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Comparison of Serum Vitamin D Levels Between Patients with Deficit and Non-deficit Schizophrenia

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ABSTRACT

Objective: Vitamin D deficiency has been proposed to play role in a series of psychiatric disorders including schizophrenia, however there have not been any knowledge regarding relationship between vitamin D deficiency and deficit syndrome schizophrenia (DS). In this study, we aimed to evaluate the relationship between vitamin D deficiency and deficit syndrome by comparing serum vitamin D levels of deficit schizophrenia patients and non-deficit schizophrenia (NDS) patients.

Methods: Sixty-six patients who had the diagnosis of schizophrenia were included. Twenty-six patients comprised the DS group, while forty patients comprised the NDS group. The severity of illness was assessed with Scale of Assessment of Negative Symptoms (SANS), Scale of Assessment of Positive Symptoms (SAPS), and Brief Psychiatry Rating Scale (BPRS). Vitamin D concentrations of both groups were measured by an electrochemiluminescence method.

Results: The groups were similar regarding age and gender ($t=1.32$; $p=0.18$ and $X^2=0.35$; $p=0.36$, respectively). The mean SANS score and BPRS was higher in DS group compared to NDS group ($t=-3.86$; $p<0.001$ and $t=-2.13$; $p=0.03$, respectively). The mean score of SAPS was found to be higher in NDS group compared with DS ($t=-2.17$; $p=0.03$). No statistically significant difference was observed between groups regarding serum 25(OH)D levels ($t=1.36$; $p=0.17$).

Conclusion: The findings of the present study may suggest that vitamin D deficiency do not play a role in etiology of DS, although previous reports imply a relation between the vitamin D deficiency and schizophrenia. Further studies are needed to clarify the role of vitamin D in subgroups of schizophrenia.

Key words: deficit, schizophrenia, vitamin D

ÖZET

Defisit ve Defisit Olmayan Şizofreni Hastalarında Serum Vitamin D Düzeylerinin Karşılaştırılması

Amaç: Vitamin D eksikliğinin şizofreni de dahil olmak üzere bir dizi psikiyatrik hastalıkta rol oynadığı ileri sürülmektedir, ancak defisit şizofreni (DS) ve vitamin D eksikliği arasındaki ilişki hakkında bilgi bulunmamaktadır. Bu çalışmanın amacı defisit ve non-defisit şizofreni (NDS) hastalarında serum vitamin D (25(OH)D) düzeylerini karşılaştırarak, defisit sendrom ve vitamin D eksikliği ilişkisinin incelenmesidir.

Yöntem: Çalışmaya şizofreni tanılı altmış altı hasta alınmıştır. NDS grubunda kırk hasta yer alırken, DS grubunda yirmi altı hasta yer almıştır. Hastalığın şiddetini ölçmede Negatif Semptomları Değerlendirme Ölçeği (SANS), Pozitif Semptomları Değerlendirme Ölçeği (SAPS), Kısa Psikiyatrik Değerlendirme Ölçeği (BPRS) kullanılmıştır. Her iki grupta da vitamin D konsantrasyonları elektrokemilüminesans yöntemi ile ölçülmüştür.

Bulgular: Gruplar yaş ve cinsiyet açısından birbirine benzerdi ($t=1.32$; $p=0.18$ ve $X^2=0.35$; $p=0.36$, sırasıyla). SANS ve BPRS ortalaması DS grubunda NDS grubuna göre daha yüksekti ($t=-3.86$; $p<0.001$ ve $t=-2.13$; $p=0.03$, sırasıyla). SAPS skor ortalaması NDS grubunda DS grubuna göre daha yüksek bulundu ($t=-2.17$; $p=0.03$). Gruplar arasında serum 25(OH)D düzeyleri arasında istatistiksel açıdan anlamlı bir fark gözlenmedi ($t=1.36$; $p=0.17$).

Sonuç: Önceki çalışmalarda vitamin D eksikliği ve şizofreni arasında bir ilişki olduğu bildirilmiş olmasına rağmen, çalışmamızda elde edilen bulgulara göre vitamin D eksikliğinin defisit sendrom şizofreninin meydana gelmesinde rol oynamadığı ileri sürülebilir. Şizofreni alt gruplarında vitamin D eksikliğinin rolünün anlaşılabilmesi için daha ileri düzeyde çalışmalara ihtiyaç duyulmaktadır.

Anahtar sözcükler: defisit, şizofreni, vitamin d

INTRODUCTION

Schizophrenia is a chronic and disabling disorder that affects approximately 1% of population.[1] There have been great efforts aimed to shed light on the underlying neurobiological mechanisms of this disorder. Among the biological factors, serum vitamin D level had given a subtle attention in terms of identifying its possible role in the etiology of disorder.[2] There may be several important and event related factors which may interfere with the possible role of vitamin D in schizophrenia. Nonetheless, there have been several reasons suggesting vitamin D as an etiological factor in schizophrenia. It has been known that prevalence of schizophrenia differs according to geographical regions. Such as; its prevalence is higher in northern sides and cold climates. Moreover, prevalence of schizophrenia is reported to be higher in blacks compared to white ethnicity and people who were born in spring or winter seasons.[3,4]

Because of this great interest about the possible association between schizophrenia and vitamin D, there have been numbers of articles which attempted to identify this relationship. A mini-meta-analysis reported that patients who were diagnosed as psychosis; particularly schizophrenia had lower vitamin D levels compared with healthy controls.[5] In a more recent meta-analysis, it has been reported that there had been a strong association between vitamin D deficiency and schizophrenia. Such as, people who had a vitamin D deficiency had 2.16 times more likely to be diagnosed as schizophrenia compared with people without vitamin D deficiency.[6]

After publication of Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5), sub-classifications of schizophrenia have been removed because of their lower reliabilities and validities.[7] However, heterogenic nature of schizophrenia is still accepted. From this point, it will be necessary to subclass of patients with schizophrenia for both clinical and research manners. Since the definition of deficit syndrome schizophrenia by Carpenter et al.,[8] this diagnosis has been used both clinically and for researches even though it has been absent in updated diagnostic manuals such as DSM-V.

In present study, we aimed to compare the serum levels of Vitamin D and related factors such as calcitonin and parathyroid hormone between schizophrenic patients with deficit syndrome (DS) and without deficit syndrome (NDS).

METHODS

Patients with schizophrenia who were diagnosed with schizophrenia according to DSM-5 and who have been followed up in Yenimahalle Education and Research Hospital, Department of Psychiatry were included into study. The inclusion criteria were as followings; being diagnosed as schizophrenia; ages between 18-60 years old, willing to participate into study. Patients with abnormal complete blood count results; abnormal sedimentation rate, thyroid hormone, vitamin B12, or ferritin levels; who had osteoporosis or systemic inflammatory and connective tissue disease; who used alcohol excessively (>40 g/d), who had diabetes, renal failure, or chronic hepatic failure or who had been on medical treatment with corticosteroids, calcitonin, estrogen, calcium, bisphosphonates, or vitamin D were excluded. Demographic and clinical characteristics, including age, sex, and body mass index (BMI), were noted.

The severity of illness was assessed with Scale of Assessment of Negative Symptoms (SANS)[9] , Scale of Assessment of Positive Symptoms (SAPS)[10] , Brief Psychiatry Rating Scale (BPRS) .[11] Patients were divided in two groups based on whether they were deficit syndrome schizophrenia according to the Schedule for the Deficit Syndrome.[12] Briefly, patients who had at least two of the following six symptoms: restricted affect, poverty of speech, curbed interests, diminished sense of purpose, diminished emotional range and diminished social drive. These symptoms had to be enduring and moderate at least 12 months duration. Additionally, these negative symptoms had to be independent of depressive disorder, anxiety, extrapyramidal side effects of drugs and mental retardation. After inclusion and exclusion criteria, 66 patients with diagnosis of schizophrenia were included in study. All patients were able to provide written informed consent and they accepted to be participate in the study. Present study was intended according to the principles of the Helsinki Declaration and was approved by the local ethics committee.

Venous blood samples (20 mL) were collected from all of the patients for the measurement of serum 25(OH)D concentrations. Serum 25(OH)D concentrations were measured by an electrochemiluminescence method (Roche Cobas E 411; Roche Diagnostics GmbH, Tokyo, Japan). Calcium, phosphor, parathyroid hormone and calcitonin were estimated with commercially available kits (Roche Cobas C 501; Roche Diagnostics GmbH).

The obtained data was assessed by Statistical Package for the Social Sciences, PC version 17.0 (SPSS, Chicago, IL). A confidence interval of 95% and two-tailed p values lesser than 0.05 were considered to be statistical significance. The numerical data was assessed by Shapiro-Wilk test for normality. The parametric numeric data between groups was assessed by Student's t test and all numerical data are presented as mean ± SD. In the case of non-parametrical numerical data, Mann Whitney U test was used to assess the difference between groups. The categorical variables were assessed by a X2 test. Relationships between parametric variables have been calculated with Pearson's correlation test.

RESULTS

The number of participants in the study was 66. Twenty-six of them were classified as DS (39.4%) and 40 of them were classified as NDS (60.4%). The mean age was 33.57±7.00 years in DS group and 35.80±6.39 years in NDS group. The mean age was similar between groups (t=1.32; p=0.18). The numbers of female participants in DS group were 13 (50%) in DS group and 23 (57.5%) in NDS groups .There was not a significant difference between groups (X^2=0.35; p=0.36). Smoking rate was also found to be similar between groups (X^2=0.15; p=0.16). The mean scores of SANS were 41.69±17.89 and 26.37±11.7 in DS and NDS groups respectively. The mean score of SANS was significantly higher in DS group (t=-3.86; p<0.001). The mean score of SAPS was 32.57±12.31 in NDS group and 25.02±12.31 in DS group. The mean score of SAPS was found to be higher in NDS group compared with DS (t=-2.17; p=0.03). The mean scores of BPRS were 26.34±11.37 and 20.15±11.52 in DS and NDS groups respectively. The BPRS score was significantly higher in DS group (t=-2.13; p=0.03). The values of BMI and chlorpromazine equivalent doses were similar between groups (Table 1).

The mean level 25(OH)D levels were 37.13±11.57 ng/mL and 32.94±13.34 ng/mL in NDS and DS groups, respectively. The levels of 25(OH)D were similar between groups (t=1.36; p=0.17). There was also not a significant difference between groups in terms of PTH, calcitonin, Ca, P levels (respectively, t=-1.21; p=0.22; t=0.92; p=0.35; t=-1.942; p=0.16; t=-0.62; p=0.53).

In correlation analysis, there was not a significant correlation between mean level of 25(OH)D and scores of SANS, SAPS, BPRS and BMI (respectively; r =-0.23, p=0.06; r=-0.03, p=0.77; r =-0.16, p=0.19 and r =-0.34, p=0.07)

DISCUSSION

In this study, we compared serum Vitamin D levels and associated factors between patients with DS and NDS.

Vitamin D is considered to have a significant role for healthy development of parts of central nervous system such as thalamus, hypothalamus, amygdala, prefrontal cortex and temporal lobe.[13] As mentioned before, individuals who were born in winter and spring, who have darker skin color and who immigrated to northern countries are more likely to develop schizophrenia.[3,4] All these factors are directly associated with lower Vitamin D levels and from this point, Vitamin D has been an important area of investigation in the etiopathogenesis of schizophrenia.[14] In a Finnish birth cohort study, it was reported that individuals who had received sufficient vitamin D supplementation during the infant period had lesser percentage of prevalence of schizophrenia compared with those who had insufficient Vitamin D supplementation.[15] Moreover, lower Vitamin D levels were reported to be associated with negative and cognitive symptoms of schizophrenia.[13]

There has been growing evidence that support the validity of deficit syndrome schizophrenia. Since the definition of deficit syndrome schizophrenia by Carpenter et al.,[8] several biological studies confirmed the discrepancy of DS compared with NDS. Albayrak et al. reported that patients with DS had increased oxidative stress and reduced total antioxidant capacity compared to NDS patients.[16] Recently, we reported decreased serum BDNF levels in patients with DS compared with NDS patients.[17] More recently, we also reported different characteristics of neurological soft signs in patients with DS compared with NDS patients and healthy subjects.[18] To our knowledge, present study is the first to compare serum vitamin D and related factors between DS and NDS patients. In the present study, we failed to find any significant differences between DS and NDS patients in terms of serum vitamin D levels. From this point, we suggest that levels of serum vitamin D and related factors such as PTH and calcitonin may not be a strong indicator or a biomarker for distinguishing DS from NDS. Although there have been consistent events that support the serum vitamin D level can be associated with symptomatology and etiology of schizophrenia,[19-21] it may not be strong tool for predicting the subtypes of schizophrenia.

Including only patients with schizophrenia to the study, matching groups in terms of age, gender, BMI and smoking status can be considered to be strengths of study. Inclusion of patients under antipsychotic treatment, relatively small numbers of participants and cross sectional method of the study are limitations of present study.

In conclusion, although deficit syndrome is considered to be a subgroup of schizophrenia, we consider that vitamin D levels may not be a good biomarker candidate for the deficit syndrome. Further and large-sample studies are needed to clarify the role of vitamin D in DS.

Table 1. Sociodemographic and clinical characteristics of participants

		NDS (N=40)	DS (N=26)	Statistic
Age (years)		35.80 ± 6.39	33.57 ±7.00	t=1.32; p=0.18
Gender	**Female**	23 (57.5%)	13(50%)	X^2=0.35; p=0.36
	Male	17(42.5%)	13(50%)	
Smoking status	**Yes**	20(50%)	9(34.6%)	X^2=0.15; p=0.16
	No	20(50%)	17(65.4%)	
BMI		26.03 ± 4.97	25.79 ± 4.11	t=0.28; p=0.83
SANS		26.37 ± 11.7	41.69 ± 17.89	t=-3.86; p<0.001
SAPS		32.57 ± 12.31	25.02 ± 12.31	t=-2.17; p=0.03
BPRS		20.15 ± 11.52	26.34 ± 11.	t=-2.13; p=0.03
Cholorpromazine equivalent dose		450.13 ± 339.13	376.88 ± 221.50	t=0.89, p=0.33

BMI: Body Mass Index, BPRS: Brief Psychiatric Rating Scale, DS: Deficit Schizophrenia, NDS: Nondeficit chizophrenia SANS: Scale for the Assessment of Negative Symptoms,SAPS: Scale for The Assessment of Positive Symptoms. Significant p values indicated in bold character.

Table 2. Comparison of serum vitamin D and associated factors between groups

	NDS (N=40)	DS (N=26)	Statistic
25(OH)D (ng/dl)	37.13±11.57	32.94±13.34	t=1.32; p=0.18
Ca (mg/dl)	9.34±0.34	9.57±0.43	t=-1.942; p=0.16
P (mg/dl)	3.33±0.60	3.44±0.62	t=-0.62; p=0.53
PTH (pg/ml)	24.33±12.44	28.78±13.87	t=-1.21; p=0.2
Calsitonin	1.89±0.86	1.79±0.88	t=0.92; p=0.35

Ca: Calcium, P: Phosphor, PTH: Parathyroid hormone DS: Deficit Schizophrenia, NDS: Nondeficit Schizophrenia.

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