

Impact of vitamin D on mobilization, pulmonary function tests, grip strength and functionality in patients with spinal cord injury: A cross-sectional study

D vitamininin omurilik yaralanmalı hastalarda mobilizasyon, solunum fonksiyon testleri, kavrama gücü ve fonksiyonellik üzerine etkisi: Kesitsel bir çalışma

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Abstract

Aim: Since vitamin D deficiency is a growing problem worldwide, insufficient levels of vitamin D were reported in patients with spinal cord injury (SCI). It was stated that levels of vitamin D may be an indirect indicator of functional status in patients with SCI. The aim of this study was to investigate the relationship between vitamin D levels and mobilization, functionality, grip strength, and pulmonary function test parameters in patients with subacute SCI.

Methods: Fifty-eight patients with subacute motor complete thoracic (T) and lumbar SCI injuries [46 males, 12 females; mean age 32.0 (11.2) years] were included. The time to complete the verticalization program on the tilt table without any orthostatic symptoms was considered as the 'time of mobilization.' Grip strength (GS) was measured using a dynamometer, pulmonary function test (PFT) parameters were measured using a spirometer, and functional status was measured using the Functional Independence Measure (FIM). For determining the levels of vitamin D, 25-hydroxy-vitamin D [25(OH)D] was measured and levels below 20 ng/mL were considered as deficiency. The patients were divided into two groups according to 25(OH)D levels, <20 ng/mL and ≥20 ng/mL. The demographic features, mobilization, PFT, GS, and FIM scores were compared according to the levels of 25(OH)D. The patients were divided into two other groups according to neurologic levels: levels between T6-10 and levels T11 and below, and then intragroup comparisons according to the levels of 25(OH)D were performed.

Results: The mean 25(OH)D level of the patients was found as 19.8 (8.3) ng/mL. When all patients were evaluated, time of mobilization was longer and FIM scores were lower in the 25(OH)D deficient group than in the other group ($P<0.001$ and $P=0.038$, respectively). When patients were evaluated separately according to their neurologic levels, time of mobilization was longer in the 25(OH)D deficient group, both in patients with a lesion level between T6-10 and the lesion levels T11 and below ($P<0.001$ and $P=0.009$, respectively). There was no statistically significant difference between the groups in terms of other clinical evaluations according to the neurologic levels of the patients.

Conclusion: Among the patients with SCI, time of mobilization of patients with vitamin D deficiency was longer than those of patients with non-deficient vitamin D levels, regardless of the neurologic level. Although the results of this study showed no statistically significant difference there may also be a relationship between vitamin D levels and pulmonary functions, GS, and FIM scores.

Keywords: Paraplegia, 25-hydroxy-vitamin D, Orthostatic hypotension, Lung function, Functional independence measure

Öz

Amaç: D vitamini eksikliği dünya çapında büyüyen bir problem olduğundan, omurilik yaralanmalı (OY) hastalarda da yetersiz D vitamini seviyeleri bildirilmiştir. D vitamini düzeylerinin, OY hastalarda fonksiyonel durumun dolaylı bir göstergesi olabileceği belirtilmiştir. Bu çalışmanın amacı, subakut dönemdeki OY hastalarda D vitamini düzeyleri ile mobilizasyon, fonksiyonel durum, el kavrama gücü ve solunum fonksiyon testi (SFT) parametreleri arasındaki ilişkiyi araştırmaktır.

Yöntemler: Subakut motor komplet torakal (T) ve lomber OY 58 hasta [46 erkek, 12 kadın; yaş ortalaması 32.0 (11.2) yıl] çalışmaya dahil edildi. Herhangi bir ortostatik semptom olmadan tilt masası ile vertikalizasyon programını tamamlama süresi "mobilizasyon zamanı" olarak değerlendirildi. El kavrama gücü dinamometre ile, SFT spirometre ile, fonksiyonel durum ise Fonksiyonel Bağımsızlık Ölçeği (FBÖ) ile değerlendirildi. D vitamini düzeylerini belirlemek için 25-hidroksi-vitamin D [25(OH)D] ölçümü yapıldı ve 20ng/mL'nin altındaki değerler eksiklik olarak değerlendirildi. Hastalar 25(OH)D seviyeleri <20 ng/mL olan ve 25(OH)D seviyeleri ≥20 ng/mL olan olmak üzere iki gruba ayrıldılar. Demografik özellikler, mobilizasyon, SFT, el kavrama gücü ve FBÖ skorları 25(OH)D düzeylerine göre karşılaştırıldı. Hastalar nörolojik seviyelerine göre de farklı iki gruba ayrıldılar: Seviye T6-T10 arası ve seviye T11 ve altı. Sonrasında 25(OH)D düzeylerine göre grup içi karşılaştırmalar yapıldı.

Bulgular: Hastaların ortalama 25(OH)D düzeyleri 19.8 (8.3) ng/mL olarak bulundu. Tüm hastalar değerlendirildiğinde, 25(OH)D eksikliği olan grupta diğer gruba göre "mobilizasyon zamanı" daha uzundu ve FBÖ skorları daha düşüktü (sırasıyla $P<0.001$ and $P=0.038$). Hastalar nörolojik düzeylerine göre ayrı ayrı değerlendirildiğinde; hem lezyon seviyesi T6-T10 arası olan grupta hem de lezyon seviyesi T11 ve altı olan grupta; 25(OH)D eksikliği olan hastalarda "mobilizasyon zamanı" daha uzundu (sırasıyla $P<0.001$ and $P=0.009$). Hastalar nörolojik düzeylerine göre ayrıldıklarında diğer klinik değerlendirmeleri açısından; gruplar arasında istatistiksel olarak anlamlı fark yoktu.

Sonuç: OY hastalarda; nörolojik seviyeden bağımsız olarak D vitamini eksikliği olan hastaların mobilizasyon süresi olmayan hastalara göre daha uzundur. Bu çalışmanın sonuçları istatistiksel olarak anlamlı bir fark göstermese de, D vitamini düzeyleri ile solunum fonksiyonları, el kavrama gücü ve FBÖ skorları arasında da bir ilişki olabilir.

Anahtar kelimeler: Parapleji, 25-hidroksi-vitamin D, Ortostatik hipotansiyon, Akciğer fonksiyonu, Fonksiyonel bağımsızlık ölçeği

Introduction

Vitamin D is an important factor in bone metabolism and neuromuscular functions. Moreover, its deficiency and insufficiency have been found to be associated with many chronic diseases including common cancers, metabolic syndrome, and cardiovascular, infectious and autoimmune diseases. Serum 25-hydroxyvitamin D [25(OH)D] is considered the best marker for assessing vitamin D status [1]. Determining the accurate thresholds for vitamin D deficiency is still a matter of debate [2]. The Endocrine Society's Clinical Practice Guideline defines vitamin D deficiency, insufficiency, and sufficiency as serum concentrations of 25(OH)D <20 ng/mL (<50 nmol/L), 21-29 ng/mL (51-74 nmol/L), and 30-100 ng/mL (75-250 nmol/L), respectively [3]. Severe vitamin D deficiency with a 25(OH)D <12 ng/mL (or 30 nmol/L) dramatically increases the risk of excess mortality, infections, and many other diseases, and should be avoided whenever possible [1].

Vitamin D deficiency is a growing problem worldwide [2,4]. It has been described as a pandemic in recent years [5]. Insufficient or severely deficient levels of 25(OH)D were reported in patients with spinal cord injury (SCI) [6-8]. Moreover, there are some studies showing that deficiency of 25(OH)D may represent an independent predictor of worsening of physical functions of people with chronic SCI [9,10].

Along with motor and sensory deficits, disturbances of the cardiovascular, bronchopulmonary, gastrointestinal, thermoregulatory, and genitourinary systems are common after an SCI [11]. Cardiovascular complications are mostly associated with dysfunctions of the autonomic nervous system. Orthostatic hypotension, irregularities of the cardiac rhythm, autonomic dysreflexia are common autonomic problems. Orthostatic hypotension is defined as a decrease in systolic blood pressure of at least 20 mm Hg, or a reduction in diastolic blood pressure of at least 10 mm Hg, upon a change in body position from a supine position to an upright posture, regardless of the presence of symptoms [12]. There are studies showing the relationship between orthostatic hypotension and vitamin D in some other diseases and in some geriatric groups [13-18]. Orthostatic hypotension seen in patients with spinal cord injury is the most important factor that negatively affects mobilization of patients. To the best of our knowledge, there is no study in the literature examining the relationship between orthostatic hypotension and vitamin D in patients with SCI.

In addition, upper extremities are very important for mobilization in patients with SCI with complete paraplegia. Therefore, in the rehabilitation program of a patient with SCI (especially patients with complete paraplegia), the most important point is to strengthen the upper extremities to the maximal level in the acute period of rehabilitation, because at the end of the acute/subacute phase, strong upper extremities are needed for independent transfers [19]. Skeletal muscle expresses vitamin D receptors and may require vitamin D for its function and there are many studies showing that vitamin D deficiency causes weakness and falls [3]. The effect of vitamin D on the limb muscles of the patients with SCI should be investigated.

However, extremity muscle strength is not the only important factor in a patient with SCI. Respiratory muscles that

affect pulmonary functions are just as important. One of the other important complications of SCI is pulmonary dysfunction. Recent studies have shown that early mobilization plays an important role in the prevention of pulmonary function decline and in the development of muscle strength [19]. Studies on some lung diseases have shown a relationship between vitamin D and pulmonary functions [20-22]. However, in some studies conducted on patients with chronic SCI, there was no association shown between pulmonary functions and vitamin D [23,24].

Thus, the purpose of this study was to investigate the relationship between vitamin D levels and mobilization, pulmonary function tests, grip strength, and the functionality of patients with subacute SCI because these parameters are closely related with each other in the rehabilitation setting.

Materials and methods

Patient selection

Fifty-eight patients with SCI, aged 18-65 years, who were admitted to the inpatient physical therapy and rehabilitation service of Ankara Physical Medicine and Rehabilitation Training and Research Hospital, which is a national tertiary referral center in Turkey, and who agreed to participate were included in the study.

In this study, patients with an SCI that resulted in complete motor paraplegia were included in order to achieve homogenization. The updated classification of the American Spinal Injury Association (ASIA) was used [25]. Patients with ASIA A and ASIA B were included in the study according to this classification. Moreover, only patients with injuries below the level of thoracic (T) 6th vertebrae (T6) were included in the study because some upper extremity functions would be studied, and some measurements should be made in a sitting position. All patients with SCI in the rehabilitation center were included in the verticalization program with the tilt table before achieving the sitting level [19]; only patients who completed the verticalization program with the tilt table were included in the study.

The exclusion criteria were as follows: Patients aged <18 or >65 years; incomplete motor SCI (ASIA C or D) or neurologic level above T6, non-traumatic spinal cord pathologies (e.g. tumor, infection, ischemia), disease duration shorter than 6 weeks or more than 6 months, additional neurologic diseases other than SCI, patients with motor impairment of the upper limbs, history of smoking, patients with pulmonary disease, using drugs that could affect vitamin D metabolism / various medications that deplete vitamin D stores, use of high-potency vitamin D supplements on a regular basis prior to initial assessment, a history of regular sunbathing, previous diagnoses of childhood rickets or history of other adult metabolic bone disorder such as osteoporosis and osteomalacia, presence of any other systemic disease (hematologic, endocrine, rheumatologic, renal, cardiovascular, gastrointestinal, pulmonary disease), presence of chronic medical disorders requiring medical treatments, active infection, history of malignancy, pregnancy/lactation, bleeding diathesis, other complications of SCI (e.g. thromboembolism, heterotopic ossification, pressure ulcers), patients who underwent therapies other than routine (e.g. elastic pressure socks, abdominal pillow, sufficient fluid intake) during verticalization program with the tilt table such as

electrical stimulation and/or medical treatment (e.g. midodrine) for the treatment of orthostatic hypotension, patients with speech disorders, communication disorders, cognitive dysfunction, severe psychological pathologies, and debility.

Before the study, permission was obtained from the local ethics committee. The participants were informed about the aim and method of the study and their written and oral consent was obtained. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Clinical measurement parameters

Demographic features

The age, sex, body mass index (BMI), etiology of SCI, time from SCI, and ASIA Impairment Scale scores of the patients were recorded. The patients were divided into two groups according to neurological levels by means of ASIA classification, because the expected functional status of patients will change according to the level of SCI: levels between T6-10 (group 1) and levels T11 and below (group 2) [19,26].

Clinical evaluation parameters

As the “mobilization time”, the ending time (means of days) of the verticalization program with the tilt table was accepted.

For defining the functionality of the patients, the Functional Independence Measure (FIM) was used [27]. FIM assesses the degree of independence of the individual in basic physical and cognitive activities in daily life. FIM consists of 18 items and basically measures two parameters: motor function and cognitive function. Each item consists of a 7-point scale in which 1 indicates total assistance and 7 shows complete independence. The ‘motor function’ section consists of self-care, sphincter, transfer, and locomotion sub-sections, and the total scoring ranges from 13 to 91. The ‘cognitive function’ section consists of communication and social cognition sub-sections, and the total scores range from 5 to 35. Total scoring of FIM ranges from 18 to 126. High scores in the scale indicate that the patient’s independence is high. The validity and reliability of the FIM is well established [28]. In this study, only the motor function section was used.

In this study, the grip strength (GS) of the upper extremities of all patients with SCI was evaluated using a Jamar® hand dynamometer (Sammons Preston, Inc., Bolingbrook, IL). For the test position, patients were instructed to sit in a wheelchair with their feet flat on the chair, and measurements were performed while the shoulder was in adduction, elbow in 90° flexion, and the forearm in the neutral position between the supine and pronation position. In the GS test, patients were required to increase their grip force smoothly and to maintain the same strength for approximately three seconds at the maximum level. The third range of the dynamometer was used as the standard when measuring and GS was measured in kilograms-force. GS was evaluated three times with one-minute rest intervals, and their averages were calculated. The dominant arm was used for the measurements.

The pulmonary function tests were defined by resting spirometric measurements including forced vital capacity (FVC), vital capacity (VC), forced expiratory volume in one second (FEV1), the ratio of FEV1 to FVC (FEV1/FVC), peak expiratory flow rate (PEF), and maximum voluntary ventilation (MVV),

which were performed using a hand-held spirometer (Vmax29 Sensormedix, Yorba Linda, CA, USA). All studies were performed with the subjects in the sitting position. Each subject performed at least three trials and the best performance was used for analysis. Measurements were expressed as percentages of the predicted values. Eighty percent of predicted maximum or greater was accepted as normal.

Laboratory measurement parameters

Due to the seasonal variation of vitamin D, this study was conducted only between September and December. Blood samples were taken from peripheral venous blood at the same time in the morning after eight hours of fasting. Routine blood tests (hemogram, liver-kidney-thyroid function tests, erythrocyte sedimentation rate, C-reactive protein) were performed in all patients in the Biochemistry Laboratory of Ankara Physical Medicine and Rehabilitation Training and Research Hospital. Patients without abnormalities in routine blood tests were included in the study. For the evaluation of vitamin D levels, serum 25(OH)D levels were determined using an electrochemiluminescence immunoassay.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) for Windows 11.5 statistical package program (IBM Corporation, Armonk, NY, USA) was used for statistical analysis. Whether the distribution of continuous and discrete numerical variables was close to normal was investigated using the Kolmogorov-Smirnov test. Descriptive statistics are shown as mean (standard deviation) (SD) or median (minimum – maximum) for continuous and discrete numerical variables, and categorical variables as number of cases and percentage (%). The significance of the difference in terms of mean values between the groups was investigated using Student’s t test and the significance of the difference in terms of median values was investigated using the Mann-Whitney U test. Categorical variables were evaluated using Pearson’s Chi-square or Fisher’s exact test. Results of $P < 0.05$ were considered statistically significant.

Results

The mean age of the patients was 32.0 (11.2) years. Some other demographic and clinical characteristics of the patients are shown in Table 1. The mean 25(OH)D level was found as 19.8 (8.3) ng/mL. The patients were divided into two groups according to their 25(OH)D levels: < 20 ng/mL and ≥ 20 ng/mL. The demographic and clinical characteristics of the patients were compared according to 25(OH)D levels (Table 2). A statistically significant difference between the two groups was observed only in ‘time of mobilization’ and ‘FIM-motor subscale ($P < 0.001$ and $P = 0.038$, respectively).

As mentioned in the methods section, the patients were divided into two groups according to neurologic levels by means of the ASIA classification: levels between T6-10 (group 1) and levels T11 and below (group 2). It was evaluated whether there was a difference in demographic and clinical characteristics between the groups according to 25(OH)D levels. In Group 1, a statistically significant difference between the two groups was observed only in time of mobilization ($P < 0.001$) (Table 3). Similarly, in Group 2, a statistically significant difference

between the two groups was observed only in time of mobilization ($P=0.009$) (Table 4). Figure 1 summarizes the relationship between mobilization time and 25(OH)D levels. There was no difference between the groups in terms of other clinical evaluations according to the neurologic levels of the patients.

Table 1: Demographic and clinical characteristics of the patients

	n=58
Age (years) [mean (SD)]	32.0 (11.2) (min:18, max:53)
Sex [n(%)]	
Female	12 (20.7%)
Male	46 (79.3%)
Body mass index (kg/m ²) [mean (SD)]	22.7 (4.0)
Disease duration (months) [median (min-max)]	4 (1.5-6)
Time of mobilization* (days) [median (min-max)]	10 (0-45)
Etiology of the injury [n(%)]	
Falling from high	24 (41.4%)
Traffic accident	27 (46.6%)
Gunshot injury	4 (6.9%)
Cutting tool injury	1 (1.7%)
Earthquake injury	2 (3.4%)
Neurological Level [n(%)]	
Levels between T6-T10	31 (53.4%)
Levels T11 and below	27 (46.6%)
FIM - Motor Subscale [median (min-max)]	53 (27-80)
Grip strength (kg) [mean (SD)]	49.7 (17.5)
25-OH Vitamin D Levels (ng/mL) [mean (SD)]	19.8 (8.3)
Pulmonary Function Tests*** [mean (SD)]	
FVC	82.5 (19.2)
FEV1	83.4 (18.8)
FEV1/FVC	102.3 (12.0)
PEF	66.3 (18.9)
VC	81.0 (18.8)
MVV	98.7 (25.1)

* The time to complete the verticalization program on the tilt table without any orthostatic symptoms was considered as the "time of mobilization", ** FIM: Functional Independence Measure, *** % predictive values of FVC: Forced vital capacity, FEV1: Forced expiratory volume at 1 second, PEF: Peak expiratory flow rate, VC: vital capacity, MVV: Maximum voluntary ventilation, T: thoracic

Table 2: Demographic and clinical characteristics of the patients according to vitamin D levels

	Vitamin D <20 ng/mL (n=28)	Vitamin D ≥20 ng/mL (n=30)	P-value
Age (years) [mean (SD)]	33.6 (11.5)	30.2 (11.1)	0.257
Sex [n(%)]			0.893
Female	6 (21.4%)	6 (20.0%)	
Male	22 (78.6%)	24 (80.0%)	
Body mass index (kg/m ²) [mean (SD)]	23.0 (2.8)	22.8 (4.4)	0.871
Disease duration (months) [median (min-max)]	3.2 (1.5-6.0)	4.5 (2.0-6.0)	0.075
Time of mobilization* (days) [mean (SD)]	18.1 (10.3)	6.1 (4.6)	<0.001
Neurologic level [n(%)]			0.110
Levels between T6-T10	18 (64.3%)	13 (43.3%)	
Levels T11 and below	10 (35.7%)	17 (56.7%)	
FIM** - Motor Subscale [median (min-max)]	51 (27-74)	56 (39-80)	0.038
Grip strength (kg) [mean (SD)]	47.7 (19.8)	51.5 (15.2)	0.432
Pulmonary Function Tests*** [mean (SD)]			
FVC	77.4 (15.8)	86.9 (20.9)	0.117
FEV1	79.6 (14.5)	86.8 (21.6)	0.233
FEV1/FVC	104.4 (12.8)	100.7 (11.7)	0.330
PEF	63.6 (16.3)	68.9 (20.9)	0.383
VC	74.8 (15.6)	85.9 (20.1)	0.062
MVV	96.2 (29.3)	99.5 (22.1)	0.675

* The time to complete the verticalization program on the tilt table without any orthostatic symptoms was considered as the "time of mobilization", ** FIM: Functional Independence Measure, *** % predictive values of FVC: Forced vital capacity, FEV1: Forced expiratory volume at 1 second, PEF: Peak expiratory flow rate, VC: vital capacity, MVV: Maximum voluntary ventilation, T: thoracic

Table 3: Demographic and clinical characteristics of patients with a neurologic lesion levels between T6-T10 (group 1)

	Vitamin D <20 ng/mL (n=18)	Vitamin D ≥20 ng/mL (n=13)	P-value
Age (years) [mean (SD)]	35.1 (12.0)	31.7 (12.3)	0.444
Sex [n(%)]			0.999
Female	4 (22.2%)	2 (15.4%)	
Male	14 (77.8%)	11 (84.6%)	
Body mass index (kg/m ²) [mean (SD)]	23.8 (3.0)	22.1 (2.7)	0.137
Disease duration (months) [median (min-max)]	3 (1.5-6)	6 (2-6)	0.115
Time of mobilization* (days) [mean (SD)]	17.0 (5.9)	8.9 (4.6)	<0.001
FIM** - Motor Subscale [median (min-max)]	47 (27-71)	53 (39-67)	0.211
Grip strength (kg) [mean (SD)]	41.7 (16.5)	47.7 (15.5)	0.326
Pulmonary Function Tests*** [mean (SD)]			
FVC	74.3 (18.3)	79.4 (20.6)	0.542
FEV1	78.5 (16.8)	81.3 (21.5)	0.735
FEV1/FVC	107.5 (12.3)	103.3 (13.1)	0.448
PEF	63.8 (12.1)	65.5 (14.9)	0.765
VC	72.9 (18.1)	78.0 (20.8)	0.547
MVV	91.5 (29.7)	93.7 (27.8)	0.860

* The time to complete the verticalization program on the tilt table without any orthostatic symptoms was considered as the "time of mobilization", ** FIM: Functional Independence Measure, *** % predictive values of FVC: Forced vital capacity, FEV1: Forced expiratory volume at 1 second, PEF: Peak expiratory flow rate, VC: vital capacity, MVV: Maximum voluntary ventilation, T: thoracic

Table 4: Demographic and clinical characteristics of patients with neurologic lesion levels T11 and below (group 2)

	Vitamin D <20 ng/mL (n=10)	Vitamin D ≥20 ng/mL (n=17)	P-value
Age (years) [mean (SD)]	31.0 (10.7)	29.1 (10.4)	0.658
Sex [n(%)]			0.999
Female	2 (20.0%)	4 (23.5%)	
Male	8 (80.0%)	13 (76.5%)	
Body mass index (kg/m ²) [mean (SD)]	21.5 (1.7)	23.4 (5.4)	0.212
Disease duration (months) [median (min-max)]	4 (1.5-5)	4.5 (2-6)	0.711
Time of mobilization* (days) [mean (SD)]	19.9 (15.3)	3.9 (3.2)	0.009
FIM** - Motor Subscale [median (min-max)]	61.5 (40-74)	72 (41-80)	0.223
Grip strength (kg) [mean (SD)]	59.9 (21.2)	54.7 (14.8)	0.484
Pulmonary Function Tests*** [mean (SD)]			
FVC	83.6 (6.8)	92.2 (20.2)	0.332
FEV1	81.8 (9.3)	90.6 (21.6)	0.354
FEV1/FVC	98.3 (12.5)	98.8 (10.6)	0.921
PEF	63.3 (24.1)	71.3 (24.7)	0.515
VC	79.2 (6.6)	91.6 (18.2)	0.159
MVV	105.5 (28.7)	103.7 (16.9)	0.859

* The time to complete the verticalization program on the tilt table without any orthostatic symptoms was considered as the "time of mobilization", ** FIM: Functional Independence Measure, *** % predictive values of FVC: Forced vital capacity, FEV1: Forced expiratory volume at 1 second, PEF: Peak expiratory flow rate, VC: vital capacity, MVV: Maximum voluntary ventilation, T: thoracic

Discussion

Vitamin D insufficiency is common in patients with SCI and the consequences of impaired vitamin D status for patients with SCI can be listed as musculoskeletal health concerning bone health (osteoporosis, fracture risk, and fracture healing), muscle health (muscle weakness, myalgia, impairments of gait and physical performance), and cardiometabolic health, which concerns hypertension, obesity, dyslipidemia, glucose intolerance, and diabetes [7]. The primary result of the present study is that there is a relation between time to mobilization of patients with SCI and vitamin D deficiency. This is another consequence that may be added to the cardiometabolic health list.

Along with motor and sensory deficits, instabilities of the cardiovascular, thermoregulatory, and pulmonary system are common after an SCI. In the acute phase of the SCI, orthostatic hypotension can be seen in 33-74% of cases [11]. In patients with orthostatic hypotension, the verticalization time with the tilt table and thus the mobilization time is prolonged. The results of this study showed that, in patients with vitamin D deficiency,

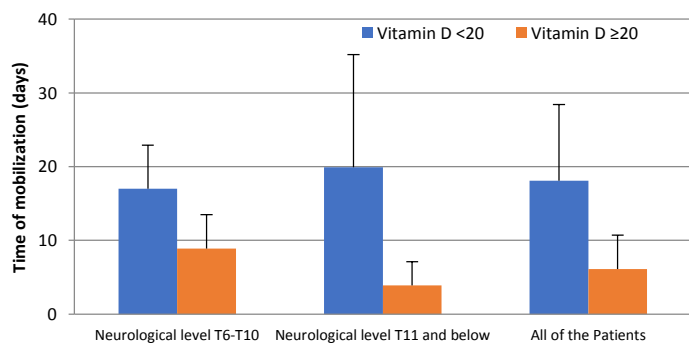


Figure 1: The relationship between mobilization time and 25(OH)D levels according to the neurologic levels of the patients

regardless of the neurologic level, the verticalization time with the tilt table is longer than in those with non-deficient vitamin D levels. In the literature, there are some studies conducted on older people [17, 18], oldest-old people [13], and patients with Parkinson's disease [14], all of which suggest that low vitamin D status is associated with orthostatic hypotension. In a systematic review and meta-analysis about hypovitaminosis D and orthostatic hypotension, it was concluded that hypovitaminosis D was associated with orthostatic hypotension, independent of potential confounders [16]. Although systolic and diastolic blood pressure values are not available in the present study, it can be assumed that the time to complete the verticalization program with the tilt table is an indirect indicator of orthostatic hypotension. In the treatment of orthostatic hypotension of patients with SCI, elastic socks, abdominal pillow, sufficient fluid intake, and gradual verticalization with the tilt table are recommended [26]. Generally, no medical treatment is required. If necessary, salt tablets or midodrine are recommended [29]. According to the results of the present study, in addition to all other beneficial effects, the level of vitamin D in patients with SCI should be checked before starting rehabilitation to prevent orthostatic hypotension, and if there is a deficiency, replacement should be initiated.

Respiratory problems after SCI continue to be the most common cause of morbidity and mortality in this patient population [23, 30]. It is known that the level and severity of injury affects pulmonary function tests in patients with SCI. Patients with high-level SCI have worse pulmonary function tests [31]. According to the results of the present study, although there was no statistical comparison, the pulmonary function test results of patients with neurologic injury levels between T6 and T10 were lower than patients with injury levels of T11 and below. This was not one of the purposes of the present study. However, one of the main aims of the study was to investigate the effects of vitamin D levels on pulmonary function tests. In almost all of the pulmonary function parameters that were studied, it was shown that in all groups with vitamin D deficiency (regardless of the neurologic level), the test results were lower than in the group with non-deficient vitamin D levels. However, these differences were not statistically significant. In some studies among patients with chronic SCI, no significant associations between levels of vitamin D and pulmonary function tests [23] and respiratory symptoms [24] were shown. The findings of the present study show similar results with the literature in patients with SCI.

Among all respiratory function test parameters, MVV has a special feature. This test is an indirect indicator of respiratory muscle strength. The authors of the present study thought a difference might be found both in MVV levels and in GS levels according to the vitamin D levels due to the potential effect of vitamin D on muscle performance. Vitamin D deficiency impairs proximal muscle function, and is thought to predispose falls, especially in the elderly, because skeletal muscle expresses vitamin D receptors and may require vitamin D for maximizing its function [3]. In a study conducted by Flueck et al. [32], athletes with SCI were subjected to vitamin D replacement and its effect on athletic performance was investigated. The authors concluded that the association between

upper body performance or muscle strength and vitamin D status remained unclear. In a cross-sectional study conducted by Barbonetti et al. [10], it was concluded that in people with chronic SCI, a low vitamin D level represented an independent predictor of poor physical function, which was assessed through functional independence in activities of daily living and leisure time physical activity. However, in another longitudinal cohort study that aimed to explore the association of baseline vitamin D levels with one-year changes in physical functional outcomes in people with chronic SCI, it was shown that a low vitamin D level might represent an independent predictor of worsening in physical function outcomes over time [9]. In the present study, functional independence was measured using the motor subscale of FIM. When patients were evaluated without being divided into groups as neurologic impairment levels, a statistically significant relationship was found between vitamin D levels and FIM scores, which showed that those with vitamin D deficiency had lower FIM scores. However, when patients were evaluated according to their neurologic injury levels (between T6 and T10, and T11 and below) there was no statistically significant relationship between vitamin D and FIM scores. The reason for all of the above results (MVV, GS, and FIM scores) may be that the patients included in the study were in the subacute period. When the disease becomes chronic, the likelihood of this effect may well increase.

Limitations

One limitation of this study is that the relationship between vitamin D levels and orthostatic hypotension was examined indirectly. The second limitation of the study is that only patients with motor deficits in their lower extremities were included in the study. Another is that it was performed only in a certain season and patients who were treated in different seasons were not compared. We suggest more comprehensive studies to evaluate blood pressure changes during verticalization programs. We also recommend conducting studies investigating the relationship between vitamin D levels and orthostatic hypotension in patients with high-level SCI because orthostatic hypotension is more common in patients with cervical injuries. There is a need for larger series of studies in which seasonal differences are also examined.

Conclusions

Among patients with SCI, the tilt table verticalization time of patients with vitamin D deficiency is longer than in those with non-deficient vitamin D levels, regardless of the neurologic level. The time to complete the verticalization program with the tilt table is an indirect indicator of orthostatic hypotension. Vitamin D levels should be checked and necessary replacement should be undertaken in patients with SCI in order to help cope with orthostatic hypotension.

References

- Amrein K, Scherkl M, Hoffmann M, Neuwersch-Sommeregger S, Kostenberger M, Tmava Berisha A, et al. Vitamin D deficiency 2.0: an update on the current status worldwide. *Eur J Clin Nutr.* 2020. Epub 2020/01/22. doi: 10.1038/s41430-020-0558-y.
- Aoun A, Maalouf J, Fahed M, El Jabbour F. When and How to Diagnose and Treat Vitamin D Deficiency in Adults: A Practical and Clinical Update. *J Diet Suppl.* 2019;1-19. doi:10.1080/19390211.2019.1577935.
- Charoenngam N, Shirvani A, Holick MF. Vitamin D for skeletal and non-skeletal health: What we should know? *J Clin Orthop Trauma.* 2019;10(6):1082-93. doi:10.1016/j.jcot.2019.07.004.
- Celep G, Durmaz ZH, Dörtok Demir H, Erdoğan Y. Vitamin D status in infancy: What is the solution? *J Surg Med.* 2019;3(8):579-82. doi: 10.28982/josam.555486.
- Holick MF. The vitamin D deficiency pandemic: Approaches for diagnosis, treatment and prevention. *Rev Endocr Metab Disord.* 2017;18(2):153-65. doi: 10.1007/s11154-017-9424-1.

6. Nemunaitis GA, Mejia M, Nagy JA, Johnson T, Chae J, Roach MJ. A descriptive study on vitamin D levels in individuals with spinal cord injury in an acute inpatient rehabilitation setting. *PM R*. 2010;2(3):202-8. doi: 10.1016/j.pmrj.2010.01.010.
7. Lamarche J, Mailhot G. Vitamin D and spinal cord injury: should we care? *Spinal Cord*. 2016;54(12):1060-75. doi: 10.1038/sc.2016.131.
8. Özgürin N, Koyuncu E, Nakipoğlu Yüzer GF, Taşoğlu Ö, Yenigün D. Is spinal cord injury a risk factor for vitamin D deficiency? *Turk J Phys Med Rehab*. 2016;62(1):57-63. doi:10.5606/tftrd.2016.39260.
9. Barbonetti A, D'Andrea S, Martorella A, Felzani G, Francavilla S, Francavilla F. Low vitamin D levels are independent predictors of 1-year worsening in physical function in people with chronic spinal cord injury: a longitudinal study. *Spinal Cord*. 2018;56(5):494-501. doi: 10.1038/s41393-017-0058-7.
10. Barbonetti A, Sperandio A, Micillo A, D'Andrea S, Pacca F, Felzani G, et al. Independent Association of Vitamin D With Physical Function in People With Chronic Spinal Cord Injury. *Arch Phys Med Rehabil*. 2016;97(5):726-32. doi: 10.1016/j.apmr.2016.01.002.
11. Hagen EM. Acute complications of spinal cord injuries. *World J Orthop*. 2015;6(1):17-23. doi: 10.5312/wjo.v6.i1.17.
12. Tesini S, Frotzler A, Bersch I, Tobon A. Prevention of Orthostatic Hypotension with Electric Stimulation in Persons with Acute Spinal Cord Injury. *Biomed Tech (Berl)*. 2013;58 Suppl 1. doi:10.1515/bmt-2013-4029.
13. Annweiler C, Schott AM, Rolland Y, Beauchet O. Vitamin D deficiency is associated with orthostatic hypotension in oldest-old women. *J Intern Med*. 2014;276(3):285-95. doi:10.1111/joim.12201.
14. Jang W, Park J, Kim JS, Youn J, Oh E, Kwon KY, et al. Vitamin D deficiency in Parkinson's disease patients with orthostatic hypotension. *Acta Neurol Scand*. 2015;132(4):242-50. doi:10.1111/ane.12390.
15. McCarroll KG, Robinson DJ, Coughlan A, Healy M, Kenny RA, Cunningham C. Vitamin D and orthostatic hypotension. *Age Ageing*. 2012;41(6):810-3. doi: 10.1093/ageing/afs088.
16. Ometto F, Stubbs B, Annweiler C, Duval GT, Jang W, Kim HT, et al. Hypovitaminosis D and orthostatic hypotension: a systematic review and meta-analysis. *J Hypertens*. 2016;34(6):1036-43. doi: 10.1097/HJH.0000000000000907.
17. Soysal P, Yay A, Isik AT. Does vitamin D deficiency increase orthostatic hypotension risk in the elderly patients? *Arch Gerontol Geriatr*. 2014;59(1):74-7. doi:10.1016/j.archger.2014.03.008.
18. Veronese N, Trevisan C, Bolzetta F, De Rui M, Zambon S, Musacchio E, et al. Hypovitaminosis D predicts the onset of orthostatic hypotension in older adults. *J Am Soc Hypertens*. 2016;10(9):724-32. doi: 10.1016/j.jash.2016.06.038.
19. Nas K, Yazmalar L, Sah V, Aydin A, Ones K. Rehabilitation of spinal cord injuries. *World J Orthop*. 2015;6(1):8-16. doi: 10.5312/wjo.v6.i1.8.
20. Brumpton BM, Langhammer A, Henriksen AH, Camargo CA, Jr., Chen Y, Romundstad PR, et al. Vitamin D and Lung Function Decline in Adults With Asthma: The HUNT Study. *Am J Epidemiol*. 2016;183(8):739-46. doi: 10.1093/aje/kwv243.
21. Ford ES. Lung function, 25-hydroxyvitamin D concentrations and mortality in US adults. *Eur J Clin Nutr*. 2015;69(5):572-8. doi: 10.1038/ejcn.2014.162.
22. Solidoro P, Bellocchia M, Facchini F. The immunobiological and clinical role of vitamin D in obstructive lung diseases. *Minerva Medica*. 2016;107:12-9.
23. Garshick E, Walia P, Goldstein RL, Teylan MA, Lazzari AA, Tun CG, et al. Associations between vitamin D and pulmonary function in chronic spinal cord injury. *J Spinal Cord Med*. 2019;42(2):171-7. doi: 10.1080/10790268.2018.1432305.
24. Walia P, Goldstein RL, Teylan M, Lazzari AA, Hart JE, Tun CG, et al. Associations between vitamin D, adiposity, and respiratory symptoms in chronic spinal cord injury. *J Spinal Cord Med*. 2018;41(6):667-75. doi: 10.1080/10790268.2017.1374020.
25. Gunduz B, Erhan B. Update for Examination Sheet of International Standards for Neurological Classification of Spinal Cord Injury. *Turk J Phys Med Rehab*. 2015;61(1):91-4. doi: 10.5152/tftrd.2015.34682.
26. Gündüz B, Turna I. Rehabilitation of the patient with spinal cord injury. *TOTBID Dergisi*. 2018;17:581-91. doi: 10.14292/totbid.dergisi.2018.77.
27. Roth E, Davidoff G, Haughton J, Ardner M. Functional assessment in spinal cord injury: a comparison of the Modified Barthel Index and the 'adapted' Functional Independence Measure. *Clin Rehabil*. 1990;4:277-85.
28. Küçükdeveci AA, G. Y., Elhan AH, Sonel B, Tennant A. Adaptation of the Functional Independence Measure for use in Turkey. *Clin Rehabil*. 2001;15(3):311-9.
29. Güzelküçük Ü, Duman İ, Yılmaz B, Tan AK. Midodrine Treatment of Orthostatic Hypotension in Patients with Acute Tetraplegia. *Turk J Phys Med Rehab*. 2012;58(Suppl 1):56-7.
30. Ordu Gökçaya NK. Pulmonary Dysfunction As a Member of Autonomic Dysfunction Family: From a Different Window. *Turk J Phys Med Rehab*. 2012;58(Suppl 1):16-20.
31. Malas FU, Koseoglu F, Kara M, Ece H, Aytekin M, Ozturk GT, et al. Diaphragm ultrasonography and pulmonary function tests in patients with spinal cord injury. *Spinal Cord*. 2019;57(8):679-83. doi: 10.1038/s41393-019-0275-3.
32. Flueck JL, Schlaepfer MW, Perret C. Effect of 12-Week Vitamin D Supplementation on 25(OH)D Status and Performance in Athletes with a Spinal Cord Injury. *Nutrients*. 2016;8(10). doi:10.3390/nu8100586.

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