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Original Article

The effects of weekly or daily oral cholecalciferol use on muscle strength, muscle thickness, and functional independence in patients with spinal cord injury

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ABSTRACT

Objectives: This study aims to evaluate the effects of vitamin D supplementation at different doses and dose intervals on upper extremity muscle strength, muscle thickness, and functional independence of patients with paraplegic spinal cord injury (SCI).

Patients and methods: This prospective controlled clinical trial included 64 paraplegic patients (45 males, 19 females; mean age: 39.7±11.5 years; range, 18 to 64 years) with serum 25-hydroxyvitamin D (25[OH]D) levels <20 ng/mL between June 2020 and June 2021. Participants were divided into three groups: control (n=20), daily supplementation with 6000 IU cholecalciferol (n=23), and weekly supplementation with 50,000 IU cholecalciferol (n=21) for eight weeks. Hand grip strength was assessed with a dynamometer, muscle thickness was measured using ultrasonography, and functional independence was evaluated with the Spinal Cord Independence Measure III.

Results: Serum 25(OH)D levels significantly increased in both supplementation groups compared to baseline (p=0.001). Nondominant hand grip strength significantly improved in both groups (daily, p=0.025; weekly, p=0.038). Muscle thickness of the biceps brachii significantly increased in the daily group (p<0.05), while triceps brachii thickness significantly improved in both groups (p<0.001). Spinal Cord Independence Measure III scores, encompassing self-care, respiratory-sphincter control, and mobility, showed significant improvements in the supplementation groups (p<0.05), but no changes were observed in the control group. No significant differences were found between daily and weekly supplementation regimens.

Conclusion: Vitamin D supplementation, whether daily or weekly, improved muscle performance and functional independence in individuals with SCI. While these findings support the inclusion of vitamin D replacement in rehabilitation programs, larger and longer-term studies are needed to confirm the benefits.

Keywords: Functional independence, muscle strength, spinal cord injury, vitamin D deficiency, vitamin D replacement.

Vitamin D deficiency prevalence is higher in individuals with chronic spinal cord injury (SCI) than in the healthy population.[1] Individuals with SCI are susceptible to vitamin D deficiency due to several reasons, including accumulation of fat mass, insufficient exposure to sunlight, use of drugs that impair vitamin D metabolism, chronic liver disease due to alcoholism, and the frequent occurrence of chronic kidney failure.[2-4] It is expected that vitamin D deficiency will have negative effects on patients during the rehabilitation of SCI. Therefore, individuals with SCI will experience difficulties in integration into social life.

After the determination of vitamin D receptor in muscle cells, the direct effect of vitamin D on muscle tissue began to be understood.[5] The vitamin D receptor has been shown to affect muscle growth through muscle cell proliferation and provide higher muscle contractility by increasing sarcoplasmic calcium.[6] In a meta-analysis of 30 randomized controlled trials examining the effects of vitamin D on muscle function, vitamin D

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supplementation had a small but positive impact on overall muscle strength.[7] The relationship between serum vitamin D levels and strength or physical performance remains a topic of investigation in 2024. In a meta-analysis conducted among athletes, upper extremity muscle strength was assessed through grip strength evaluation.[8]

Skeletal muscle contraction, muscle strength, and postural stability are known to be associated with circulating vitamin D levels, and skeletal muscle weakness appears to be a common symptom of vitamin D deficiency. Vitamin D also has a protective and bioactive effect on neurological disorders involving the musculoskeletal system, such as SCI. In the meta-analysis published in 2023, the accelerating and contributing effect of vitamin D on the rehabilitation of chronic SCI individuals was mentioned.[9] The authors focused on studies suggesting that low levels of vitamin D may be associated with reduced physical performance, cardiopulmonary disease, heterotopic ossification, and depression in patients with chronic SCI.

In individuals with thoracic spinal cord injuries, the preserved function of upper extremity muscles plays a critical role in the rehabilitation process. Paraplegic patients rely on the coordinated use of upper limb flexor and extensor muscles to perform essential functional tasks, such as bed mobility and transfers between the bed, wheelchair, and toilet. The effective use of manual wheelchairs and crutches also depends heavily on upper extremity strength and functionality.[10] Strengthening these muscle groups not only enhances the performance of these critical activities but also reduces the risk of upper extremity overuse injuries, decreases the likelihood of shoulder pain, and ultimately improves the capacity to perform daily activities.[11]

Few studies in the literature have investigated the effect of vitamin D supplementation on upper extremity muscle performance in individuals with SCI.[12] Some studies reported a positive impact of vitamin D on the rehabilitation of individuals with SCI, while others mentioned the need for further studies.[13-17] In a study conducted on elite athletes with SCI, an improvement in grip strength was observed in athletes who received vitamin D supplementation, whereas no significant changes were noted in wheelchair sprint performance.[17] Most studies utilized grip strength to evaluate upper extremity muscle strength, while assessments using ultrasonography and muscle thickness measurements have not been reported.

The primary aim of this study was to investigate the effects of different vitamin D replacement protocols on upper extremity muscle strength and muscle thickness in paraplegic patients with vitamin D deficiency during their rehabilitation process. The secondary aim was to evaluate the impact of vitamin D replacement on the functional independence of individuals with SCI.

PATIENTS AND METHODS

This prospective controlled clinical trial included a total of 64 paraplegic patients (45 males, 19 females; mean age: 39.7±11.5 years; range, 18 to 64 years) with serum 25-hydroxyvitamin D (25[OH]D) levels <20 ng/mL and hospitalized in the rehabilitation clinic of the İstanbul Physical Medicine and Rehabilitation Training and Research Hospital between June 2020 and June 2021. Since upper extremity muscle evaluation was planned to be performed. Spinal cord injury patients with complete/incomplete, traumatic/nontraumatic, and neurological levels between T2 and T12 were accepted. Patients with a medical history of chronic liver disease, chronic kidney disease, hypothyroidism, hyperparathyroidism, hypogonadism, rheumatoid arthritis, ankylosing spondylitis, multiple myeloma, leukemia, inflammatory bowel disease, and malabsorption syndrome were excluded from the study. Patients were questioned about the use of drugs that induce CYP3A4, such as carbamazepine, phenytoin, and rifampicin, which may interact with vitamin D. Patients who had used bisphosphonate, teriparatide, denosumab, calcium or vitamin D supplements, or corticosteroids in the last six months were excluded from the study, as these agents could have altered vitamin D and serum calcium levels. Obese patients with a body mass index >30 were excluded from the study, as obesity may impact vitamin D levels. Parameters that may cause myopathy, including magnesium (mg/dL), triglyceride (mg/dL), total cholesterol (mg/dL), low-density lipoprotein (mg/dL), albumin (g/L). C-reactive protein (mg/L), erythrocyte sedimentation rate (mm/h), and thyroid stimulating hormone, were evaluated to avoid any difference between study groups, and patients with pathological values were excluded from the study. Written informed consent was obtained from each participant. The study protocol was approved by Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (Date: 16.03.2020. No: 2020-06-29). ClinicalTrials Identifier: NCT04400747. The study was conducted

in accordance with the principles of the Declaration of Helsinki.

Those with high serum calcium levels (>10.6 mg/dL; n=4). kidney, ureter, and bladder stones in urinary ultrasonography (USG; n=6), and those who did not want to take vitamin D treatment (n=10) were included in the control group (n=20). Other patients were randomized using a computed-based system to receive 6000 IU of cholecalciferol daily (n=21) and 50,000 IU of cholecalciferol weekly (n=23) for eight weeks. Treatment groups were given a calcium-rich diet of 1000 mg daily for eight weeks during the study. The rehabilitation program was applied to all patients by the same physiotherapist for 1 h, six days a week, for eight weeks (Figure 1).

In the treatment of vitamin D deficiency, the American Endocrine Society recommends using 50,000 IU weekly or 6000 IU daily for eight weeks, and follow-up assessment at the end of eight weeks.[18] In our study, serum 25(OH)D levels of daily and weekly vitamin D treatment groups were examined at the end of eight weeks. Determination of 25(OH)D3 was performed using the electrochemiluminescent method on the Cobas analyzer (Roche Diagnostics, Mannheim, Germany).

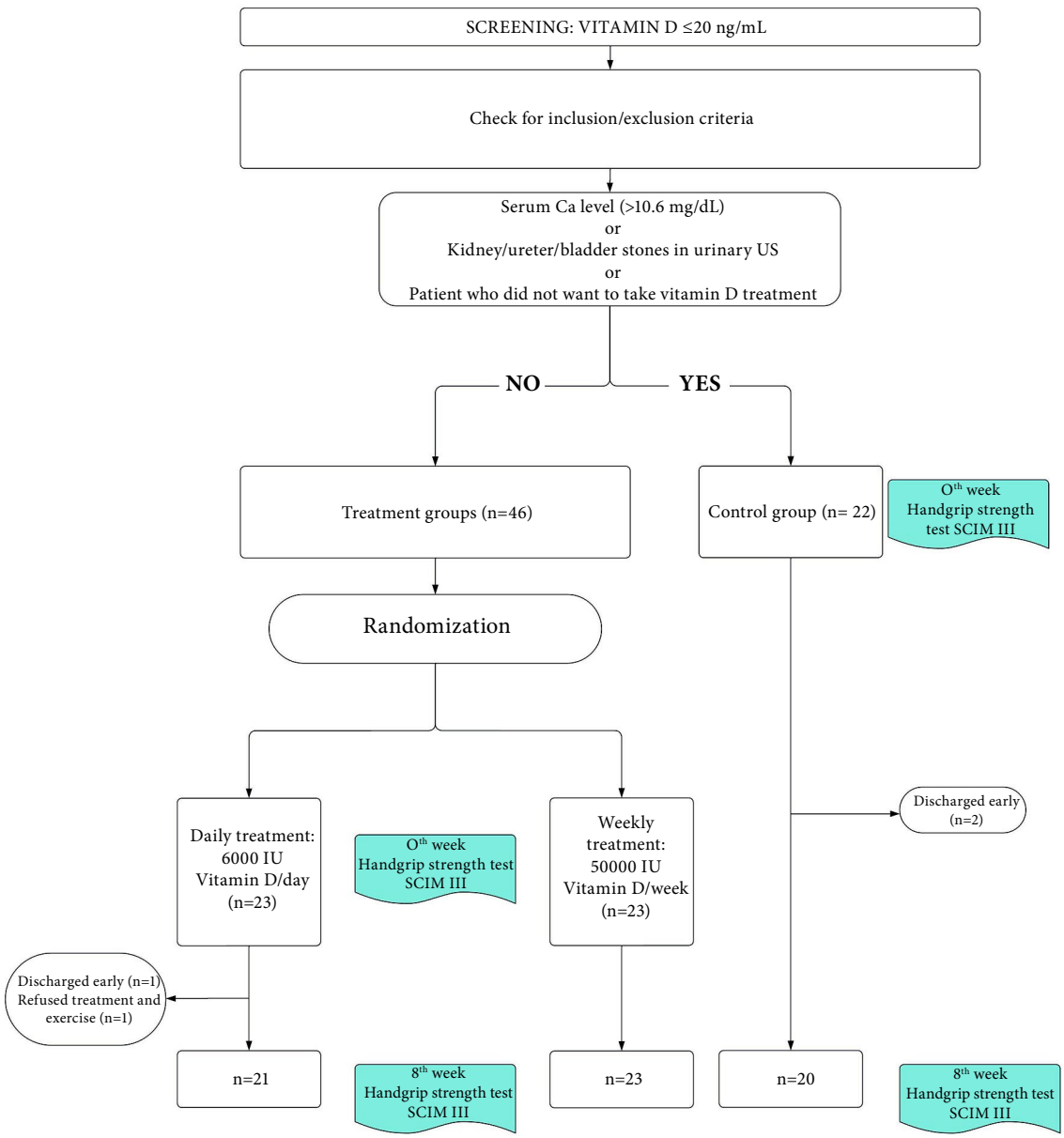

Figure 1. Flowchart of patient groups.

US: Ultrason; SCIM III: Spinal Cord Independence Measurement Version III.

In our study, the Jamar Plus hydraulic hand grip dynamometer (Sammons Preston, Inc., Bolingbrook, IL., USA) was used to evaluate the hand grip strength at the beginning and the end of eight weeks. The test was performed for dominant and nondominant upper extremities. All patients were evaluated 30 min after meals, before exercise, and while sitting in their wheelchairs. The test was performed with the shoulder in full adduction, elbow flexed at 90°, and forearm in mid-prone neutral position. The dynamometer was squeezed with maximal force three times, and the mean of these three measurements was used to assess grip strength measured in kilograms.[19]

All ultrasonographic measurements were made by the same person using a diagnostic USG device (Arietta 65; Hitachi, Tokyo, Japan) and a linear probe. Before evaluating the measurements, all muscle measurements were repeated at different times to determine whether the results of the researcher who performed the examinations were consistent, and intraclass correlation (ICC) analysis was performed between the two measurements. The intraclass correlation coefficient was excellent in all tested muscles. Biceps brachii (BB) and triceps brachii (TB) muscle thicknesses were measured in the bilateral upper extremity. Bilateral upper extremity measurement points were determined with the help of a tape measure beforehand. The transducer was placed at the midpoint between the elbow crease and greater tubercle of the humeral head for the BB and halfway between the olecranon and lateral edge of the scapular spine for the TB. The point between the uppermost part of the bone echo of the humerus and the superficial fascia of the muscles was measured. The measurement was made in a sitting position in the patient's wheelchair, with the arm parallel to the body, the elbow flexed at 90°, and the forearm and hand in the neutral position. A generous amount of contact gel was used to minimize the required pressure of the transducer on the skin. Each measurement was repeated thrice, and the mean value was used in the analysis.[20]

Spinal Cord Independence Measurement Version (SCIM) III, which is used in the functional evaluation of individuals with SCI, was performed in all patients included in the study at baseline and the eighth week. The patients were evaluated in three subscales. A total of 17 items about self-care, respiration-sphincter, and mobility were questioned by the clinician. Higher scores indicated a higher independence rate. The SCIM III is accepted as the most sensitive, valid, and reliable functional assessment scale for disability in individuals with SCI.[21] The Turkish adaptation and validity study of this scale was carried out by Kesiktas et al.[22]

Statistical analysis

The required sample size was determined with a power analysis based on the findings of Gupta et al.[19] using the G.Power version 3.1.9.4 software (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany). In Gupta et al.'s study, the effect size of 1.33 was calculated from the change in hand grip muscle strength between the vitamin D group (3.1±2.5) and the control group (0.3±1.59). For the present study, calculations were performed with an alpha level of 0.05, power of 0.95, and number of groups set to three, and the required sample size was determined as 18 per group.

The data were analyzed using NCSS (Number Cruncher Statistical System) 2007 (NCSS LLC, Kaysville, UT, USA) software. The normality of the data distribution was tested using the Shapiro-Wilk test. Descriptive statistics were applied for both categorical and continuous variables, Continuous variables were summarized as mean ± standard deviation, median, minimum, and maximum values, while categorical variables were presented as frequencies and percentages. The chi-square test and Fisher exact test were used for categorical variables, as appropriate. For comparisons of continuous variables that did not meet the normality assumption, the Kruskal-Wallis test was applied for group comparisons, and the Mann-Whitney U test was used for post hoc pairwise comparisons. To account for multiple comparisons. Bonferroni correction was applied to the p-values obtained from the Mann-Whitney U test. To evaluate within-group changes over time, the Wilcoxon signed-rank test was performed for continuous variables that were nonnormally distributed. Additionally, Cohen's d effect sizes were calculated to evaluate the magnitude of the observed changes in key outcomes, including BB muscle thickness and SCIM III scores, where moderate effects were observed. Effect sizes provided a practical measure of the clinical significance of the findings, complementing p-value interpretations. The type 1 error rate (alpha) was set at 0.05, and p-values <0.05 were considered statistically significant.

TABLE 1
Comparison of demographic characteristics and comorbidities by groups

	Daily group (n=21)		Weekly group (n=23)		Control group (n=20)		
	n	%	n	%	n	%	*p*
Sex							
Female	5	23.8	8	34.8	6	30.0	0.728[a]
Male	16	76.2	15	65.2	14	70.0	
Smoke							
No	11	52.4	9	39.1	7	35.0	0.495[a]
Yes	10	47.6	14	60.9	13	65.0	
Diabetes mellitus							
No	19	90.5	20	87.0	17	85.0	0.865
Yes	2	9.5	3	13.0	3	15.0	
Hypertension							
No	20	95.2	20	87.0	19	95.0	0.505[b]
Yes	1	4.8	3	13.0	1	5.0	
Coronary artery disease							
No	20	95.2	23	100.0	20	100.0	0.353[b]
Yes	1	4.8	0	0.0	0	0.0	
Asthma							
No	21	100.0	22	95.7	20	100.0	0.404[b]
Yes	0	0.0	1	4.3	0	0.0	
Constipation							
No	17	81.0	17	73.9	17	85.0	0.656[b]
Yes	4	19.0	6	26.1	3	15.0	
ASIA Impairment Scale							
A	9	42.9	14	60.9	9	45.0	0.891[b]
B	4	19.0	3	13.0	4	20.0	
C	6	28.6	4	17.4	4	20.0	
D	2	9.5	2	8.7	3	15.0	

[a] Pearson chi-square test; [b] Fisher exact test.

RESULTS

Table 1 and Table 2 shows the sociodemographic properties of all the groups, such as age, sex, body mass index, smoking, and the classification of patients according to the American Spinal Injury Association Impairment Scale. There were no significant differences in these variables between these three groups. The time elapsed after injury, additional disease, constipation, and serum 25(OH)D, calcium. C-reactive protein, erythrocyte sedimentation rate, thyroid stimulating hormone, total cholesterol, triglyceride, fasting blood glucose, albumin, and magnesium values did not show any statistically significant difference in the participants according to the groups examined at baseline (p>0.05). Phosphorus values showed statistically significant differences according to the groups (p=0.038; Table 2). In post hoc analysis, a p-value of 0.029 was observed between the weekly and control groups.

Serum 25(OH)D vitamin levels of four participants in the group receiving 6000 IU of vitamin D daily were <30 ng/mL after eight weeks. In the group that received 50,000 IU of vitamin D weekly, serum 25(OH)D levels of two participants in total remained <30 ng/mL after eight weeks. In both the daily and weekly groups, the increase in serum 25(OH)D levels in the eighth week compared to the initial measurement was statistically significant

TABLE 2
Comparison of demographic characteristics and blood values by groups

	Daily group (n=21)			Weekly group (n=23)			Control group (n=20)			
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	p^a
Age (year)	38.14±10.82	37	20-60	41.91±12.61	40	18-64	38.75±11.09	42	20-59	0.607
Body mass index (kg/m^2)	25.79±3.19	26.37	17.92-28.83	26.55±4.23	27.78	17.24-29.86	24.75±2.28	24.16	20.07-29.39	0.119
Time since injury (mo)	43.95±18.46	37	19-85	43.39±41.15	30	8-168	42.10±25.11	33	11-88	0.363
25(OH)D3 (ng/mL)	12.48±4.09	13	5-20	12.91±4	12	6-20	14.15±5.18	15.5	30-20	0.416
Ca (mg/dL)	9.5±0.49	9.49	8.73-10.41	9.36±0.64	9.2	8.1-9.84	9.65±0.73	9.33	8.84-11.16	0.392
CRP (mg/L)	6.9±6.98	3.3	0.4-23	7.3±8.56	3.9	0.8-39	7.4±6.71	5	0.3-22	0.965
ESR (mm/h)	7.67±5.21	7	2-23	10.48±8.67	6	1-36	13.83±13.35	9.5	1.61-58	0.373
TSH (mIU/mL)	2±0.92	2.31	0.47-3.59	2.24±1.08	2.17	0.42-5.14	2.3±1.07	2.13	0.97-4.41	0.792
Total kolesterol (mg/dL)	173.24±30.88	170	124-234	170.87±52.13	187	50-266	167.35±62.7	157.5	98-335	0.503
Trigliserid (mg/dL)	164.24±70.87	173	44-285	140.87±54.97	132	70-266	136.7±58.57	130	35-273	0.343
FBS (mg/dL)	98.33±15.87	96	83-152	106.43±25.73	98	72-162	101.15±16.52	96.5	78-154	0.511
Albumin (g/L)	41.92±3.42	42	34-50	41.03±3.31	41	35-51	41.25±3.14	41	35-47	0.385
Phosphorus (mg/dL)	4.05±0.79	4.07	3-5.73	4.16±0.7	4.18	2;82-5.77	3.57±0.71	3.57	2.12-4.89	0.038*
Magnesium (mg/dL)	2.11±0.41	2.03	1.65-3	2.18±0.42	2.05	1.81-3.15	2.16±0.4	2.09	1.58-3.07	0.726

SD: Standard deviation; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; TSH: Thyroid stimulating hormone; FBS: Fasting blood sugar; [a] Kruskall-Wallis test; Ca: Calcium; * p<0.05.

TABLE 3
Comparison of hand grip strength within and between groups

	Daily group (n=21)			Weekly group (n=23)			Control group (n=20)			
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	p *between groups*[a]
Dominant										
Beginning	32.36±11.57	30.5	18.1-57.8	31.82±13.32	27	16-61.9	31.47±9.13	30.85	19.8;49.7	0.973
8th week	33.77±11.19	29.9	17-58.5	31.74±13.6	26.8	12.5-58.6	31.82±8.28	29.9	19;49	0.715
p in group[b]		0.067			0.976			0.432		
Non-dominant										
Beginning	33.53±11.8	33.5	14.9;61.6	30.89±13.78	26.1	12.9-60.1	31.47±9.13	30.85	19.8;49.7	0.613
8th week	35.08±11.18	35	13.4;61.1	31.76±13.96	26.8	11.4-62.4	31.82±8.28	29.9	19;49	0.337
p in group[b]		0.025*			0.038*			0.632		

SD: Standard deviation; [a] Kruskall-Wallis test; [b] Wilcoxon signed ranks test; * p<0.05.

TABLE 4
Comparison of BB and TB muscle thicknesses within and between groups

	Daily group (n=21)			Weekly group (n=23)			Control group (n=20)			
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	p *between groups*[a]
Left BB muscle thickness										
Beginning	25.15±4.87	24.2	18-33.9	25.39±7.08	26.8	12.3-39.8	24.07±5.69	26	16.5-32.6	0.706
8th week	27.4±4.61	28	18.8-31.1	25.24±6.93	26.6	14.1-39.9	24.44±5.51	25.5	15.8-32	0.276
p in group[b]		0.003*			0.615			0.167		
Right BB muscle thickness										
Beginning	26.42±5.34	25.4	18-38	26.06±5.92	25.5	15.8-38	25.88±7.56	23.55	16.4-38	0.843
8th week	27.61±5.61	26.5	18.6-37.4	26.68±5.95	27	16-37	25.5±7.29	23	15-38.1	0.556
p in group[b]		0.038*			0.059			0.140		
Left TB muscle thickness										
Beginning	27.68±8.27	25.2	16.1-43.1	23.95±7.47	24	12.2-41	25.88±7.56	23.55	16.4-38	0.287
8th week	29.97±10.52	25.8	17.3-51.9	25.62±8.31	24.7	13-44.2	25.5±7.29	23	15-38.1	0.269
p in group[b]		<0.001*			<0.001*			0.931		
Right TB muscle thickness										
Beginning	26.5±9.08	24.8	14.7-43.8	23.57±8.66	21.3	13.7-45.1	25.18±8.5	24.3	10.1-42.8	0.511
8th week	28.42±9.16	27.5	15-43.1	25.3±8.67	24.5	13.7-45.3	26.34±8.96	27.4	10.2-42	0.469
p in group[b]		<0.001*			<0.001*			0.093		

BB: Biseps brachii; TB: Triceps bracii; SD: Standard deviation; [a] Kruskall-Wallis test; [b] Wilcoxon signed ranks test; * p<0.05.

TABLE 5
Comparison of SCIM III scores within and between groups

	Daily group (n=21)			Weekly group (n=23)			Control group (n=20)			
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	p *between groups*[a]
Self-care										
Beginning	16.29±2.94	16	10-20	16.09±3.8	17	10-20	17.25±3.54	18	10-20	0.425
8th week	17.52±2.93	19	9-20	17.48±3.2	19	9-20	17.35±4.03	19.5	10-20	0.878
p in group[b]		0.013*			0.002*			0.394		
Respiration and sphincter management										
Beginning	29.1±9.8	28	10-40	28.87±9.37	27	10-40	32.95±8.18	37	19-40	0.368
8th week	32±7.77	32	16-40	32.57±7.26	32	16-40	33.05±8.68	36.5	13-40	0.817
p in group[b]		0.016*			<0.001*			0.623		
Mobility										
Beginning	19.14±8.18	18	8-33	18.3±8.36	18	8-34	19.25±8.17	19	3-29	0.768
8th week	22.19±7.17	19	9-37	21.22±7.23	20	10-37	19.65±8.02	18.5	3-30	0.668
p in group[b]		<0.001*			<0.001*			0.590		
Total score										
Beginning	64.00±18.68	59	34-93	63.26±19.79	64	30-94	69.45±17.46	75.5	29-89	0.548
8th week	71.71±15.73	71	34-92	71.26±15.62	71	34-95	70.05±19.22	75	23-90	0.998
p in group[b]		<0.001*			<0.001*			0.605		

SD: Standard deviation; [a] Kruskall-Wallis test; [b] Wilcoxon signed ranks test; * p<0.05.

(p<0.001). The mean serum 25(OH)D levels increased from 12.48±4.0 ng/mL to 33.62±8.0 ng/mL in the daily supplementation group and from 12.91±4.0 ng/mL to 34.96±4.9 ng/mL in the weekly supplementation group. In the evaluation between the groups, serum 25(OH)D level measurement value in the eighth week did not show a statistically significant difference (p>0.05).

The increase in the nondominant hand grip strength in the eighth week was statistically significant compared to the initial measurement in the daily group (p=0.025). The increase in the nondominant hand grip strength in the eighth week was statistically significant compared to the initial measurement in the weekly group (p=0.038). The eighth week measurement value of both dominant and nondominant hand grip strength did not show a statistically significant difference between the groups (p>0.05) (Table 3).

Compared to the initial measurement of left and right BB muscle thickness in the daily treatment group, the increase observed in the eighth week was statistically significant (p=0.013; p=0.038). Compared to the initial measurement of left and right BB muscle thickness in the weekly treatment group, the increase in the eighth week measurement was not statistically significant (p>0.05). In the control group, the increase in bilateral BB muscle thickness in the eighth week was not statistically significant compared to the initial measurement (p>0.05). In the daily and weekly groups, the increase in bilateral TB muscle thickness in the eighth week was statistically significant compared to the initial measurement (p<0.001). In the control group, the increase in bilateral TB muscle thickness in the eighth week was not statistically significant (p>0.05; Table 4).

The SCIM III scale, which was completed at baseline and the eighth week, was evaluated under three subscales: breathing, sphincter control, and mobility. In the daily and weekly treatment groups, the increase in all scores in the eighth week measurement was statistically significant, However, no statistically significant difference was found in the control group (Table 5).

The effect size for the BB muscle thickness in the daily supplementation group was 0.46, indicating a moderate effect of vitamin D replacement on muscle thickness. In contrast, the effect size for the SCIM III scores was 0.41 in the daily group and 0.40 in the weekly group, suggesting a moderate improvement in functional independence following vitamin D supplementation.

DISCUSSION

The prevalence of insufficient serum 25(OH)D levels in individuals with SCI admitted to rehabilitation centers has been found to range from 67 to 93%.[23] The SCI population is considered to be at high risk for vitamin D deficiency, and treatment methods should be determined based on the most current published guidelines.[18,24] In this special population of individuals with disabilities, vitamin D deficiency has been implicated as a contributing factor to conditions such as widespread muscle pain, early-onset muscle weakness, challenges experienced during the rehabilitation process, and delays in achieving independence in activities of daily living (ADL).[1,9,25,26] In this study, we investigated the effects of vitamin D supplementation on upper extremity performance and independence in ADL in SCI individuals with vitamin D deficiency who were treated in a rehabilitation clinic. Different protocols of vitamin D supplementation (weekly/daily) resulted in statistically significant differences in muscle strength, muscle thickness, and functional independence compared to the control group.

Bauman et al.[14] instructed individuals with SCI to use 800 IU of cholecalciferol daily and they could not reach a sufficient level of 25(OH)D. The same author increased 25(OH)D levels to >30 ng/mL within 12 weeks by giving 2000 IU of cholecalciferol daily to individuals with SCI.[15] Flueck et al.[16] gave 6000 IU of cholecalciferol daily for 12 weeks to athletes with SCI and evaluated upper extremity muscle strength and performance. Vitamin D levels reached a sufficient level (>30 ng/mL) in these athletes using wheelchairs, and no signs of toxicity were observed.

In our study, we divided our vitamin D replacement group into two. At the end of eight weeks, serum 25(OH)D vitamin levels of four patients from the daily group and two patients from the weekly group remained below 30 ng/mL. Except for these patients, patients in the replacement group achieved values above 30 ng/mL. Serum 25(OH)D level measurement has become a controversial issue in the literature, as the measured 25(OH)D is a reserve form bound to the circulating vitamin D-binding protein. All changes related to vitamin D-binding

protein can change the measured serum 25(OH)D level.[27] In addition, since the half-life of 25(OH)D is weeks, it is possible to overestimate the body's stored vitamin D level.[28] These are parameters that are overlooked in epidemiological and interventional studies. As in our study, we conclude that laboratory results in interventional studies cannot give precise information about the level of active vitamin D used by the body.

In a study conducted by Apaydin et al.,[29] different doses of vitamin D3 were given to 60 postmenopausal healthy women, and muscle strength was evaluated by isokinetic evaluation at the fourth and 12th weeks. Although the increase of serum 25(OH)D levels appeared to be more significant with a single dose of high-dose vitamin D3, the quadriceps muscle strength score increased significantly at four weeks and the hamstring muscle strength score at 12 weeks in the daily treatment group. In a study conducted by Dhanwal et al.,[30] a positive correlation was found between low vitamin D and hand grip strength in a population of 95 hip fractures. In another study, hand grip strength was increased in the group receiving vitamin D compared to placebo, as in our study.[19]

In addition to these, studies without improvement in upper extremity muscle strength have also been published in the literature. In a pilot study conducted by Amorim et al.,[23] 14 SCI patients were followed for eight weeks in a rehabilitation center. There was no increase in hand grip strength in the vitamin D group, and it was stated that the reason for this was impaired hand control. When the study is examined in detail, it is observed that SCI patients with cervical lesions were also included in the study. In the study of Flueck et al.,[16] the vitamin D levels in the patients reached the optimal level (>40 ng/mL). However, due to the absence of the placebo group and the inclusion of athletes with cervical lesions in the study, a conclusion could not be reached on whether vitamin D affects upper extremity muscle performance. Since all our study participants were paraplegic, the hand grip dynamometer, which can evaluate the upper extremity muscle strength globally, could be used easily, and the results were more reliable than other studies. There was no difference in the control group, but the change in strength at eight weeks in the vitamin D groups was a small effect observed in the present study. Since there was no difference between the groups at the beginning, and the same exercises and diet were given to each group, we believe that the increase in muscle strength was the effect of vitamin D.

There were few studies in the literature examining the relationship between vitamin D and muscle thickness. In a cross-sectional study conducted by Ata et al.,[31] skin, fat, and muscle thickness were examined by USG and compared between groups with serum 25(OH)D levels <20 ng/mL and >20 ng/mL. There was no difference between the groups in terms of muscle thickness and grip strength. The fact that the study did not have a control group and that it was evaluated without vitamin D replacement follow-up is an important limitation.

There is only one prospective study in the literature that measured muscle thickness after vitamin D replacement. In the study of Cuellar et al.,[32] 50.000 IU cholecalciferol replacement was given weekly to the participants for 12 weeks, and their trunk muscle thickness was evaluated with USG. There was no significant difference between the groups in the change in the size or function of the abdominal or multifidus muscles after 12 weeks of vitamin D supplementation. Bilateral TB muscle thicknesses evaluated in our study showed a statistically significant difference at the end of eight weeks in the intragroup evaluation in both vitamin D replacement groups. However, the change observed in the control groups was not significant.

In our study, it is notable that the TB muscle showed a more pronounced positive response to vitamin D replacement compared to the BB muscle. Han et al.,[8] evaluated the effects of vitamin D supplementation on healthy athletes and reported the most significant impact on the quadriceps muscle group. It has been demonstrated that vitamin D intake enhances the diameter and number of type II skeletal muscle fibers, particularly type IIa fibers.[33] This observation may explain the varying degrees of muscle strength improvement and muscle fiber hypertrophy across different muscle groups. Specifically, in upper extremity muscles that undergo morphological changes following SCI, the effects of vitamin D may differ.[34,35] Further studies are required to establish definitive conclusions in this area.

The negative interaction between vitamin D and physical function in individuals with SCI should be considered. Due to muscle wasting and disability, people with SCI lose their functional

independence in ADL and their ability to perform physical activity. The most valuable study on this issue belongs to Barbonetti et al.[26] In the study of 100 chronic SCI individuals, an independence assessment was done by SCIM III. As a result of the study, lower 25(OH)D levels were associated with poorer SCIM III scores. From this study, it is not possible to determine whether vitamin D supplementation improves physical performance in individuals with SCI. Our study differed from the literature by assessing SCIM III score before and after vitamin D supplementation in individuals with SCI. A statistically significant difference was found within the group in the self-care, respiratory, sphincter control, and mobility parts of the scale between the baseline and the eighth week in both groups receiving vitamin D supplementation. The moderate effect sizes observed for SCIM III scores (0.41 for daily and 0.40 for weekly supplementation) reflect meaningful improvements in the participants' ability to perform ADL. However, while statistically significant, these effects were not large, suggesting that the overall impact of vitamin D supplementation on functional outcomes and muscle structure may be modest in the short term.

It is necessary to mention some limitations of this study. First, there was a limited sample size and a short follow-up period. Therefore, we believe that the effect size in our study was low to moderate. Second, the eight-week vitamin D serum levels were not analyzed in the control group. It was accepted that the 25(OH)D levels of the untreated group did not change. Third, although the treatment group of the study was designed randomly, the control group patients were not randomized.

In conclusion, this study evaluated the effects of vitamin D on muscle performance, including muscle strength, muscle thickness, and functional independence. Daily and weekly vitamin D treatment provided minimal improvement in upper extremity performance and functional assessment in individuals with SCI. There was no significant difference in dose and interval in vitamin D replacement.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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