizophrenia. This study aimed to analyze the difference in serum vitamin D levels between schizophrenia patients and healthy people without mental disorder and to analyze the correlation between cognitive function and vitamin D serum level in schizophrenia patients.

Design

The study was a case-control study, at the psychiatric outpatient service of West Java Province Mental Hospital, Indonesia. Thirty-one (31) schizophrenia patients and 30 healthy control participated in this study. Cognitive function was assessed using the Montreal Cognitive Assessment Indonesian version (MoCA-Ina) and serum vitamin D levels were examined using electrochemiluminescence binding assay (ECLIA) for the in-vitro determination of total 25-hydroxyvitamin D.

Results

The results showed that almost all of the schizophrenic subjects have a cognitive impairment. Serum Vitamin D levels in all schizophrenia subjects are low, which is insufficient (35,5%) and deficient (64,5%), and the levels are lower significantly compared to the control group (p=0,010). The results of data analysis using the Pearson test shows no correlation between cognitive function and serum vitamin D levels in schizophrenia (r=0,092, p=0,312).

Conclusions

Serum vitamin D levels of schizophrenia patients are low and significantly lower than normal people. There is no correlation between cognitive function and serum vitamin D level in schizophrenia

INTRODUCTION

Schizophrenia is a severe mental disorder with prevalence in the world of around 1% [1, 2]. Impaired cognitive function is a core deficit of schizophrenia [3, 4]. Most schizophrenia patients experience impaired cognitive function. Disturbances in cognition affect the clinical presentation, daily functioning, and are a major cause of disabilities in work, social, and economic [1-8]. Antipsychotic therapy is unsatisfactory in improving cognitive function, so it is necessary to look for additional alternative therapies that can help improve cognitive function. For this reason, it is important to understand the mechanism of cognitive function disorders in schizophrenia clearly. Vitamin D has long been thought to play a role in the development of schizophrenia. Several studies found that risk factors for the occurrence of schizophrenia including factors related to low exposure to the sun, such as births during spring or winter, living in higher latitudes area and migrations from lower latitudes to areas with higher latitude and having darker skin color which impaired the synthesis of vitamin D in the skin [9-12].

The source of vitamin D mainly comes from synthesis on the

skin, from 7-dehydrocholesterol converted to provitamin D3 with ultraviolet B from sunlight [12, 13]. Provitamin D3 will isomerize into vitamin D3. Synthesis of vitamin D requires sun exposure, so there is a suspicion that the birth season of schizophrenia patients is associated with low levels of vitamin D [9, 10, 14]. Previous study shows that patients with psychiatric disorders such as schizophrenia are more likely to lack vitamin D compared to the general population. Patients with schizophrenia, in particular, are more likely to have low vitamin D levels compared to individuals with other psychiatric disorders. [9, 11, 12, 15] The study aimed to compare the levels of serum vitamin D between schizophrenia patients and healthy controls, and to examine the correlation between serum vitamin D levels and cognitive function in the patient's group.

PATIENTS AND METHODS

The subjects of this study were 31 patients diagnosed with schizophrenia using the Diagnostic and Statistical Manual of Mental Disorders V (DSM V) criteria at the psychiatric outpatient service of West Java Province Mental Hospital, Indonesia. The control group was a healthy person without a mental disorder. Ethical approval was obtained from the Ethics Committee of Faculty of Medicine, Padjadjaran University (Letter number 1390/UN6.KEP/EC/2018). The subjects were selected consecutively. Informed consent was obtained from the patients, their parents or legal guardians, and the control group. The inclusion criteria were male, age between 18 and 45 years old, scores of each subscale of PANSS EC≤3, and using atypical antipsychotics. The exclusion criteria were having an intellectual disability or neurological disorders that can interfere with cognitive function, consuming vitamin D supplements, and using psychiatric medication other than atypical antipsychotics. Characteristic data such as education, marital status, occupation, history of previous hospitalization, duration of illness, were obtained by filling out a questionnaire. Body mass index (BMI) was obtained by measure the subject's height and body weight and calculated using BMI formula. The current medication was obtained from the patient's medical record. Cognitive function was administered to the schizophrenia group, using the Montreal Cognitive Assessment (MoCA) that has been validated in the Indonesian language. The MoCA scores ranged from 0 to 30. The MoCA scores ≥ 26 means the cognitive functions are normal, and scores <26 means there is an impairment in cognitive functions. A blood sample was collected on the same day. Serum vitamin D levels (total 25-hydroxyvitamin D) were measured using electrochemiluminescence binding assay (ECLIA) in both the schizophrenia patients and the control group. Vitamin D levels were classified as sufficient if the value of 25(OH)D was ≥30 ng/ml, insufficient if the value was <30 ng/ml, and deficient if the value was 20 ng/ml.

Data on the subject's characteristics such as education, marital status, occupation, history of previous hospitalization, duration of illness, and medication received were analyzed using descriptive statistics that presented in numbers and percentages. Data in the form of age, duration of illness and body mass index were presented in the mean and standard deviation. The difference between serum vitamin D levels of schizophrenia patients with the control group will be analyzed using an independent T-test. While the statistical analysis of the correlation between serum vitamin D levels with the cognitive function will use Pearson correlation analysis if the data are normally distributed, or the Spearman correlation analysis if the data are not normally distributed.

RESULTS

Data collection was carried from February to April 2019. The mean age of the patients was 35.22±6.83 years old, while the mean age of the control group was 35.37±6.92 years old. The majority of the patients are single (71%), graduated from senior high school (64.5%), have no job (61.3%), and had a history of the previous hospitalization caused by their mental illness (64.5%). The duration of illness was varying with the mean is 10.35±6.79 years. Most of the patients received antipsychotic risperidone (70,97%), and the rest received risperidone and clozapine combination. All of the patients received anticholinergic trihexyphenidyl.

Characteristic data are summarized in Table 1.

Table 1

Characteristic Data

	Schizophrenia		Healthy Control	
	(Mean ± SD)	n (%)	(Mean ± SD)	n (%)
Age (years)	35.22±6.83		35.37±6.92	
Education				
- Elementary school	6	6 (19.3)		
- Junior high school	9	3 (9.7)		
- Senior high school	12	20 (64.5)		
- College	16	2 (6.5)		
Marital Status				
- Single		22(71.0)		
- Married		8(25,8)		
- Divorced		1(3,2)		
Occupation				
- Un employee		19(61.3)		
- Employee		12(38.7)		
Body Mass Index	22.6±3.3			
Duration of illness (years)	10.35±6.79			
Previous Hospitalization:				
- No		11 (35.5)		
- Yes		20 (65.5)		
Treatment:				
Risperidone, Trihexyphenidyl		22 (70.97)		
Risperidone, Clozapine, Trihexyphenidyl		9 (29.03)		

Group comparison of the levels of vitamin D levels

In this study, we found that serum vitamin D levels in schizophrenic subjects are low, which is insufficient or deficient, while in the control group, almost half of them had normal vitamin D levels. Vitamin D levels in schizophrenia patients were lower significantly compared to the control group (p=0,010). The group differences and the statistical values are summarized in Table 2.

Table 2

Serum Vitamin D level

	Schizophrenia	Healthy Control	*p*-value
Serum vitamin D level	16,7 ± 5,6	31.93±10.51	0,01
- Normal	-	14 (46,7)	
- Insufficiency	11(35,5)	15(50)	
- Deficiency	20(64,5)	1(3,3)	

Almost all of the schizophrenia patients have impairment in their cognitive function (96,8%), with the mean of MoCA scores is 20 ± 4 (Table 3)

Table 3

Cognitive Function of Schizophrenia Patients

	(Mean ± SD)	n (%)
MoCA scores	20 ± 4	-
- No impairment		1(3,2)
- Impaired		30(96,8)

We did not find any correlations between the serum vitamin D levels and cognitive function measured with MoCA-Ina. We also did not find any correlation between the serum vitamin D levels and all of the cognitive domains of MoCA-Ina scores (attention, executive functions, memory, language, visuospatial skills, and orientation). The correlation analyses are summarized in Table 4.

Table 4

Correlation between cognitive functions with serum vitamin D levels

	Serum Vitamin D Level	
	r	*p*
Total MoCA-Ina Scores	0,092	0,312
MoCA-Ina Cognitive Domains		
- Attention	0,170	0,181
- Executive functions	0,151	0,208
- Memory	0,42	0,412
- Language	0,12	0,475
- Visuospatial skills	0,147	0,214
- Orientation	-0,160	0,195

DISCUSSION

In this study, almost all of the subjects (96,8%) show impaired cognitive functions according to MoCA-Ina, with an average score of 20±4. This finding is consistent with previous studies that schizophrenia patients had a significant decline in cognitive function compared to normal subjects.[3, 4, 6, 16-19]

All of the subjects having low vitamin D levels both in the category of vitamin D deficiency and insufficiency, with the mean level of 16.67±5.6 ng/mL. This is similar to previous studies that individuals with schizophrenia tend to have a low vitamin D level and have lower vitamin D levels

compared to healthy controls [9, 10]. Pearson test showed no association between serum vitamin D levels and cognitive function (r=0,092 , p= 0,312). This finding is different from studies from Graham and Nerhus that reported a significant association between vitamin D levels and cognitive deficits in schizophrenia[10, 11, 14, 20] Data analysis also shows no association found between serum vitamin D levels and each of the MoCA cognitive domains (attention, executive functions, memory, language, visuospatial skills, and orientation). Our different results in this study compared to others might be caused by several factors.

The hypothesis from Barnett et al. states that cognitive reserve (CR) is a factor that affects the risk of developing mental disorders, the clinical features, and daily functions in individuals with mental disorders. Cognitive reserve explains individual differences to maintain cognitive function in the presence of pathology in the brain. Cognitive reserve is difficult to measure experimentally and dependent on several factors such as premorbid IQ, education and employment. Education influences the completion of a task which involves attention, executive functions, memory and construction abilities. The length of formal education reflects the premorbid function, the level of intelligence and the level of information processing. Schizophrenias with high education can perform cognitive tasks well because of inherent cognitive abilities. The cognitive reserve of schizophrenia patients could be an important confounding factor in this study [21].

Vitamin D measured in this study was 25-hydroxyvitamin D(25(OH)D), while the active form of vitamin D was Calcitriol (1,25(OH)2D) which was converted from 25-hydroxyvitamin D(25(OH)D) in the kidney [22]. If the subject having impaired kidney function, it will affect the conversion of 25(OH)D into active metabolites of 1,25(OH)2D. Ideally, subjects with impaired renal function are excluded from the study, because in such condition, serum D(25(OH)D) level is not associated with the level of (1,25(OH)2D).

All of the schizophrenia patients received trihexyphenidyl, an anticholinergic agent. It is widely known that anticholinergic could impair cognitive function. Even though all subjects in this study consumed trihexyphenidyl, but the adverse effect in decreasing cognitive function might be different in one subject compared to another. This can also interfere with the results of this study. The last and powerful factor was genetic, which could affect cognitive function extensively, in many neuronal pathways, receptors, enzymes, neurotransmitters, and response to antipsychotics treatment. [8, 23]

This study has limitations. First, there were confounding factors discussed previously that could influence the result of this study. Second, we only matched control subjects to patients based on age. Future research on the relationship of vitamin D levels with cognitive function is needed, using better methodologies, measuring tools for examining more sensitive cognitive functions, using homogeneous antipsychotics and getting rid of the use of anticholinergic drugs.

CONCLUSION

Schizophrenia patients have low serum vitamin D levels and the levels are lower significantly compared to the healthy control group. There is no correlation between cognitive function and serum vitamin D levels in schizophrenia.

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