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Original Article

Effect of a resistance-power training and vitamin D supplementation on serum IGF-1 concentration and physical function in elderly women

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Abstract

Background: This research examined the effect of a period of resistance-power training and vitamin D supplementation on serum insulin-like growth factor 1 (IGF-1) concentration and physical function in elderly women.
Objectives: This study aimed to evaluate the effect of 12 weeks of resistance-power training and vitamin D supplementation on serum IGF1, vitamin D concentrations, and physical function of elderly women.
Methods: In total, 44 elderly volunteered women were randomly assigned to four groups of training+placebo (TP), training+vitamin D (TS), vitamin D (Vit D), and placebo (P). The training groups performed a weight training program for 12 weeks (three sessions per week). People in the Vit D group took one 50,000 IU vitamin D jelly tablet every two weeks, and the P group took one placebo capsule (rice flour). Blood samples were taken from all subjects before and after training; moreover, serum vitamin D, IGF-1, and physical function indices were measured in this study. Data were analyzed in SPSS (version 25) and R3.5.2 software through the analysis of variance of weighted repeated measures.
Results: Serum vitamin D was significantly increased in the TS and Vit D groups in comparison with the control group, while it is meaningfully decreased in the TP group ($P \le 0.05$). Training and supplementation interventions had no significant effects on serum IGF-1 ($P \ge 0.05$). There was a significant increase in the physical function indices of the TS and TP groups, compared to those in the control group ($P \le 0.05$); meanwhile, there was no significant difference between the two groups.
Conclusion: Resistance-power training in the elderly improved the physical function indices; however adding vitamin D supplementation to the training had no significant effect on physical function.

Keywords: Aging, IGF-1, Physical function, Resistance-power training, Vitamin D

1. Background

Aging is a progressive and irreversible process that is associated with reduced physiological functions (1). During this period, a gradual decrease occurs in lean body mass, muscle strength, and motor performance (2). Numerous factors, such as inactivity, vitamin D (25-hydroxyvitamin D) deficiency, reduced growth factors, chronic inflammatory status, and changes in the neuromuscular junction (NMJ) contribute to the development of this condition in old age (3). Aging is also associated with decreased levels of anabolic hormones, especially IGF-1, which is an important primary arbitrator of growth hormone-related signaling pathways (4). Due to the important role of IGF-1 in regulating cell metabolism, growth, proliferation, and apoptosis in several organ systems (5), decreased level of this makes the elderly susceptible to sarcopenia, muscle atrophy (6), as well as neurodegenerative diseases, such as Alzheimer's and Parkinson's diseases, and functional dependencies (5). Therefore, the maintenance of optimal circulating IGF-1 levels is critical to good health.

On the other hand, poor vitamin D status is common in adult and aged populations (7). Severe atrophy of type 2 muscle fibers and internal infiltration of fat into skeletal muscle has been observed in patients with vitamin D deficiency (7, 8). Recently, a positive association has been reported between serum IGF-1 and vitamin D status (9, 10). Vitamin D appears to accelerate the production of IGF-1, IGF-1 receptors, and possibly IGFBP-3 (IGF-binding protein). Although several studies have shown that vitamin D treatment significantly increased serum IGF-1 levels (9, 11), the result of a study conducted by Meshkini et al. did not support these findings (12).

Moreover, IGF-1 has a progressively more powerful trophic impact, compared to growth hormone, on sensory and motor neurons, neuronal growth, and recovery. IGF-1 plays an important role in the development of peripheral and central nervous system (5). Vitamin D increases IGF-1 gene expression in the nervous system, and IGF-1 produced in Schwann cells leads to NMJ integration (13).

According to studies, physical exercise, especially strength training and proper nutrition, due to its positive effects on the muscular and nervous systems, is the most effective way to treat the consequences of aging with minimal side effects (14, 15). Resistance training can increase strength, power, and muscle volume (1). Some research has also reported that resistance training can increase serum IGF-1 levels (15, 16). Although these claims contradict research findings that report reduced or no effects of IGF-1 (17), the use of standard resistance training is effective in improving physical function by maintaining or even increasing muscle strength in the elderly. On the other hand, researchers reported that muscle power has a greater effect on physical function and daily activities in old age than muscle strength. Moreover, increasing muscle power is more useful and effective for the elderly than increasing muscle strength and mass. Therefore, when the goal is to increase the ability to perform physical functions, a power training program that focuses on improving muscle power is likely to be more effective (18).

As it was mentioned, resistance training, especially power training, stimulates and activates NMJ frequently and increases strength and physical function, which can cause significant changes in the function and morphology of neuromuscular junction and ultimately improve NMJ performance and muscle function (19, 20). Therefore, more research is needed to examine the influence of resistance-power training on the performance indicators of the elderly. Findings of nutritional studies in the elderly have also shown that vitamin D supplementation has positive effects on muscle strength, physical function, and prevention of falls and fractures in the elderly female population (3, 7, 8).

Furthermore, Drey et al. found that vitamin D could play an effective role in improving and stabilizing NMJ and increasing the performance of the elderly (19). However, the factors affecting this therapeutic intervention, such as dose, frequency of injections, and supplementation period have not been fully known yet and more research is needed in this area (7). Interestingly, some studies have shown that exercise training combined with vitamin D supplementation increases the positive influence of exercise on muscle function (13, 15). In contrast, Uusi-Rasi et al. stated that vitamin D consumption did not increase the effects of exercise on the performance of older women (21).

The positive effect of exercise and vitamin D on growing muscle power, strength, volume, and physical function in the elderly has been somewhat elucidated; however, the confirmation of the additive effects of exercise due to vitamin D intake in combined exercise+ supplement intervention programs requires further research. Accordingly, and considering the need for treatment and prevention of worsening physical condition of elderly people who have suffered from muscle wasting and decreased motor function due to decreased mobility and poor nutrition, it is needed to perform a research to evaluate the effects of resistance-power training and vitamin D supplementation for physical function in the elderly.

2. Objectives

This study was aimed to evaluate the effect of 12 weeks of resistance-power training and vitamin D supplementation on serum IGF1, vitamin D concentrations, and physical function of elderly women.

3. Methods

Participants and Experimental design

This double-blind randomized trial was conducted based on a placebo-controlled design. The statistical population of the study included all elderly women in Mashhad, Iran, who were selected by distributing announcements in cyberspace, as well as the area of the gym. The sample size was determined using G-power software (version 3.1.9.7) with a power of 0.85 and an effect size of 0.30 at a significance level of 0.05. In total, 44 healthy elderly women participated in this study.

Afterward, the individuals were randomly assigned into four groups of 11 cases per group, including resistance-power training+placebo (TP), resistance-power training+vitamin D supplement (TS), vitamin D supplement (Vit D), and placebo (P).

The inclusion criteria were being over 50 years of age and ability to perform exercises with the pieces of equipment. On the other hand, the participants with cardio and renal diseases, high blood pressure, and medical conditions preventing exercise (severe back pain and severe knee pain), and those who were taking medications that affected the amount of vitamin D serum, such as antiepileptic drugs, glucocorticoids, bile acid sequestrants, and lipase inhibitors, as well as cases who participated in regular exercise and had a history of taking vitamin D supplements in the last six months were excluded from the study.

In this study, the intervention lasted 12 weeks. One week before the start of the training program, the subjects were given the necessary information about the research procedure and objectives, the type of exercises, the type of supplement, and how to perform the research steps; moreover, they received two introductory sessions with research interventions (including weight training and tests). After explaining the procedure, written consent was completed by the research subjects. A physical-activity readiness questionnaire was also given to the individuals. Subjects were asked to refrain from any changes in their diet and physical activity during the study. At the beginning of the study, pretest subjects included body composition (e.g., height, weight, and body mass index [BMI]), lower and upper body muscle strength tests, and agility tests. Subsequently, two experimental groups were asked to participate in three sessions per week. In addition to their normal daily activities, they performed a power training program. One group received vitamin D supplementation, and the other group was given a placebo. The training program was completely supervised and carried out under the supervision of a researcher and by experienced trainers. The Vit D and the P groups did not perform any resistance training after the pretest. At the end of 12 weeks, all tests were taken again from all samples. The subjects' blood samples were taken before the start of training and 48 hours after the last training session following 8-10 hours of fasting at a rate of 5 cc. Participant's serum samples were prepared and stored in a freezer at -80°C until use. The study protocol was approved by the Ethics Committee of Hakim Sabzevari University, Sabzevar, Iran.

Training program

The training program was resistance-power and included five movements of leg press, chest press, leg extension, leg curl, and shoulder press with a range of 4-10 repetitions and 3-4 sets, which was performed in a circle. The rests between the stations and the sets were 60-90 seconds and 2-3 minutes, respectively. The individuals practiced three sessions per week for 12 weeks. From the fourth week, the participants were asked to perform all concentric movements at the maximum possible speed (<1 second) then stop for one second and complete the eccentric part at a slow and controlled speed (2-3 seconds) (22). During the first three weeks, the concentric section was performed at an average speed of 1-2 seconds. The duration of each power training session was about 45 minutes (warm-up with soft running, stretching and kinetic movements, performing a circle of resistance exercises with light weights for 10 minutes, weight training program for 30 minutes, and cooling for 5 minutes).

Complementary program

Individuals in the Vit D group received an oral vitamin D capsule (a capsule of cholecalciferol, 50000 IU) with a meal every two weeks. The subjects in the P group took one placebo capsule (containing rice flour) every two weeks.

Demographic characteristics

To evaluate the demographic characteristics, height and weight were first measured by gauges and scales; moreover, body mass index was obtained by dividing the weight (kg) by the square of the height (m).

Biochemical variables

Serum vitamin D and IGF-1 levels were measured using ELISA kits purchased from Monobind Inc (USA) and Mediagnost Inc (Germany), respectively.

Physical function

Jones and Rikli (2002) set of functional tests were used to measure the physical function of the subjects (23). Accordingly, three tests used from this set included Chair Stand for 30 seconds to measure lower body muscle strength, Arm Curl to measure upper body strength, and 8-Foot Up-and-Go test to assess agility. Subjects performed each test three times at one-minute rest intervals. In the end, the best result out of three attempts was recorded as an individual record.

30-Second Chair Stand

To assess lower body strength, the subject was asked to sit for 30 seconds with the arms crossed on the chest, stand up, and sit back in a chair (standard height 45 cm). The number of correct stands during this period was calculated as the individual record.

Arm Curl

In order to evaluate the upper body strength, the subject was asked to bend the arm sitting for 30 seconds while holding a weight of 2.27 kg. The number of bicep curls in 30 seconds was recorded as an individual record.

Timed-Up-and-Go (TUG)

To assess agility, each subject sat on a chair and then got up from the chair with the steering wheel and began to walk at a distance of 2.44 meters and then returned to the path. The time it took to get up from a chair and sit back on it was recorded as a person's record.

Statistical analysis

SPSS software (version 24.0) and R 3.5.2 were used for data analysis. Quantitative variables were presented as mean±SD. To evaluate the normality, Shapiro-Wilk and Kolmogorov-Smirnov tests with Lilliefors correction were used. Repeated measures analysis of variance (RM-ANOVA) was also applied to test the research hypotheses. If the underlying hypotheses related to the analysis of variance were not established, weighted RM-ANOVA was used. In case of significant interaction between groups and times, the Tukey post hoc test was employed to determine the location of the pair-wise differences between mean values. A p-value less than 0.05 was considered statistically significant.

4. Results

Characteristics of participants

Table 1 tabulates the demographic characteristics of the participants. Mean age, height, and BMI values of the participants were obtained at 55.84±4.70 years, 155±5 cm, and 29.61±4.26 kg/m^2, respectively. The results of RM-ANOVA for weight and BMI showed that group and time had significant interaction effects (P=0.03 and P=0.04, respectively). Based on the Tukey post hoc test, the weight groups of TS (P=0.001) and Vit D (P=0.009) had a significant decrease, compared to the control group. The TP group also showed a significant decrease, compared to the TS group (P=0.026). In contrast, the TP group was not significantly different from the Vit D (P=0.134) and control groups (P=0.933); moreover, the TS group was not significantly different from the Vit D group (P=0.029).

Regarding BMI, the results of the Tukey post hoc test showed that the supplement group experienced a significant decrease, compared to the TS group (P=0.03). No significant difference was observed among other groups (P>0.05).

Changes in serum concentrations of Vit D3 and IGF-1

Table 2 summarizes the changes in biochemical variables of subjects before and after interventions. The results indicate the significant effects of group and time interaction on Vit D (P=0.005). In contrast, the interaction effects of group and time were not significant for IGF-1 (P>0.05). Therefore, there was no significant difference among the groups in terms of the IGF-1 concentration.

Regarding Vit D, the results of the Tukey post hoc test revealed that all three experimental groups were significantly different from the control group (P=0.0001). Furthermore, a significant increase was observed in TS and Vit D groups compared to the control group, while A significant decrease was observed in TP group compared to the control group (P=0.0001). Moreover, the TS group revealed a significant increase, compared to the Vit D group (P=0.0001).

Physical function

The mean of physical function variables of subjects before and after interventions are presented in Table 3. The results of RM-ANOVA showed that group and time had significant interaction effects on lower and upper body functional strength and agility. Regarding lower and upper body functional strength, the findings of the Tukey post hoc test revealed that the TP and TS groups had a significant increase in comparison with the control group (P<0.001); however, the two groups were not significantly different (P>0.05). Moreover, no significant difference was observed between the supplement and control groups (P>0.05). Regarding agility, the results showed that the TP and TS groups had a significant improvement, compared to the Vit D group (P<0.0001). Meanwhile, the two groups were not meaningfully different (P>0.05).

Table 1. Mean of demographic characteristics of the participants in the studied groups before and after interventions

Variable	Time	Groups				F	p-value
		TP	TS	Vit D	P		
Age (years)		55.4+00	55.4±3.8	57.4±4.8	55.8±4.7	N/A	
Height (cm)		158±3	156±5	151±5	157±5	N/A	
Weight (kg)	Before	74.4±7.8	69.7±8	68.95±12.8	75±13.9	3.07	0.03
	After	72.5±5.9	69.2±7.5	68±11.5	75.1±13.4		
	% of changes	-2.5	-0.7	-1.3	0.1		
BMI (kg/m2)	Before	29.8±3.7	28.6±3.1	29.9±5	30.11±5.3	2.88	0.04
	After	29.1±2.8	28.4±2.9	29.5±4.5	30.14±5.2		
	% of changes	-2.3	-0.6	-1.3	0.09		

Table 2. Mean of biochemical variables of subjects in the studied groups before and after interventions

Variable	Time	Groups				F	P-value
		TP	TS	Vit D	P		
Vit D3 (ng/ml)	Before	32.73±6.74	32.85±12.49	22.59±14.67	19.91±9.43	4.87	0.005
	After	19.94±9.1	44.63±17.4	28.39±18.05	20.2±14.02		
IGF-1 (ng/ml)	Before	221.6±79.5	196.1±53.7	196±79.3	207.9±76.5	2.00	0.13
	After	195.6±66.5	194.8±84.9	172.7±55.4	167.4±66		

Table 3. Mean of physical function variables of subjects in the studied groups before and after interventions

Variable	Time	Group				F	P-value
		TP	TS	Vit D	P		
Lower body functional strength (n)	Before	17.3±3.8	15.9±1.8	15.3±2.5	15.7±2.9	7.67	0.0001
	After	27.8±7.2	28.2±4.9	18.2±3.6	19±5.5		
Agility (Sec.)	Before	5.3±1.1	5.1±0.7	5.7±0.7	5.5±0.6	3.98	0.01
	After	4.7±0.6	4.8±0.4	5.5±0.7	5.6±0.8		
Upper body functional strength (n)	Before	27.9±6.3	28.7±4.6	23.2±4.4	25.2±5.4	8.22	0.0001
	After	39.7±5.2	35.6±6.1	24.3±5	23.6±4.6		

5. Discussion

This study aimed to examine the effect of resistance-power training and vitamin D supplementation on serum IGF-1 concentration and physical function in elderly women. Based on the results, serum vitamin D levels decreased in the TP group and increased in the TS and Vit D groups. Previous studies have shown that taking vitamin D supplementation increases serum vitamin D levels (19, 24-26). Since the supplementation in the present study was in the form of vitamin D tablets with a dose of 50,000 IU every two weeks, or approximately 3,000 IU/day almost in accordance with the clinical guidelines (27), an increase in the serum vitamin D and close return to normal levels was predictable in supplement-consuming subjects.

In the present study, a significant decrease in the level of serum vitamin D was observed in the training group. Since muscle is an important source of vitamin D, lack of muscle hypertrophy after exercise training can be one of the reasons for the lack of improvement in vitamin D status (28). However, other factors, including the use of fatty acids, such as linoleic acid in the diet, the use of fat-lowering drugs, estrogen depletion, and the reduction of calcium, magnesium, and iron micronutrients can lower vitamin D levels. These factors cause damage to the pathways of absorption, synthesis, activation, and metabolism of vitamin D (29). It is possible that exercise training through some of these factors causes a decrease in the serum levels of vitamin D in the subjects in the training group. In the present study, serum levels of these micronutrients were not measured; however, it is possible that their possible changes may have reduced serum vitamin D levels in the training group.

The results of the study revealed no significant difference among the studied groups regarding the serum IGF-1. This result agrees with the results of a study conducted by Trummer et al. that found no changes in IGF-1 after taking vitamin D (26) and the findings of a study performed by Hofmann et al. after resistance training (30). However, it was inconsistent with the results of other studies conducted on increasing IGF-1 after resistance training (16, 31), the consumption of vitamin D (9, 11), and the combination of training and vitamin D (15).

Several mechanisms have been hypothesized for the way IGF-1 levels are modulated by physical activity. Stimulation of growth hormone as a result of physical activity can lead to increased IGF-1 levels (16). On the other hand, another possible mechanism is the enlargement or regeneration of muscle cells following resistance training that may increase IGF-1 (32). Therefore, it is possible that in the present study, no increase in muscle volume caused any changes in IGF-1 levels. Various studies have addressed several factors that explain differences in IGF-1 levels following vitamin D supplementation. Accordingly, IGF-1 binds to its binding proteins (IGFBPs), which positively correlates with the IGFBP-3 and negatively with the IGFBP-1 (33). Vitamin D has been shown to mediate the increased production of IGFBP-3 resulting in a decrease in the IGF-1/IGFBP-3 ratio in some studies following vitamin D supplementation (34).

On the other hand, bodyweight may affect IGF-1 levels. IGF-1 as a systemic growth factor is mainly synthesized in the liver, although it is also produced in other tissues, including muscles (35). According to studies, different effects on the body composition of the subjects can cause different results in IGF-1 levels (36). In the present study, it is possible that different IGF-1 isoforms underwent simultaneous decreasing and increasing changes so that their serum levels remained unchanged. Studies have shown different results on the association between IGF-1 and 25-hydroxyvitamin D (25 (OH) D) (9, 12). Therefore, the relationship between IGF-1 and 25 (OH) D is still unclear and needs further research.

In the present study, improvement in physical function tests was observed in training groups. Many studies have reported a significant increase in physical strength and function following resistance and power training (19, 22, 37, 38). The maintenance of muscle strength in old age is more dependent on maintaining muscle mass. At the same time, it seems that muscle strength has a greater effect on health status in old age than muscle volume (39). Regular physical activity increases muscle strength and volume by increasing protein synthesis, the number of myofibrils, and the cross-sectional area of the fibers (40). An important anabolic pathway for protein synthesis is PI3K/AKT activation, which stimulates mTOR for protein synthesis. This pathway is up-regulated by anabolic stimuli, such as IGF-1 and exercise (41, 42). However, due to the lack of significant changes in IGF-1 levels in the present study, it seems that other factors in addition to muscle growth and hypertrophy have improved physical function.

In this regard, Hofmann et al. stated that improvements from resistance training in physical function appear to be due to inhibition of muscle degradation pathways rather than muscle growth occurring through IGF-1 (30).

In the present study, unlike training, vitamin D consumption had no significant effect on improving subjects' physical function. This was contrary to many studies that have shown the effect of taking vitamin D on the improvement of muscle function and strength, as well as reduction of the risk of falls and even death (3, 7, 13, 15, 19). In line with the results of this study, Pirotta et al. reported that consuming vitamin D supplementation for 10 weeks increased 25 (OH) D levels and muscle strength in the elderly; however, it had no effects on muscle power and function (25). Furthermore, in the study carried out by Uusi-Rasi et al., vitamin D intake did not increase the effects of exercise training on physical function (21).

There are several factors involved in the lack of improvement of physical function in groups taking vitamin D supplements. The effects of vitamin D supplementation are probably dependent on basal serum vitamin D levels. In such a way that if the serum level is more than 10 ng/ml, the supplementation has no effect or may have a limited effect (43). Nevertheless, several studies have reported conflicting results. Moreira-Pfrimer et al. observed a positive effect of vitamin D supplementation on lower limb muscle strength in people with inadequate levels of vitamin D (10-20 ng/ml) (44). Many studies state that the target vitamin D concentration level to meet the needs of human tissues containing vitamin D receptors is about 40 ng/ml (27, 45). In the present study, serum levels of vitamin D in the Vit D and TS groups at the end of the period were about 28 and 44 ng/ml, respectively, which showed an increase in muscle function. Therefore, the lack of change in muscle composition following supplementation is a probable reason for the lack of improvement in muscle function (43)

In this study, subjects in the Vit D group observed no improvement in physical function, whereas physical function improved in the training and supplement+training groups. This improvement can be attributed to the positive effects of training, such as increasing muscle strength and power, as well as maintaining or increasing muscle mass. It seems that vitamin D consumption cannot increase the improvements from resistance-power training in the physical function of the elderly.

Study Limitations

On the other hand, lack of control over the level of motivation during the performance of exercises and tests, as well as the effect of learning on how to perform the tests were among the limitations of the study. Furthermore, despite the advice to the subjects to not change their daily physical activity during the study, it was possible that some did not fully follow this advice.

Strength of the study

One of the strengths of the study is the type of exercise training program that was of the resistance-power type since the muscle power factor for adults and the elderly to improve physical function is more important than other physical factors, such as muscle strength. The other one is the use of vitamin D supplementation due to its effect on the muscular and nervous systems, which declines structurally and functionally with age.

6. Conclusion

Based on the results, training without change in IGF-1 levels improved physical function in the elderly. In contrast, vitamin D supplementation had no effect on physical function and IGF-1 levels of elderly women. Therefore, it can be said that resistance-power training can increase muscle and physical function in the elderly. Interestingly, taking vitamin D supplementation at the same time does not increase these changes. It seems that the amount and duration of vitamin D supplementation were not sufficient to be effective. Therefore, it is recommended that future studies examine the effect of training and vitamin D supplementation on the population of older people with different indicators and interventions, such as dose and duration of consumption, intensity, and duration of training.

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Conflicts of interest

The authors declare no conflict of interest.

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