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Original Article

Vitamin D supplementation attenuates exercise induced muscle damage: A meta-analysis of randomized control trials

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Abstract
Purpose: This meta-analysis evaluated the effectiveness of vitamin D (Vit D) supplementation in reducing muscle damage, inflammation, and perceived muscle soreness. **Methods:** A structured literature search was performed Web of Science, Scopus, and Google Scholar databases to identify relevant randomized controlled trials. Six studies comprising 209 participants (155 males, 54 females) met the inclusion criteria. Outcome measures included creatine kinase (CK), lactate dehydrogenase (LDH), serum cytokines, and visual analog scale (VAS) for muscle soreness. Post-exercise muscle damage was assessed by comparing the Vit D supplementation and placebo groups using participant numbers, mean differences, and standard deviations. Cohen's d was used to compute the standardized mean differences (SMDs) for each study group. These values were then weighted based on the inverse of their variance to give more importance to studies with more precise results. A random effects model was selected to estimate the total effect size along with a 95% CI. **Results**: The analysis revealed a moderate effect of Vit D supplementation on muscle damage markers (CK = -0.46, 95% CI: -0.94, 0.02, LDH: -0.28, 95% CI: -0.87, -0.30) and inflammatory markers (Serum Cytokines: -0.50, 95% CI: -0.90, -0.11). Strongest impact was observed on perceived muscle soreness (Visual Analogue Scale: -1.34, 95% CI: -1.91, -0.77). Notable improvements were highlighted in Vit D dosage and intervention duration but lacked consistency among the outcomes which contributing further variation in findings. **Conclusion**: Vit D demonstrated a moderate effect on muscle damage and inflammatory processes, its strongest impact was observed on perceived muscle soreness. However, inconsistencies in dosage, intervention duration, and study protocols limit the ability to draw robust conclusions. Future research should emphasis on standardized protocols, larger sample sizes, and consideration of factors such as skin biosynthesis of Vit D, climatic conditions, and controlled muscle damage models to enhance the reliability of findings.
Keywords: Vitamin D, Ergocalciferol, Cholecalciferol, exercise-induced muscle damage, muscle soreness, muscle recovery

Introduction

Vitamin D (Vit D) is a group of structurally related *lipophilic vitamin* responsible for absorption of magnesium, phosphate and calcium including numerous other biological functions (Holick et al., 2011). Various types of Vit D exist, with the two major forms being Vit D_2 (ergocalciferol) which comes from the plants, and Vit D_3 (cholecalciferol) comes from animals and synthesized by the skin (Hossein-Nezhad & Holick, 2013). The main natural way humans get Vit D_3 is through its production in the skin where 7-DHC (7-dehydrocholesterol) follows a two-step process of reactions including ultraviolet-B (UV-B) irradiation to form pre-Vit D_3 followed by a subsequent thermal isomerization to Vit D_3 (Pludowski et al., 2018).

Vit D is processed in the body through a specific pathway. First, it is carried in the blood by a protein called Vit D Binding Protein. It then travels to the liver, where it is changed into 25 – hydroxyvitamin D [25(OH)D], which is the main compound found in the blood. Any extra Vit D that the body does not need right away is stored in the liver, muscles, and fat tissues. After that, 25(OH)D goes to the kidneys, where it is converted into its active form, called 1,25-dihydroxyvitamin D^3 [$1,25(OH)_2D_3$], or calcitriol (Henry, 2011).

This activation process is carefully regulated by two hormones: Parathyroid Hormone (PTH), which increases Vit D activation when calcium levels are low, and Fibroblast Growth Factor-23 (FGF-23), which inhibits Vit D activation to prevent excess calcium in the bloodstream (Saponaro et al., 2020).

The main role of Vit D is to control calcium and phosphorus levels, ensuring strong and healthy bones. It improve calcium immersion in the small intestine by approaching with Vit D Receptors in intestinal cells,

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which then activate calcium transport channels. When calcium levels are too low, Vit D also helps release calcium from bones by activating osteoclasts, bone cells responsible for breaking down bone tissue. This process is mediated through the *Receptor Activator of Nuclear Factor Kappa B Ligand protein*, which signals osteoclasts to release stored calcium into the blood (Laird et al., 2010; Lips, 2012; Need et al., 2008).

Beyond the functions of bones, Vit D has several other essential functions in the body. It strengthens the immune system by improving the activity of immune cells, reducing the risk of infections and autoimmune diseases (Prietl et al., 2013). It also impact on heart functioning by regulating blood pressure and reducing inflammation, which may help lower the risk of cardiovascular diseases (Pilz et al., 2011; Zittermann & Koerfer, 2008). Additionally, Vit D is involved in brain function, influencing mood and cognitive health, and may play a role in preventing conditions such as depression and neurodegenerative diseases (Anjum et al., 2018; Croll et al., 2021; Navale et al., 2022).

It also supports insulin regulation, potentially reducing the risk of type-2 diabetes by increasing insulin sensitivity (Al-Shoumer & Al-Essa, 2015; Grammatiki et al., 2017). Overall, Vit D is a vital nutrient that supports various physiological functions, and maintaining adequate levels is essential for overall health.

Globally, Vit D deficiency is exceedingly prevalent, with significant proportions of populations across all age groups displaying suboptimal levels. Severe Vit D deficiency i.e., [25(OH)D < 30 nmol/L or 12 ng/ml] has been reported in 5.9% of the US population, 7.4% in Canadian population (Sarafin et al., 2015), and 13% in Europeans (Cashman et al., 2016).

When considering levels below '50 nmol/L (20 ng/ml)', the prevalence rises to 24% in the US, 37% in Canada, and 40% in Europe. Deficiency rates are typically higher in children, the elderly, and nonwhite individuals. In countries like India, Pakistan, Afghanistan and Tunisia over 20% of the population has 25(OH)D levels below 30 nmol/L, with approximately 490 million people affected in India alone (Amrein et al., 2020; Cashman, 2020).

This concern is not limited to the general population, studies indicate that a substantial number of athletes and sportspersons also exhibit insufficient or deficient Vit D levels, despite their high levels of physical activity. A study followed North Indian region explored that out of three hundred sixty-nine athletes aged 18-25 years 69% were Vit D deficient and further lead to low bone mineral density and high parathyroid hormone (Gupta et al., 2021).

Vit D plays a crucial role in muscle function, recovery, and repair. It has been included in several physiological processes, including protein synthesis, immune modulation, and inflammation regulation, all of which are essential for muscle health. However, despite growing interest in the association between Vit D and exercise-induced muscle damage, the evidence remains limited and inconclusive.

Several studies have highlighted that Vit D may influence muscle damage biomarkers such as creatine kinase (CK), lactate dehydrogenase (LDH), serum cytokines, and perceived soreness (Ke et al., 2016; Larson-Meyer et al., 2018; Petersen et al., 2001; Rojano-Ortega & Berral-de la Rosa, 2023a; Todd et al., 2015), yet findings are inconsistent across different populations, supplementation protocols, and exercise modalities.

Given the conflicting evidence and the increasing interest in Vit D as a recovery aid in sports and exercise science, a comprehensive synthesis of the existing literature is warranted. The absence of clarity in existing literature highlights the need for a comprehensive and systematic assessment of the available evidence. Given the potential of Vit D to mitigate muscle damage and enhance recovery, it is crucial to determine its precise impact on key biomarkers of muscle damage.

Therefore, the objective of the present meta-analysis is to systematically evaluate the effect of Vit D supplementation on CK, LDH, serum cytokines, and perceived soreness, providing a more robust understanding of its role in muscle recovery and post-exercise inflammation.

By synthesizing data from multiple studies, this meta-analysis aims to clarify inconsistencies, identify potential dose-response relationships, and offer practical insights for athletes, clinicians, and researchers in the field of sports science and exercise physiology.

Materials and Methods

Literature Search

An electronic search of the related literature was conducted in three online databases namely, Scopus, Web of Science and Google Scholar.

The following terms were used as keywords for search the relevant articles: ("Vitamin D" OR "Cholecalciferol" OR "Calcitriol") AND ("Delayed Onset Muscle Soreness" OR "DOMS" OR "Exercise-Induced Muscle Damage" OR "EIMD") AND ("Recovery" OR "Muscle Pain" OR "Soreness" OR "Inflammation").

In addition, bibliography included in the articles were also explored thoroughly to search the additional relevant studies that were not electronically recognized.

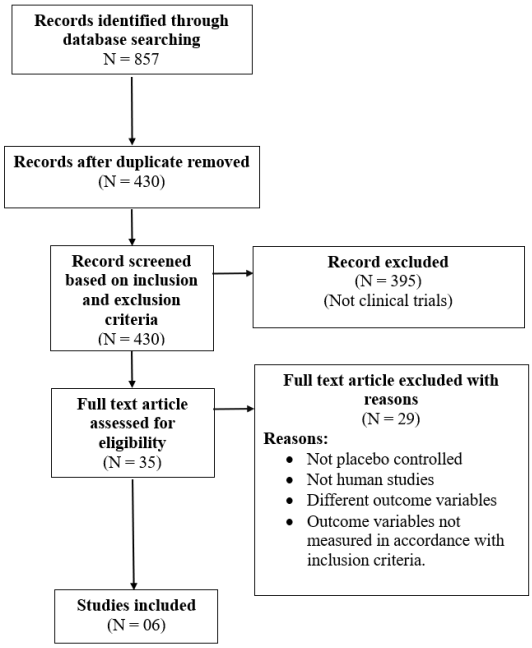

Figure 1 Study Identification and Selection Pathway

Outcome Variables

The available literature was reviewed to evaluate how Vit D supplementation influences markers of muscle damage, focusing on outcome variables that are most commonly used in research on Vit D and exercise-induced muscle damage (EIMD). Vit D supplementation, muscle soreness, muscle damage biomarker (structural/inflammatory). Supplementation included any existing form of Vit D (ergocalciferol or cholecalciferol) with proper dose of intake and intervention period. Measurement of muscle damage biomarker included delayed onset muscle soreness (DOMS), which were obtained using visual analogue scale, and other blood biomarkers such creating kinase (CK), lactate dehydrogenase (LDH), serum cytokines (inflammatory markers) obtained from capillary or venous sampling.

Criteria adopted for Inclusion and Exclusion of the Studies

Following criteria were used to selected the studies: (1) subjects were randomized into a Vit D supplementation and placebo group where both groups were blinded to the supplementation received; (2) Studies were included if they measured at least one relevant outcome and conducted assessments both at baseline and again either 1 hour or 24 hours after the exercise session; (3) no gender and training restriction were applied; (4) participants with hypovitaminosis D but healthy and able to perform physical activity. Studies were excluded if: (1) the supplementation period of Vit D was too short (less than 1 weeks); (2) Studies were excluded if the supplementation group received more than one type of treatment or if the control group engaged in any activity that might enhance recovery; (3) there was insufficient data and (4) participants with severe health conditions; (4) Article published other than English language were also excluded.

Extraction of the Data

Mean, Standard Deviation (SD), and sample size were extracted from the included studies. The posttest (1 hour/ or 24 hours) scores of both groups (Vit D/or Placebo) were used for further computations. Risk of bias was calculated in accordance with the Cochrane Collaboration Guidelines (Cumpston et al., 2019).

Coachrane Collaboration Guidelines were implemented to assess risk of bias

Statistical Analysis

To compare results from different studies that used various measurement scales, effect sizes were calculated using standardized mean differences (SMDs), along with 95% confidence intervals (CIs). The size of the effect was interpreted using Cohen's guidelines: an SMD less than 0.50 was considered small, between 0.50 and 0.80 was seen as moderate, and anything above 0.80 was viewed as a large effect (Cohen, 1988). Statistical heterogeneity, which shows how much of the variation between study results is due to real differences in methods or study populations rather than chance, was measured using the I^2 statistic (Borenstein et al., 2009). I^2 values of 25, 50, and 75% represent low, medium, and high heterogeneity (Higgins et al., 2003), respectively. If moderate or high heterogeneity is found, it may lead to further analysis by dividing the studies into subgroups based on certain factors, such as when the measurements were taken (e.g., 1 hour or 24 hours after exercise), the dose of Vit D given (e.g., 1000 to 8000 IU), and how long the supplementation lasted (e.g., 3, 6, or 12 weeks), even if the overall results are not statistically significant. A Z-test was performed to determine the overall significance of the pooled effect size, with statistical significance set at $p < 0.05$. Additionally, potential publication bias was assessed through funnel plot inspection. All calculation carried out using Review Manager

(RevMan) 5.4 (*Review Manager (RevMan)*, 2020). All sub-group calculations generated by RevMan software were further illustrated in two forest plots (figure 3 & figure 4) respectively.

Results

Article search

Through selected electronic search databases 857 publications were initially identified (see Figure 1). However, only six articles fulfil the inclusion criteria and selected for final data synthesis. Out of the 857 initially identified articles, 427 were duplicates and were subsequently removed. From the remaining 430 articles, 395 were excluded as they were not clinical trials. Among the 35 remaining studies, 29 were further excluded for not being conducted in humans, lacking a placebo-controlled design, or not assessing selected muscle damage biomarkers and outcomes variables did not measured in accordance with inclusion criteria.

Studies Characteristics

A total six studies were included in this meta-analysis as provided in Table 1 respectively. The training status of participates varied among the studies and ranged from untrained to competitive athletes. In three studies participants were Basketball player (Stojanović et al., 2022), national level ultramarathon runner (Zebrowska et al., 2020), and competitive Football players (Todd et al., 2017). Two studies included healthy moderate to vigorously active participants (Barker et al., 2015; Pilch et al., 2020), while one included study conducted the intervention on obese women having perceived myalgia (Ahmed et al., 2021). The status of 25-hydroxyvitamin D was also varied among the studies.

Three studies (Ahmed et al., 2021; Pilch et al., 2020; Stojanović et al., 2022) included the participants with inadequate Vit D status. All studies were double blinded randomized control trials followed by a Vit D supplementation group and placebo group which ensured the blinding of the participants to the groups. In one study (Ahmed et al., 2021) divided the participants into three groups (Aerobic + Vit D supplementation, Vit D Supplementation and Placebo), while another study (Pilch et al., 2020) divided the participants as per status of Vit D (25-hydroxyvitamin D) and categorized each group (treatment or control) into optimal and suboptimal (see table 1) respectively. Further, one study (Barker et al., 2015) categorized the participants on different dose of Vit D supplementation (4000 IU/ or 8000 IU) followed by a placebo or control group. The dose of Vit D supplementation was varied and ranged from 1000 IU/day to 8000 IU/day. Similarly, the supplementation period was ranged between 3 to 12 weeks. Some studies measured the outcomes in pre and post timelines (Ahmed et al., 2021; Barker et al., 2015; Stojanović et al., 2022; Todd et al., 2017) while some studies expended measurement timelines into 1hour, 24 hours post muscle damage exercise protocol (Pilch et al., 2020; Zebrowska et al., 2020). The total participants in the dataset were 209 (n = 155 male, and n = 54 female) with a mean and SD age of 28.52 (4.24) years. Additional details of outcome's variables and exercise protocol for muscle damage for each study were provided in table no 1, respectively

Table 1 Studies Characteristics

Study	Participants	Study Design	Group (N) / (Age)	Vit D Content	Suppl. Period	Data assessed	Outcome Measures	Exercise protocol to induce muscle damage
(Stojanović et al., 2022)	Basketball Player (Female) having Vit D deficiency	Double Blind RCT*	VITD (12)/ (19.4±4) PLCB (12)/ (19.8±4.6)	Cholecalciferol 4000IU/day	6 weeks	Pre and Post	LDH, CK	8 to 10 h basketball drills along with two basketball matches in a week
(Ahmed et al., 2021)	Participants were obese women (BMI 30.0 to 34.9 kg/m^2) and perceived myalgia along with Vit D deficiency (serum25(OH) D levels<30ng/mL and<10ng/mL)	A single-blinded RCT	Aerobic + VITD (15)/ (34.8±2.64) VITD (15)/ (35.01±2.39) CON (15)/ (35.4±2.69)	Cholecalciferol 50000 IU/Week	12 weeks	Pre and Post	VAS	Aerobic interval training at 50% to 70% maxHR for 40 minutes follow 3 times in a week
(Zebrowska et al., 2020)	ultramarathon (male) runners with 7 years of competitive experience	double-blind placebo-controlled study	VITD (12) 33.7±7.5 PLCB (12) 35.9±5.3	Cholecalciferol (2×1000IU/day)	3 weeks	Rest, 1h after, 24h	CK, LDH, TNFα, IL-6	downhill running test (Intensity 70% of max VO_2) (treadmill declination = 16%)
(Pilch et al., 2020)	Healthy physically active	Not reported	*Sub optimal>VIT	Cholecalciferol 1000 IU/day	12 Weeks	1h before,	CK, LDH	Eccentric exercise

	(1385±116) MET-min/week, on average) male volunteers who were able to perform exercise test		D (15) Sub optimal>PLCB (15) *Optimal>VITD (15) Optimal>PLCB (15)			1h after, 24 after		test on treadmill inclined at -10%. Participants loaded with weight (5% of body mass). Intensity was equal to 60±2% of peak VO_2
(Todd et al., 2017)	Participants were competitive male footballers	double-blind, randomised, placebo controlled trial	VITD (22) (20±2) PLCB (20) (20±2)	Cholecalciferol 3000 IU/day	12 weeks	Pre and Post	IL-8, TNFα, CRP	Routine football training
(Barker et al., 2015)	Participants were modestly active healthy male (i.e., 30 min of continuous physical activity at least 3 times per week)	Double Blind RCT*	VITD 4000 IU (15) (34±5) VITD 8000 IU (14) (32±7) PLCB (17) (29±7)	Cholecalciferol 4000 IU/day 8000 IU/day	5weeks	Pre and Post	TNFα, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12, IL-13	Fifty isokinetic contractions involving concentric knee extension and flexion at a speed of 120˚/s, performed using the dominant leg.

VITD = Vit D Group, PLCB = Placebo Group, CON = Control Group, *Sub-optimal = (Vit D level ↓30ng/ml), *Optimal = (Vit D level ↑30ng/ml), LDH = lactate dehydrogenase, creatine kinase, TNFα = Tumour Necrosis Factor alpha, CRP = C- reactive protein, IL = interleukin, VAS = visual analogue scale, RCT = randomized control

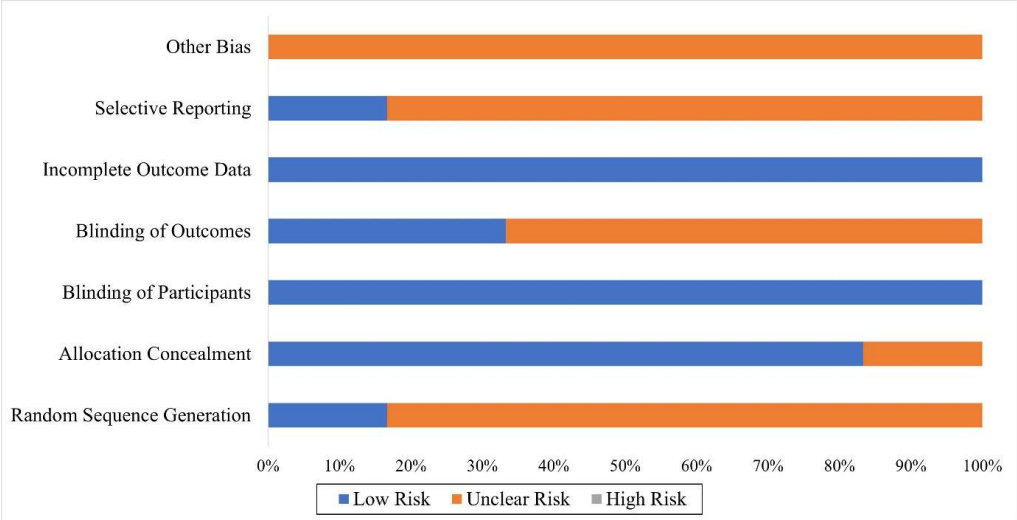

Figure 2 Risk of bias summary in context of Cochrane collaboration guidelines

Risk of Bias Outcomes

The risk of bias assessment, illustrated in Figure 2, was conducted using Cochrane guidelines. The evaluation indicated that random sequence generation, which ensures participants were assigned to groups using a valid method, was predominantly unclear, with the exception of a single study (Zebrowska et al., 2020) that explicitly reported using a random number generator for group allocation.

Similarly, blinding of outcomes, which prevents participants from being aware of group assessments, was frequently unclear or unreported. Additionally, selective reporting, a measure of reporting bias, and other potential biases were also largely unclear, highlighting gaps in methodological transparency across the included studies.

Table 2 Summary of Meta-Analysis

Subgroups	N	SMD	95% CI	I^2	(Z)
CK (1h)	03	-0.20	-0.68, 0.28	2%	0.82 (P = 0.41)
CK (24h)	03	-0.74	-1.60, 0.12	49%	1.68 (P = 0.09)
Total	06	-0.46	-0.94, 0.02	49%	1.86 (P = 0.06)
LDH (1h)	03	-0.49	-1.66, 0.67	81%	0.83 (P = 0.40)
LDH (24h)	03	-0.10	-0.67, 0.47	30%	0.34 (P = 0.73)
Total	06	-0.28	-0.87, 0.30	65%	0.94 (P = 0.94)
Serum Cytokines (1h)	04	-0.68	-1.34, -0.01	60%	2.00 (P = 0.05)
Serum Cytokines (24h)	04	-0.34	-0.34, 0.15	30%	1.35 (P = 0.18)
Total	08	-0.50	-0.90, -0.11	45%	2.48 (P = 0.01)
VAS	02	-1.34	-1.91, -0.77	0%	4.63 (P = .000)
1000 IU/Day	06	-0.48	-1.11, 0.15	69%	1.49 (P = 0.14)
2000 IU/Day	03	-0.57	-1.35, 0.22	62%	1.42 (P = 0.16)
3000 IU/Day	02	-0.22	-0.65, 0.21	0%	1.01 (P = 0.31)
4000 IU/Day	04	-1.05	-2.33, 0.22	88%	1.62 (P = 0.10)
8000 IU/Day	04	-1.25	-1.64, -0.86	0%	6.27 (P = .000)
Total	19	-0.74	-1.08, -0.39	72%	4.15 (P = .000)
3 Weeks	03	-0.57	-1.35, 0.22	62%	1.42 (P = 0.16)
5 Weeks	04	-1.63	-2.30, -0.95	61%	4.71 (P = .000)
6 Weeks	02	0.04	-0.53, 0.61	0%	0.14 (P = 0.89)
12 Weeks	10	-0.59	-1.02, -0.16	66%	2.69 (P = 0.007)
Total	19	-0.74	-1.08, -0.39	72%	4.15 (P = .000)

N = Number of outcome measure; SMD = summary effects in terms of standardized mean difference; 95 % CI = Confidence limits (lower, upper), I^2 = Test for heterogeneity, Z = Test for overall effect

Sub-group Analysis

A total 6 studies with 40 outcomes measures were retained for the final analysis. As per the obtained outcomes and characteristics, outcomes were further divided into sub-groups in reference to different biomarkers of muscle damage as well as time points of the measurements. The graphical representation in terms of forest plot was revealed in Figure 3 respectively.

The effect of Vit D supplementation on CK on different time points revealed mixed effects. At 1 hour post intervention the SMD was -0.20 (95% CI: -0.68, 0.28) with an I^2 of 2%, indicating low heterogeneity and no significant effects (Z = 0.82, P = 0.41). At 24 hours, the SMD was -0.74 (95% CI: -1.60, 0.12) with an I^2 of 49%, suggesting moderate heterogeneity. The Z-score of 1.68 and P-value of 0.09 indicate a trend toward CK reduction, though the effect did not reach statistical significance. When both time points were combined, the overall effect size was -0.46 (95% CI: -0.94, 0.02) with an I^2 of 49%, and the test for overall effect (Z = 1.86, P = 0.06) approached significance.

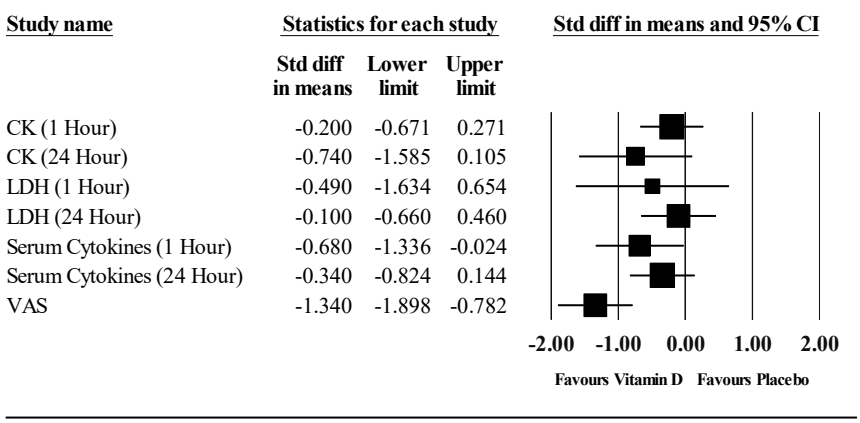

Figure 3 Forest plot depicted sub-groups analysis for muscle damage biomarkers including CK (creatine kinase), LDH (lactate dehydrogenase), Serum Cytokines and VAS (visual analogue scale) at different time points (1 hour, 24-hour post exercise)

The analysis of lactate dehydrogenase (LDH) at different time points also shown mixed effects. At 1 hour post intervention, the SMD was -0.49 (95% CI: -1.66, 0.67) with I^2 of 81%, indicating high heterogeneity and no significant effects (Z = 0.83, P = 0.40). At 24 hours post intervention, the effects are almost negligible with SMD -0.10 (95% CI: -0.67, 0.47), with moderate heterogeneity (I^2 = 30%) and non-significant Z value (Z = 0.34, P = 0.73). The overall impact of Vit D supplementation on LDH was small with SMD of -0.28 (95% CI: -0.87, 0.30) along with I^2 of 65% indicating moderate heterogeneity. The Z value for overall summary effect was (Z = 0.94, P = 0.73) not significant.

Serum cytokines are inflammatory markers of muscle damage. The present meta-analysis includes Interleukin-1β, IL-6, IL-8 and TNFα as measuring outcome variables. The SMD for 1 hour was -0.68 (95% CI: -1.34, -0.01), with moderate amount of heterogeneity (I^2 = 60%). The effects were consistent among the included studies (Z = 2.00, P = 0.05) showing significant effect of Vit d supplementation on reduction of inflammatory markers.

Delayed onset muscle soreness (DOMS) was assessed in terms of visual analogue scale (VAS) used to measure the pain perception in both groups. DOMS were assessed in baseline and post measurements only. No additional time point i.e., 1 hour post, 24-hour post exercise was reported in the study. The pain perception assessed using 10 cm Likert scale (0 = no pain, 10 = severe pain) at baseline and after 12 weeks followed by Vit D supplementation and placebo. The SMD of VAS was -1.34 (95% CI: -1.91, -0.77) with I^2 of 0% and Z (4.63, P = 0.000) indicating significant impact of Vit D supplementation on DOMS.

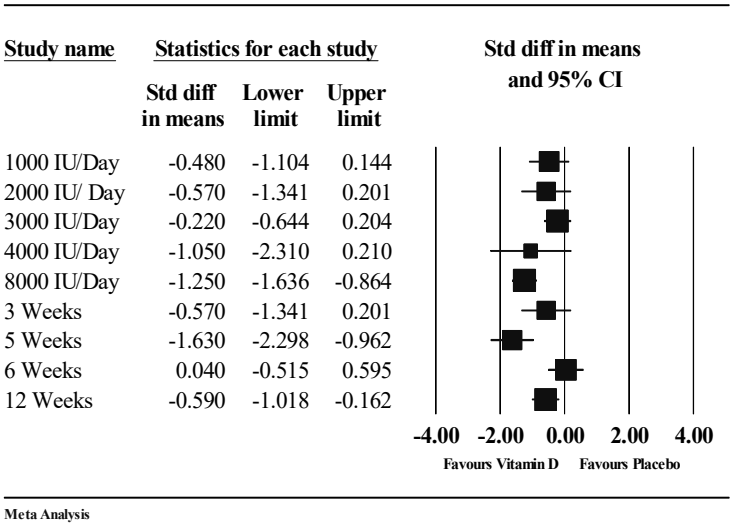

Figure 4 Sub-Groups analysis for Vit D supplementation at various dose (IU = international units) and different duration of an intervention.

The dose of Vit D intake was consistently significant (See figure 4, & table 2) at different amount. The effects are consistently improved except the dose 3000 IU/day and SMD was ranged from -0.22 to -1.25 followed by the different doses of Vit D intake. The higher dose of Vit D intake [8000 IU (SMD -1.25 (95% CI: -1.64, -0.86, I^2 = 0%, Z = 6.27, P = .000) shown greater impact on muscle damage markers. The SMD of overall impact was -0.74 (95% CI: -1.08, -0.39, I2 = 72%, Z = 4.15, P = .000) and indicating significant impact of Vit D supplementation on muscle damage. But the results are inconsistent to the length of supplementation period. Higher impact of intervention length for Vit D supplementation was revealed at 5 weeks of supplementation followed by the lowest impact at 6 weeks. The SMD at 5 weeks was -1.63 (95% CI: -2.30, -0.95, I^2 = 72%, Z = 4.71, P = 0.000) and shown significant impact of Vit D intake. The SMD of overall impact of intervention length was -0.74 (95% CI: -1.08, -0.39, I2 = 72%, Z = 4.15, P = .000) respectively.

Discussion

The use of antioxidant and anti-inflammatory supplements is widely prevalent in sports to mitigate exercise-induced muscle damage (EIMD) and enhance recovery post-exercise (Ortega et al., 2020; Peake et al., 2007). Vit D is well known for its properties of anti-inflammatory, and recent research has explored its potential role in reducing muscle damage and promoting recovery after exercise.

This meta-analysis evaluates the effectiveness of Vit D supplementation in enhancing recovery following exercise-induced muscle damage (EIMD) in humans. A total of six studies, involving 209 participants (155 males and 54 females), met the inclusion criteria.

To conclude the final outcomes, there are several key points which need to be discuss before. First, the overall SMD (Effect Size) of each sub-group indicated small to large effects of Vit D intake on muscle damage biomarkers. The obtained effects sizes are ranging from -0.28 (small) to -1.34 (large) among the selected recovery biomarkers. Lowest effects were revealed in LDH an enzyme which help in energy production converting glucose into energy simultaneously used as a muscle damage biomarker. Whereas the large effects were revealed in perceived pain assessment. These outcomes reported Vit D supplementation as an effective nutritional means to improve muscle recovery by reducing muscle damaging biomarkers. A recent systematic review (Rojano-Ortega & Berral-de la Rosa, 2023b) supported the outcomes that reported Vit D supplementation to be an efficacious strategy for reducing damage through muscle and inflammation after exercise. The review also highlighted that a minimum dose of 2000 IU/day of Vit D supplementation for more than one week intervention is sufficient to promote muscle health. Another study (Mastali et al., 2022) reported significant

reduction in CK and LDH biomarker in Vit D supplementation group included 24 untrained men. However, A meta-analysis conducted by Bello et al. containing 9 studies for LDH concentration evident non-significant effects of Vit D supplementation (Bello et al., 2021). A variation among the different biomarker used for muscle damage was identified in the literature. Vit D supplementation significantly reduced CK and inflammatory cytokines, while the effects were not consistent in context of LDH among the available literature.

Second, the consistency of the results varied among the studies included in the present meta-analysis. The Z statistic evaluates the overall effect size in a meta-analysis, testing whether the combined effect across studies significantly differs from zero. The studies used CK and LDH biomarkers shown non-significant Z values (see table 2) in subgroups analysis, indicated, the lack of strong evidence to conclude the definitive effects of Vit D on such parameters. On the other hand, effects are consistent in reference to inflammatory cytokines and perceived soreness. This suggests that Vit D supplementation has a meaningful impact on reducing perceived muscle soreness (VAS) and modulating serum cytokines, which are markers of inflammation. Whereas inconsistent outcomes were reported in context of dose of Vit D and supplementation period. Results were consistent at different doses except the studies used 3000 IU/day (Todd et al., 2017). The effects were improved by dose of Vit D from 1000 IU/day to 8000 IU/day on different muscle damaging biomarkers. Likely, no pattern was identified in intervention period. After 5 weeks of supplementation notable and higher effects were noticed, while the studies used 6 weeks have no effect on muscle damage biomarkers and moderate effects were noticed after 12 weeks. The results were also moderate but significant at lowest time point (5 weeks). A systematic review reported that a minimum of 1 week's supplementation is enough to produce the significant effects (Rojano-Ortega & Berral-de la Rosa, 2023a). Similar inconsistencies were reported in a recent systematic review conducted to assess the effects of Vit D supplementation on inflammatory cytokines (IL-6, TNFα). The review found that only two out of six studies showed noticeable changes in IL-6 levels, while the other four reported no significant differences in interleukin-6 or TNF-alpha levels after Vit D supplementation in athletes (Saedmocheshi et al., 2024).

Third and important aspect was the exercise protocol used to induce the muscle damage significantly impact the outcomes. Two studies with four outcomes did not used specific exercise protocol and did not report any significant impact at different biomarkers. The study conducted by stojanovic et al. used routine basketball match and drills for muscle damage (Stojanović et al., 2022). The biomarkers include CK, and LDH levels were not significant. While Todd et al. used routine football training was used as a muscle damaging protocol (Todd et al., 2017) and the mean difference of the biomarker IL-8 and TNFα were not significant. Rest of studies used specific eccentric muscle damage protocol involving, pre-defined intensity, angle of limbs, rest between sets, and velocity to ensure the proper muscle damage. Proper fatigue assessment is a crucial factor in studies analyzing recovery indices (Nara et al., 2023; Nara, Kumar, Rathee, & Kumar, 2022; Nara, Kumar, Rathee, Kumar, et al., 2022). This study emphasizes the importance of confirming muscle damage status in research focused on recovery, ensuring accurate evaluation of the recovery process. No sufficient literature is available to justify the fact. Additionally, the status of Vit D (25-hydroxyvitamin D levels) before the supplementation and control on the synthesis of Vit D_3 (cholecalciferol) through sun exposure during intervention period are the crucial factors which might have been considered before the intervention. Only 3 studies out of the total 6, reported the Vit D status before the intervention (Ahmed et al., 2021; Pilch et al., 2020; Stojanović et al., 2022). The absence of information regarding key environmental factors, such as the time of year, climatic conditions, and the surface area of skin exposed to sunlight during the intervention period, introduces potential bias in the study outcomes. Seasonal variation plays a crucial role in endogenous Vit D synthesis, and inadequate reporting of these factors makes it challenging to compare results across different studies. Without accounting for these variables, fluctuations in baseline and post-intervention Vit D levels may not be solely attributed to supplementation, thereby influencing the overall interpretation of its efficacy. Consequently, the lack of standardized reporting on sun exposure conditions limits the reliability and generalizability of findings in studies assessing the effects of Vit D supplementation on recovery and muscle damage.

Conclusion

Vit D supplementation appears to have a moderate effect on reducing EIMD, particularly in alleviating muscle soreness and supporting muscle recovery. However, the current body of evidence is limited by notable inconsistencies in study design, including variations in dosage, duration, participant characteristics, and assessment protocols. These factors make it difficult to draw firm conclusions. Nevertheless, the findings highlight the potential utility of Vit D, especially for individuals with existing deficiencies, such as athletes or those with limited sun exposure. Given the global prevalence of Vit D deficiency and its known role in musculoskeletal health, incorporating supplementation into recovery strategies could offer practical benefits. Standardizing intervention protocols should be a key goal in future investigations, include larger and more diverse populations, and consider external influences such as geographic location and sun exposure to better clarify the relationship between Vit D and muscle recovery.

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