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Effects of cholecalciferol supplementation on inflammatory markers and muscle damage indices of soccer players after a simulated soccer match

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ABSTRACT

Objectives: Soccer-induced muscle damage and inflammation lead to a reduction in athletic performance. The aim of this study was to determine whether supplementation with cholecalciferol would reduce inflammation and muscle damage in soccer players after a simulated soccer match.
Methods: Twenty-two soccer players (median age 27 y, interquartile range 5 y) were divided randomly into two groups, as follows: a cholecalciferol group (n = 11) and a placebo group (n = 11). Cholecalciferol supplements (50 000 IU/wk) or placebos were administered to the groups by an independent co-worker. After 8 wk, the athletes participated in a simulated soccer match, and perceived exertion and heart rates were measured during the trial. Blood samples were obtained presupplementation, postsupplementation, immediately after, and 2- and 24-h postexercise for measurement of lactate dehydrogenase, creatine phosphokinase, C-reactive protein (CRP), and interleukin (IL)-6.
Results: The intervention group demonstrated a significant increase in serum 25-hydroxyvitamin D levels (53.93, 10.68 ng/mL, $P < 0.0001$), which is the best indicator of vitamin D levels in the body, with no change in the circulating markers of muscle damage and CRP ($P > 0.05$) but showed increased IL-6 ($P = 0.034$). In addition, the ratings of perceived exertion and heart rates were not altered by vitamin D compared with placebo ingestion ($P = 0.155$ versus $P = 0.261$; $P = 0.600$ versus $P = 0.983$).
Conclusion: The study showed that 50 000 IU/wk of cholecalciferol supplementation for 8 wk increased the 25-hydroxyvitamin D levels, with no effect on muscle damage indices or CRP. However, The IL-6 concentration was generally higher in the intervention group.

Introduction

Inflammation, muscle damage, and muscle pain are the most common problems seen in athletes [1,2]. Hence, although vigorous exercise results in beneficial effects on their health, it also can lead to a loss of energy, inflammation, oxidative stress, and muscle damage, which can have adverse effects on some organs of the body and negative effects on general health [3–5]. Soccer is considered one of the most popular and lucrative sports in the world; it requires muscle strength, aerobic capacity, and high speed [6,7]. At the same time, playing soccer leads to fatigue and muscle damage, suggesting that achieving the right balance between stress and recovery is of the utmost importance in maximizing the performance and health of athletes [8]. Currently, antiinflammatory drugs, antioxidant supplements, immobilization periods, and ultrasound therapy are used to relieve the pain associated with the injuries mentioned here [9,10]. However, other strategies for accelerating recovery include a personalized diet, as well as the consumption of certain supplements [11].

Vitamin D is an essential micronutrient for muscle strength and control of calcium homeostasis [12]. Recent evidence has shown that vitamin D has roles in health, athletic performance, inflammation modification, and immune function [13]. At present, there is no consensus on healthy serum concentrations of 25-hydroxyvitamin D (25[OH]D); however, the Endocrine Society Committee (ESC) has defined 25(OH)D concentrations ≥ 30 ng/mL (≥ 75 nmol/l)

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as sufficient, 21–29 ng/mL (52.5–72.5 nmol/l) as insufficient, and ≤ 20 ng/mL (≤ has defined 25(OH)D concentrations 30 ng/mL (75 nmol/L) as sufficient, 21 to 29 ng/mL (52.5–72.5 nmol/L) as insufficient, and 20 ng/mL (50 nmol/L) as deficient [14,15].

Because inflammation and free radical production are associated with muscle fatigue during prolonged exercise, supplementation with vitamin D may lead to a delay in fatigue [16]. Calcitriol, the active form of vitamin D, is produced by the hydroxylation of 25(OH)D in the body. It modulates the activation, proliferation, and differentiation of immune and inflammatory cells [17,18]. These cells also convert 25(OH)D to calcitriol [17,19]. Vitamin D promotes a T-cell shift from T-helper 1 cells to T-helper 2 cells. This effect results in a decreased production of type 1 proinflammatory cytokines, such as interleukin (IL)-12, interferon-γ, IL-6, IL-8, tumor necrosis factor (TNF)-α, IL-17 and IL-9, and an increased production of type 2 anti-inflammatory cytokines, such as IL-4, IL-5, and IL-10 [17,18,20]. Vitamin D is also involved in reducing oxidative status by increasing reactive oxygen species–scavenging pathways and decreasing the source of oxidative stress [21,22].

Several in vitro studies and studies that used animal models demonstrated the immunomodulatory effects of vitamin D; however, these studies used supraphysiological concentrations of 1,25 (OH)2-D3 [5,20]. Some studies involving human participants also agreed that a reverse correlation exists among vitamin D levels, and C-reactive protein (CRP) and IL-6 concentrations, and a number of inflammatory markers; however, because the studies presented dissimilar underlying causes of inflammation and used different techniques for the measurement of cytokines, the findings are largely contradictory, thus highlighting the need for additional research especially in athletes [23–26]. Vitamin D receptors (VDRs) have been found in all body tissues, including skeletal muscle tissue, suggesting a potential role of the vitamin in muscle performance and regeneration [27]. In multiple studies, the effects of vitamin D supplementation on athletes' recovery and performance have been investigated, but the results indicated incongruence in the groups selected as samples, evaluated parameters, type and dose of the supplementation, circumstances of the intervention, or intervention duration across the studies [28–34].

To our knowledge, sufficient research has not been conducted on the effects of vitamin D on inflammation and muscle damage in soccer players. Studies that have been conducted have reported contradictory results. Consequently, the motivation for the present study was to investigate whether 50 000 IU/wk of cholecalciferol would reduce the inflammatory markers and muscle damage indices in soccer players after a simulated soccer match [35].

Methods

This randomized, double-blind, placebo-controlled study was approved by the Human Research Ethics Committee at the Urmia University of Medical Sciences, Iran. After describing the nature of the study to the athletes, written informed consent was obtained from each participant. Professional, healthy soccer players (N = 22) from a first-division team affiliated with Urmia's local league participated voluntarily in the study. The participants met the inclusion criteria if they did not smoke or abuse alcohol and were free from disease. Potential participants were excluded if they were taking any dietary supplements or foods high in vitamin D, using certain drugs, or traveling to sunny areas during the study period. The data were collected during the winter in Urmia, Iran.

Before any testing, participants completed questionnaires in which they reported their demographic variables and medical history. For eliminating confounding factors, at the beginning and end of the study, 3 d of 24-h recall questionnaires, a physical activity questionnaire, and a sunlight exposure questionnaire, which covered various criteria, were completed. The sun exposure questionnaire was derived from McCarty et al.'s [36] and adapted to Iran's culture and conditions. Moreover, the categorized physical activity questionnaire that was used was valid and reliable for Iran and Europe [37,38]. The participants' dietary records were analyzed for total energy, carbohydrate, protein, fat, and vitamins D, C, E and β-carotene content using a computer-aided nutritional program (Modified NUT4 version 1).

Before the study, blood samples were taken to evaluate basal serum concentrations of 25(OH)D. Anthropometric measurements were carried out using a body composition analyzer in the Nutrition Department of Imam Khomeini Hospital (Urmia, Iran; InBody 770-BIA- South Korea). Based on the criteria of the baseline 25(OH)D concentration and average duration of physical activity per week, the participants were randomly assigned into two groups, with cholecalciferol (50 000 IU/wk; Zahravi®, Tehran, Iran; n = 11) or placebo (Paraffin, Zahravi; n = 11), taken once weekly for 8 wk (Fig. 1). The participants and study investigators were unaware of the treatment allocation.

In the first week of the study, to estimate the participants' maximal oxygen uptake capacity (VO_2 max), they completed a multistage shuttle run test [39]. The average VO_2 max estimated for the team was then used to calculate the running speeds corresponding to 55% and 95% VO_2 max using the tables for predicting VO_2 max values. In week 2, the participants were familiarized with the test protocol. They were asked to eat and exercise as they would do normally in preparation for a soccer match and then refrain from strenuous physical activity and consuming caffeine, or any other substance that could influence the results, for 72 h before the test. On the day of the test, two equipped phlebotomists at the stadium collected the athletes' blood samples and transferred them to the Imam Khomeini Hospital laboratory in a cold box as soon as possible for measuring serum concentrations of 25(OH)D, creatine phosphokinase (CPK), lactate dehydrogenase (LDH), IL-6, and CRP.

The test was conducted on a football pitch. After 15 min of warming up, the participants completed the Loughborough intermittent shuttle test (LIST), which is designed to simulate individuals' metabolic and physiological responses in a soccer match [40]. The test protocol consisted of two parts (Fig. 2). For each part, an audio voice was designed, and the athletes set their pace according to its instructions. Part A represented a fixed period comprising five 15-min exercise periods, with each period followed by 3 min of recovery. Each exercise period consisted of a set pattern of running with specific rates, as follows:

- 3 × 20 m at a walking pace (13.5s for 20 m);
- 1 × 20 m at maximal running speed (3.90s for 20 m);
- 4s recovery;
- 3 × 20 m at a running speed corresponding to 55% of the group's predicted VO_2 max (2.36 m/s); and
- 3 × 20 m at a running speed corresponding to 95% of the group's predicted VO_2 max (3.4 m/s).

After 3 min of rest, the athletes started part B. In this part, the athletes were required to run at speeds corresponding to 55% and 95% of the group's predicted VO_2 max, with the speeds alternating every 20 m. This exercise pattern was repeated continuously until the athletes could not complete two consecutive shuttles. After every 15-min period, the athletes' heart rates and levels of fatigue were measured using the Borg scale of perceived exertion [41].

The blood samples were collected immediately and 2-h after LIST. At 24-h postexercise, the athletes presented to the laboratory for final blood sample collection and anthropometric measurements. The concentrations of CRP (latex immunoturbidimetric assay), LDH (photometrics), and CPK (photometrics) were measured using an automatic biochemical analyzer (BT4500, Italy). The IL-6 concentration was determined using enzyme-linked immunosorbent assay, following the manufacturer's instructions (IBL International GMBH, Hamburg, Germany). The serum 25(OH)D concentration was analyzed using an immunoassay analyzer (Cobas E 411 Analyzer, Germany) with electrochemiluminescence technology.

The results are presented as the median and interquartile range. To identify any confounding variables, single-variable tests, including the χ^2, Fisher's exact, and Mann–Whitney U tests, were used; variables that were compared between the two groups and had a $P < 0.25$ were selected as confounding variables for the multivariate analysis. For the multivariate analysis, the marginal longitudinal model and generalized estimating equations (GEEs) were used. To investigate the main effect of the experimental group, the main effect of the time factor, and the interaction between the experimental group and time factor, two separate covariance analysis models were used, as follows: In model 1, the effects of the confounding variables were not modified; in model 2, in addition to adjusting the effect of the base values of the response variables, the effects of the confounding variables were modified.

Results

The baseline characteristics, including age; serum 25(OH)D concentration; physical activity level; body mass index (BMI); skeletal muscle mass (SMM); and dietary vitamin D, E, C, β-carotene, energy, carbohydrate, protein, and fat intake were relatively well

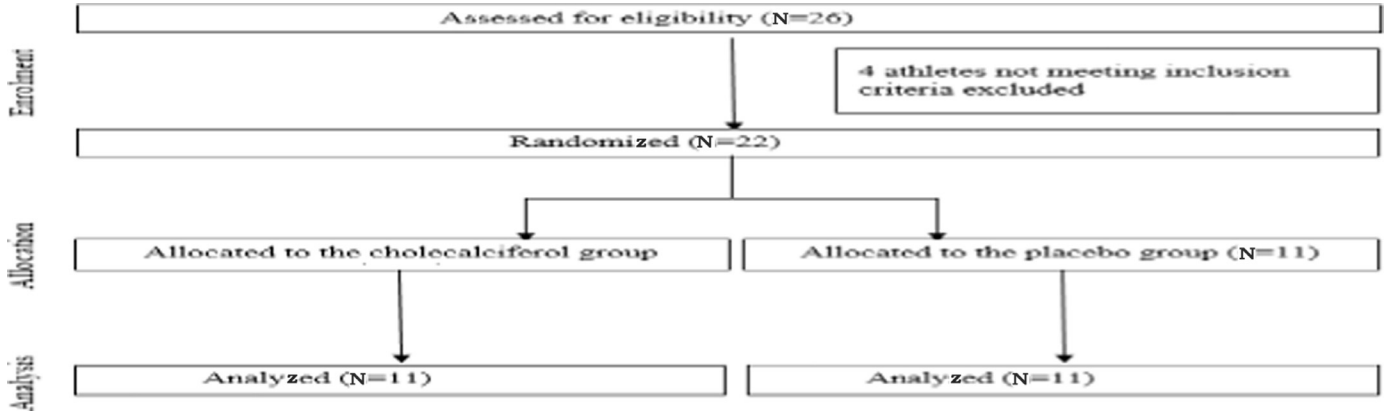

Fig. 1. Flow diagram of the progress.

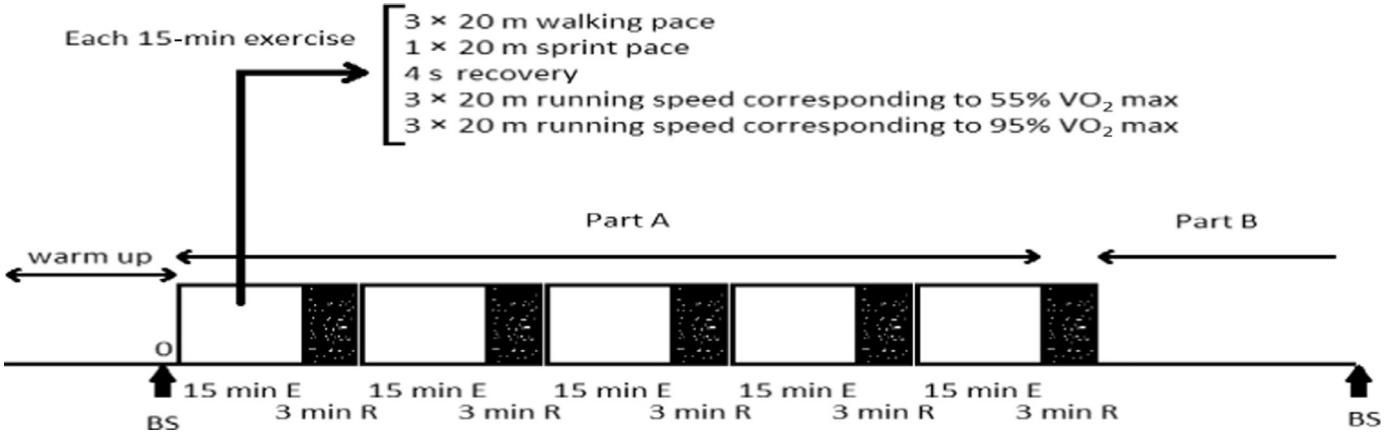

Fig. 2. Schematic of the Loughborough intermittent shuttle test (LIST). BS, blood sample; E, exercise; R, rest.

balanced between the groups (Table 1). However, the groups differed in terms of dietary vitamin D intake and BMI variables, and they were considered as confounding factors ($P < 0.25$).

According to the baseline assessment of serum 25(OH)D concentration, five participants were insufficient in terms of serum 25 (OH)D levels (22.7–27.4 ng/mL), and 17 had deficient serum 25 (OH)D levels (≤20 ng/mL) [14]. Both GEE models showed that 8 wk of supplementation with 50 000 IU of cholecalciferol versus a placebo significantly increased the serum 25(OH)D values (53.93 versus 10.68 ng/mL; $P < 0.0001$).

GEE model 1 showed that the main effects of supplementation on the IL-6 concentration of the intervention group was not significant ($P = 0.49$; Table 2); however, GEE model 2 showed that the concentration of IL-6 was generally about 0.92 pg/mL higher in the intervention group than the control group ($P = 0.03$). In addition, neither the interaction effect of the experimental group nor the factor of time was significant ($P = 0.30$). Both GEE models showed that the CRP concentration did not differ between the groups ($P = 0.33$, $P = 0.44$; Table 2). However, the interaction effect on the level of CRP was quite significant ($P = 0.11$, $P = 0.11$); In other words, in the first to third stages, the CRP concentrations in the intervention group were clearly higher than they were in the control group, whereas in the fourth stage, the CRP concentration in the intervention group was slightly lower than that in the control group. In terms of both models, the pattern of increase between the vitamin D and placebo groups did not differ significantly for serum LDH ($P = 0.62$, $P = 0.41$). However, after adjusting for the effect of confounding variables, the LDH concentration in the intervention group was generally about 7.760 U/L lower than that in the control group, but this result was not statistically significant. For both GEE models, the main effect of the experimental group on the CPK concentration was not significant ($P = 0.68$, $P = 0.07$; Table 2). In the first to third stages, the CPK concentrations in both groups were relatively equal, whereas in the fourth stage, the CPK concentration in the intervention group was clearly lower than that in the control group.

For both models, the recorded heart rates during the simulated soccer match did not show a difference between the groups ($P = 0.60$, $P = 0.98$), but the main effect of the time factor on the heart rate was significant ($P < 0.0001$, $P < 0.0001$). The athletes' level of fatigue did not differ between the groups ($P = 0.15$, $P = 0.26$), but it increased significantly after each stage of the test ($P < 0.0001$, $P < 0.0001$; Table 3).

Discussion

Recent evidence has broadened interest in the role of vitamin D in reducing inflammation and increasing muscle strength in athletes, but knowledge on the potential effects of vitamin D supplementation on improving these conditions remains limited [42–44]. The researchers conducted this study to examine the effects of vitamin D3 supplementation (50 000 IU/wk, for 8 wk) on muscle damage and inflammation in soccer players.

Cellular and animal studies on vitamin D and the immune system demonstrated VDR expression in T-helper cells [20]. The active form of vitamin D, 1,25(OH) 2-D, can suppress the proliferation of T-helper cells and diminish their production of proinflammatory cytokines (e.g., IL-1 and TNF-α) [18,20]. Exercise-induced muscle damage and oxidative stress upregulate proinflammatory cytokine production, which stimulates IL-6 production. IL-6, in turn, leads to the production of acute-phase proteins, including CRP [45]. Whether CRP has proinflammatory effects or not is being debated [46]. Skeletal muscle has been identified as an endocrine organ that produces and releases cytokines, which are called "myokines" and include IL-6, IL-8, and IL-15; these myokines exert paracrine, autocrine, or endocrine effects [47]. Strenuous muscle contractions during exercise also induce mechanical muscle damage, which triggers the release of large amounts of intracellular enzymes, including CK and LDH, into the circulation. In vitro and animal studies suggested that vitamin D reduces tissue damage after intense exercise by lowering peroxidation levels and increasing mitochondrial oxidative phosphorylation [30,42,48]. Despite the insights provided by these studies, however, the vitamin D pathways that affect the reduction of muscle damage still need further investigation.

The present study showed that supplementation with cholecalciferol increased the serum 25(OH)D level of the intervention group to 53.93 ng/mL but did not improve the athletes' muscle damage indices (Table 2). Although the level in the intervention group was less than that in the placebo group, this difference was not significant. Both IL-6 and CRP concentrations were higher in the intervention group than in the placebo group; the differences

Table 1
Comparison of athletes' baseline characteristics

Variable	Placebo (n = 11)					Cholecalciferol (n = 11)					*P*-value†	*P*-value‡
	Pre		Post		*P*-value*	Pre		Post		*P*-value*		
	Median	IQR	Median	IQR		Median	IQR	Median	IQR			
Age (y)	27	4	–	–	–	27	5	–	–	–	0.94	–
BMI, kg/m^2	24.8	2.7	25.1	3.51	0.13	22.6	3.7	22.9	2.95	0.28	0.17	0.72
Skeletal muscle mass, kg	35.1	4.4	34	4.4	0.85	31.8	8.2	31.9	6.7	0.63	0.37	0.47
Physical activity level, METs.h/wk	181	83.8	183	83.8	0.25	186	85.5	173	93.1	0.92	0.94	0.75
Dietary vitamin D intake, μg/d	2.13	1.58	2.10	1.15	0.42	2.33	0.91	2.65	0.92	0.76	0.23	0.9
Dietary energy intake, kcal/d	2156	476	2200	500	0.68	2098	485	2100	392	0.47	0.51	0.37
Dietary carbohydrate intake, g/d	288	40.8	293	80.9	0.79	283	65.4	288	81.9	0.79	0.37	0.88
Dietary protein intake, g/d	91.6	23.8	89.3	15.1	0.65	84.6	33.3	85.4	15.9	0.59	0.3	1.0
Dietary fat intake, g/d	71.2	22.9	74.7	15.5	0.65	66.7	17	66.8	8.5	0.72	0.67	0.52
Dietary vitamin C intake, mg/d	99.4	69.1	103	64.9	0.47	114	44.2	112	52.2	0.92	0.87	0.93
Dietary vitamin E intake, mg/d	10.2	3.38	10.2	5	0.95	10	12.4	9.9	10.5	0.79	0.97	0.66
Dietary β-carotene intake, ug/d	173	76.6	177	73.4	0.79	178	75.8	207	121	0.85	0.92	0.82
Serum 25(OH)D level, ng/mL	14	6.83	12.9	9.02	0.07	15.6	12	53.9	10.6	0.01	0.94	0.00

BMI, body mass index; IQR, interquartile rate; METs, metabolic equivalent of tasks.
Data are presented as median and interquartile rates.
*Denotes differences between pre- and postsupplementation within the groups.
†Denotes differences between the groups at the beginning of the study.
‡Denotes differences the changes between the groups.

Table 2
Comparison of Inflammatory markers and muscle damage indices after 8 wk of weekly supplementation with 50 000 IU of cholecalciferol or placebo

Variable			Placebo								Cholecalciferol							
			Stage 1		Stage 2		Stage 3		Stage 4		Stage 1		Stage 2		Stage 3		Stage 4	
			Mdn	IQR	Mdn	IQR	Mdn	IQR	Mdn	IQR	Mdn	IQR	Mdn	IQR	Mdn	IQR	Mdn	IQR
IL-6 (pg/mL)	Total		0.06	1.31	3.82	2.25	4.96	5.43	0.53	2.51	1.27	1.74	2.62	3.29	3.10	3.82	1.13	1.87
	Model 1	*P*-value*									0.49							
		P-value†									<0.0001							
		P- value‡									0.30							
	Model 2	*P*-value*									0.03							
		P-value†									<0.0001							
		P- value‡									0.30							
CRP (mg/L)	Total		1.45	1.66	1.50	1.21	2.20	1.19	6.89	13.0	0.78	2.68	3.21	1.08	3.03	1.05	6.67	8.98
	Model 1	*P*-value*									0.44							
		P-value†									<0.0001							
		P- value‡									0.01							
	Model 2	*P*-value*									0.35							
		P-value†									<0.0001							
		P- value‡									0.01							
LDH (U/L)	Total		31	36	39	91	39	67	38	152	32	66	40	141	36	110	35	116
	Model 1	*P*-value*									0.62							
		P-value†									<0.0001							
		P- value‡									0.27							
	Model 2	*P*-value*									0.41							
		P-value†									<0.0001							
		P- value‡									0.27							
CPK (U/L)	Total		19	119	30	84	33	179	48	268	0	103	30	299	36	280	37	331
	Model 1	*P*-value*									0.68							
		P-value†									<0.0001							
		P- value‡									0.01							
	Model 2	*P*-value*									0.07							
		P-value†									< 0.0001							
		P- value‡									0.01							

CPK, creatine phosphokinase; CRP, C-reactive protein; IL, interleukin; IQR, interquartile rate; LDH, lactate dehydrogenase; Mdn, median.
Data are presented as median and interquartile rates In model 1, confounding variables were not modified. In model 2, confounding variables were adjusted.
*Denotes the main effect in the intervention group.
†Denotes the main effect of time.
‡Denotes the interaction between the intervention group and time.

in IL-6 and CRP levels between the groups were significant and not significant, respectively. Oxidative stress and inflammation are associated with harmful biological events, although they also are essential to the adaption and optimal functioning of cells and it is stated that cytokine cascade induced by exercise markedly differs from the cytokine cascade induced by infections [47,49,50]. During exercise, the contracting muscle releases significant amounts of IL-6, which has been suggested to have anti-inflammatory properties and is not involved in inflammatory responses [47,51,52]. Exercise-induced elevations in levels of IL-6 cause a transient increase in the concentrations of two anti-inflammatory cytokines, IL-1 ra and IL-10, and may prevent inflammation-induced elevations in TNF-α [53,54]. Researchers also believe that IL-6 is able to stimulate the hypothalamic-pituitary-adrenal axis and increases the secretion of cortisol, which also has anti-inflammatory effects [55,56]. In this study, vitamin D supplementation increased the concentration of IL-6, which acted as a metabolic mediator in the athletes. It mediates hepatic glucose production during exercise or lipolysis in adipose tissue [47]. Several epidemiologic studies indicated that low levels of 25(OH)D were associated with high concentrations of pro-inflammatory cytokines. Nevertheless, hypovitaminosis D might be the consequence of some inflammatory diseases and not the cause of inflammatory conditions; inflammation induced by exercise differs from other inflammatory conditions [57]. Furthermore, some in vivo studies on human inflammatory diseases reported conflicting results regarding the effects of vitamin D supplementation [17,58,59].

The results of the present study indicated that supplementation with vitamin D had no effect on the muscle damage indices of the intervention group but that their CK and LDH concentrations at the fourth stage were generally lower than those of the placebo group. Nevertheless, the difference between the groups was not significant.

Some studies suggested that serum 25(OH)D levels of 120 to 225 nmol/L are required to create physiological response in skeletal muscles, and the 25(OH)D goal of 40 ng/mL is recommended for athletes because at this level, vitamin D begins to be stored in the muscle and fat for future use [13,60]. In the current research, all athletes exhibited insufficient and deficient concentrations of vitamin D according to the ESC definitions, but after supplementation the serum vitamin D concentration in athletes increased to up to 53.93 ng/mL (134.8 nmol/L). Ke et al. [42] reported that postexercise calcitriol injection (2 mcg/mL) in rats decreased muscle damage indices (CPK, LDH), tissue damage, and peroxidation induced by exhaustive exercise. One remarkable difference between the study by Ke et al. and the present study was the use of calcitriol, the active form of vitamin D; in addition, the supplementation was done in the form of a bolus dose given after intense exercise. In a study by Barker et al. [30], participants with sufficient vitamin D concentrations (M = 30.8 ng/mL) ingested cholecalciferol (4000 IU/d)

Table 3
Comparison of heart rate and Borg's fatigue test changes after 8 wk of weekly supplementation with 50,000 iu cholecalciferol or placebo

Variable			Borg's fatigue						Heart rate					
			Total	Model			Model 2		Total	Model			Model 2	
				P-value*	*P*-value†	*P*- value‡	*P*-value*	*P*-value†	*P*- value‡		*P*-value*	*P*-value†	*P*- value‡	*P*-value*	*P*-value†	*P*- value‡
Placebo	Stage1	Mdn	3	0.15	<0.001	0.01	0.26	<0.001	0.01	116	0.6	<0.001	0.75	0.98	<0.001	0.75
		IQR	3							10						
	Stage2	Mdn	4							116						
		IQR	3							10						
	Stage3	Mdn	5							118						
		IQR	2							6						
	Stage4	Mdn	6							118						
		IQR	1							6						
	Stage5	Mdn	7							120						
		IQR	1							6						
	Stage6	Mdn	8							122						
		IQR	0							2						
Cholecalciferol	Stage1	Mdn	2							118						
		IQR	0							4						
	Stage2	Mdn	2							118						
		IQR	1							4						
	Stage3	Mdn	4							120						
		IQR	1							6						
	Stage4	Mdn	6							120						
		IQR	2							6						
	Stage5	Mdn	8							120						
		IQR	1							6						
	Stage6	Mdn	8							122						
		IQR	1							4						

IQR, interquartile rate; Mdn, median.
Data are presented as median and interquartile rates. In model 1, confounding variables were not modified. In model 2, confounding variables were adjusted.
*Denotes the main effect in the intervention group.
†Denotes the main effect of time.
‡Denotes notes the interaction between the intervention group and time.

for 35 d, and after 28 d of supplementation, they completed an exercise protocol. Circulating biomarkers were measured before and after (immediately, 1, 24, 48, 72, and 168 h) the test protocol. The test protocol was such that the amount of exercise was likely to vary between the participants, and they were not block randomized according to their baseline vitamin D status. The authors reported that supplementation with vitamin D attenuated the muscle damage indices (aspartate transaminase, alanine transaminase) and enhanced recovery. Of possible theoretical mechanisms, vitamin D supplementation may improve the speed of recovery. First, it can increase oxidative phosphorylation, and the production of extracellular matrix proteins, and manage the inhibition of apoptosis. Second, supplemental vitamin D increases VDR expression in skeletal muscle cells, thereby affecting muscle regeneration and function. Third, cytochrome P450 27 B1 increases in regenerated skeletal muscle cells and elevates the concentration of 1,25(OH)D, thus potentially contributing to muscle regeneration [30].

In the present study, the results indicated that vitamin D supplementation enhanced the concentration of IL-6, which is involved in different adaptations and accelerated the recovery of athletes after strenuous exercise. These issues also require further investigation.

Certain limitations of the study are worth discussing. The first is the small sample, in which the number of participants was equal to the number of players in a football team. Second, the differences in baseline BMI between the groups; however, its effect on the results was adjusted. Our study's strengths included the randomized, double-blind, placebo-controlled design. Moreover, the palatability and appearance of the supplement and placebo were similar, and we used the LIST, which is a valid and reliable test. It has been shown that this test can properly simulate soccer match conditions. Future studies with different doses of vitamin D supplementation and duration are warranted to determine whether vitamin D supplementation can improve inflammation and muscle damage in athletes with different 25(OH)D levels.

Conclusion

The unexpected finding in the present study was that supplemented athletes exhibited no improvement in muscle damage and CRP concentration after a simulated soccer match. However, supplementation with 50 000 IU cholecalciferol for 8 wk increased the serum 25(OH)D and IL-6 concentrations significantly.

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