

Effect of ultraviolet on vitamin D and quality of life in postmenopausal women: a randomized controlled study

Type

Original paper

Keywords

quality of life, vitamin D, aerobic exercises, ultraviolet radiation

Abstract

Objective

To determine the influence of ultraviolet radiation on vitamin D plasma levels and quality of life in postmenopausal women with vitamin D deficiency

Subjects and Methods

In a single blinded randomized controlled trial design, thirty postmenopausal women were chosen suffering from a progressive, generalized muscle weakness, associated with decrease in physical function and poor quality of life. Subjects were aged between 45 and 65 years and were randomly assigned into group (A), treated by ultraviolet radiation in addition to regular aerobic exercises; and group (B), receiving solely aerobic exercises. All participants had 3 sessions per week for three months. Outcome measures measured before and after three months of intervention were vitamin D level and the SF-36, a specific quality-of-life questionnaire

Results

A significant increase in vitamin D was observed along with an improvement in quality of life in group A compared with group B after the treatment period.

Conclusions

twelve week program of ultraviolet radiation in addition to regular aerobic exercises yielded improvement in vitamin D and quality of life more than aerobic exercises alone in the management of postmenopausal chronic musculoskeletal disorders.

Explanation letter

all comment were considered and corrected with highlighted

Effect of ultraviolet on vitamin D and quality of life in postmenopausal women: a randomized controlled study

Abstract. [Purpose] To determine the influence of ultraviolet radiation on vitamin D plasma levels and quality of life in postmenopausal women with vitamin D deficiency. [Subjects and Methods] In a single blinded randomized controlled trial design, thirty postmenopausal women were chosen suffering from a progressive, generalized muscle weakness, associated with decrease in physical function and poor quality of life. Subjects were aged between 45 and 65 years and were randomly assigned into group (A), treated by ultraviolet radiation in addition to regular aerobic exercises; and group (B), receiving solely aerobic exercises. All participants had 3 sessions per week for three months. Outcome measures measured before and after three months of intervention were vitamin D level and the SF-36, a specific quality-of-life questionnaire. [Results] A significant increase in vitamin D was observed along with an improvement in quality of life in group A compared with group B after the treatment period. [Conclusion] twelve week program of ultraviolet radiation in addition to regular aerobic exercises yielded improvement in vitamin D and quality of life more than aerobic exercises alone in the management of postmenopausal chronic musculoskeletal disorders.

Key words: vitamin D, quality of life, ultraviolet radiation, Aerobic exercises

INTRODUCTION

Menopause is the interruption of menstruation for more than one year as a result of degenerative changes at the level of the ovaries and follicles, and is usually associated with changes in the ovarian hormone levels. The part of life after menopause is commonly termed postmenopausal period in female life [1]. The clinical picture associated with menopause is usually the presence of hot flushes, irregular menses, and excessive night sweats. While some women report no major signs other than the discontinuation of menses [2], many others tend to report many somatic and psychological symptoms often designated as postmenopausal syndrome. It is well documented that age is linked to a decline in physiological functions particularly the loss of bone mass density (BMD) in addition to a drop in muscle strength and mass termed sarcopenia. Such decline in muscle mass has been accused to induce functional impairment especially those related to activities of daily living, in addition to increased

34 risk of falling and nonvertebral fractures [3]. Vitamin D deficiency is well documented
35 in postmenopausal women at which parathyroid hormone is suppressed and is
36 associated with increased intestinal calcium absorption, reduced BMD, increase bone
37 loss, and increase fracture rate. Various risk factors were identified including age,
38 decreased dietary intake, diminished sunlight exposure, wintertime, nursing home
39 environment, reduced skin thickness, a decline in the ability of the skin to fabricate
40 vitamin D, impaired intestinal uptake, and decreased hydroxylation in both kidneys and
41 liver [4]. Vitamin D deficiency is usually asymptomatic, but research conclusions
42 reported generalized muscle weakness, lengthened time to peak contraction in addition
43 to augmented time to muscle relaxation, in post-menopausal women. Clinically, such
44 associated changes are often described by affected women as heaviness in the legs,
45 tiring easily, difficulty when performing some activities of daily living particularly
46 rising from a seated or squat position, mounting stairs, or lifting objects [5]. Diagnosis
47 of vitamin D deficiency is crucial since it may lead to impairment in quality of life
48 (QoL) even if no specific symptoms are present [6]. Vitamin D supplementation is
49 commonly used as a medical intervention but overdose may cause hypercalcemia, with
50 associated anorexia, nausea, vomiting and diarrhea, polyuria, polydipsia, weakness,
51 weight loss, insomnia, irritability, nervousness, severe depression, pruritus, proteinuria,
52 and potential calcification in the kidneys, and ultimately renal failure [7]. Non-
53 pharmaceutical treatment as ultraviolet radiation and exercises are used to address
54 postmenopausal symptoms especially that chronic musculoskeletal disorders has been
55 well correlated with diminished quality of life scores. Such modalities are regarded as
56 natural and safe in managing postmenopausal syndrome and being less invasive than
57 medications [8]. Ultraviolet is an electromagnetic energy, which falls between visible
58 rays and X-rays and has a wavelength between 10 nm and 400 nm. It is divided into;
59 UVA: Wavelength range between 315 and 400 nm., UVB: Wavelength range between
60 280 and 315 nm., and UVC: Wavelength below 280 nm [9]. The skin absorbs UVB
61 radiation and uses it to convert skin sterols precursors, such as 7- dehydrocholesterol,
62 to cholecalciferol (Vitamin D₃). In the liver and kidneys, this latter is converted to active
63 metabolites form 1,25(OH)₂ D₃. It has been agreed for many years that, exposure to
64 artificial UV radiations or artificial sun light can be curative for vitamin D deficiencies
65 [10]. In the same context, aerobic exercise has been claimed to be efficient in the
66 management of a number of post-menopausal signs and symptoms including hot
67 flushes, osteoarthritis, hyperlipidemia, fibromyalgia, depression, and diabetes mellitus

[11]. Regular aerobic activities were also reported to maintain and improve quality of life, decrease fatigue sensation, and lessen the rate of depressive disorders [12]. Researches trying to figure the relation between vitamin D deficiency and skeletal muscle strength concluded opposing results. Such conflicting results might be caused by research methodologies differences, genetic causes and research participant's characteristics. Additionally, vitamin D deficit has been found to be one of the correlated risk factors for osteoporosis, high fall risk and fractures, and was accused to affect negatively the patient's quality of life. Thus, the present study aimed to study the effect of ultraviolet radiation and aerobic exercise on muscle strength and consequently the quality of life in women in their postmenopausal life period.

SUBJECTS AND METHODS

This was a prospective, single-blinded, pre and post-test, randomized controlled trial. Thirty-six postmenopausal females were enrolled from the women's health outpatient clinic at faculty of physical therapy, Cairo University, outpatient clinic of obstetrics and gynaecology department. Eligible participant's age ranged between 45 and 56 years old, and their body mass index (BMI) ranged between 28 and 30 kg/m² and reporting a decrease in their physical function and quality of life. Exclusion criteria consisted of women reporting any inclusion in any physical activity, even in leisure time, for the last 12 months or suffering from any acute or chronic metabolic, hormonal, neurological, musculoskeletal, gastrointestinal, or urinary disorder or disease. In addition, subjects included in the study, were chosen not taking any vitamin D supplements, osteoporosis treatment, or current or previous intake of hormone replacement therapy. Prior to any evaluation, signed informed consent was collected from all participating women. The study was granted the approval from the institutional review board of the at Faculty of physical therapy, Cairo University with a reference number (P.T.REC/012/001543). The study abided to the guidelines of the declaration of Helsinki and was performed between September 2017 and October 2018.

Intervention

All participants were given a brief demonstration about the study and the tasks to be performed. An independent research assistant unwrapped closed casings containing a random cards generated automatically by a computer and divided the participants into two identical groups A and B. The study did not record dropouts after the randomization. Group A received ultraviolet radiation in addition to regular aerobic exercises. Ultraviolet sessions were performed three times per week for three months,

104 and were achieved while the patient was lying down comfortably. The aerobic exercises
105 were implemented 3 times per week for three months. Group (B) received solely
106 aerobic exercises, three sessions per week for three months. For both groups, aerobic
107 exercise session was performed as follows: 40 minutes of treadmill walking, as follows:
108 warm up (10 minutes), followed by exercising (20 minutes) and ended by cooling down
109 (10 minutes). Intensity of the exercise session was fixed at 60–70% of maximum heart
110 rate (HR max) calculated as $220 - \text{age}$ [13].

111 **Outcome measures**

112 Vitamin D level was measured by blood analysis before and after 3 months of
113 intervention in both groups. The plasma levels of Vitamin D were recorded before and
114 after 3 months of intervention. Vitamin D concentrations were taken through high-
115 performance liquid chromatography (HPLC) (Shimadzu, Japan). Kits used allowed the
116 chromatographic determination of 25-OHD on a simple isocratic HPLC system with
117 ultra violet detection. Interfering components were removed and analytes were
118 concentrated through efficient protein precipitation and selective solid phase extraction.
119 The limit of detection was 2.5 ng/ml and the coefficient of variation was <7 %. It has
120 been found that serum 25-hydroxyvitamin D can be considered as one of the most valid
121 markers of vitamin D status. It has been also agreed that vitamin D is considered
122 deficient with levels less than 20 ng/ml (50 nmol/l) of 25-hydroxyvitamin D, while the
123 range 21 to 29 ng/ml (52.5 to 72.5 nmol/l) is considered as vitamin D insufficiency,
124 while the ideal level was set as 30 ng/ml (75 nmol/l). In this study, a level less than 20
125 ng/ml of 25-hydroxyvitamin D levels was considered as marker of vitamin D deficiency
126 [14]. Additionally, the quality of life was judged by the SF-36 a tool considered generic
127 and multidimensional, and evaluating a person's overall satisfaction with life and
128 health. This tool has been translated and validated into many languages including
129 Arabic [15]. The Arabic version of the questionnaire was self-administered and all
130 subjects completed it at their routine clinical visit after they had accepted to participate
131 in the study. SF-36 is a measure of physical and mental status for the last four weeks,
132 and consists of three levels: first level containing 36 items, the second level comprising
133 eight sub-scales that aggregate 2-10 items, and the third level involving two summary
134 scales that aggregate sub-scales. These two latter, aggregate four sub-scales each: the
135 first addressing the physical component, and the other addressing the mental component
136 score. General health, vitality and social functioning have correlation with both of the

138 summary scales. The higher score means better QoL, with score ranging between 0 and
139 100.

140 **Data analyses**

141 Using Statistical Package for Social science (SPSS) program version 23, the data
142 recorded were analyzed. Before concluding analysis, data was evaluated for normality
143 assumption, homogeneity, and occurrence of extreme scores. Such analysis was
144 performed as preliminary measure before parametric calculations of the analysis of
145 difference. We recorded a linear relationship between the dependent variables using
146 scatterplot, and no proof of multicollinearity using Pearson correlation ($|r| < 0.9$).
147 Additionally, no univariate outliers were observed in the data through boxplot, and no
148 multivariate outliers, as evidenced by Mahalanobis distance. Vitamin D and quality of
149 life were normally distributed, as demonstrated by Shapiro-Wilk's test ($p > .05$).
150 Levene's test assured the homogeneity of variances ($p > .05$) for all dependent
151 variables. Consequently, 2×2 MANOVA (mixed design) was considered to match the
152 recorded variables for groups and at various periods. Alpha level was set at .05. **The**
153 **sample size (30 participants) was calculated to yield an 85% power and $\alpha=0.05$.**

154 **RESULTS**

155 Thirty participants were involved in the final analysis after recording drops of six
156 volunteers related to personal willingness of the participants (fig 1). They were
157 previously allotted into two groups; 15 patients (group A) receiving ultraviolet radiation
158 in addition to regular aerobic exercises, and the group B comprising 15 patients
159 receiving aerobic exercises. The independent t-test showed no significant differences
160 ($p > .05$) when comparing mean values of different personal characteristics in both
161 groups (table 1).

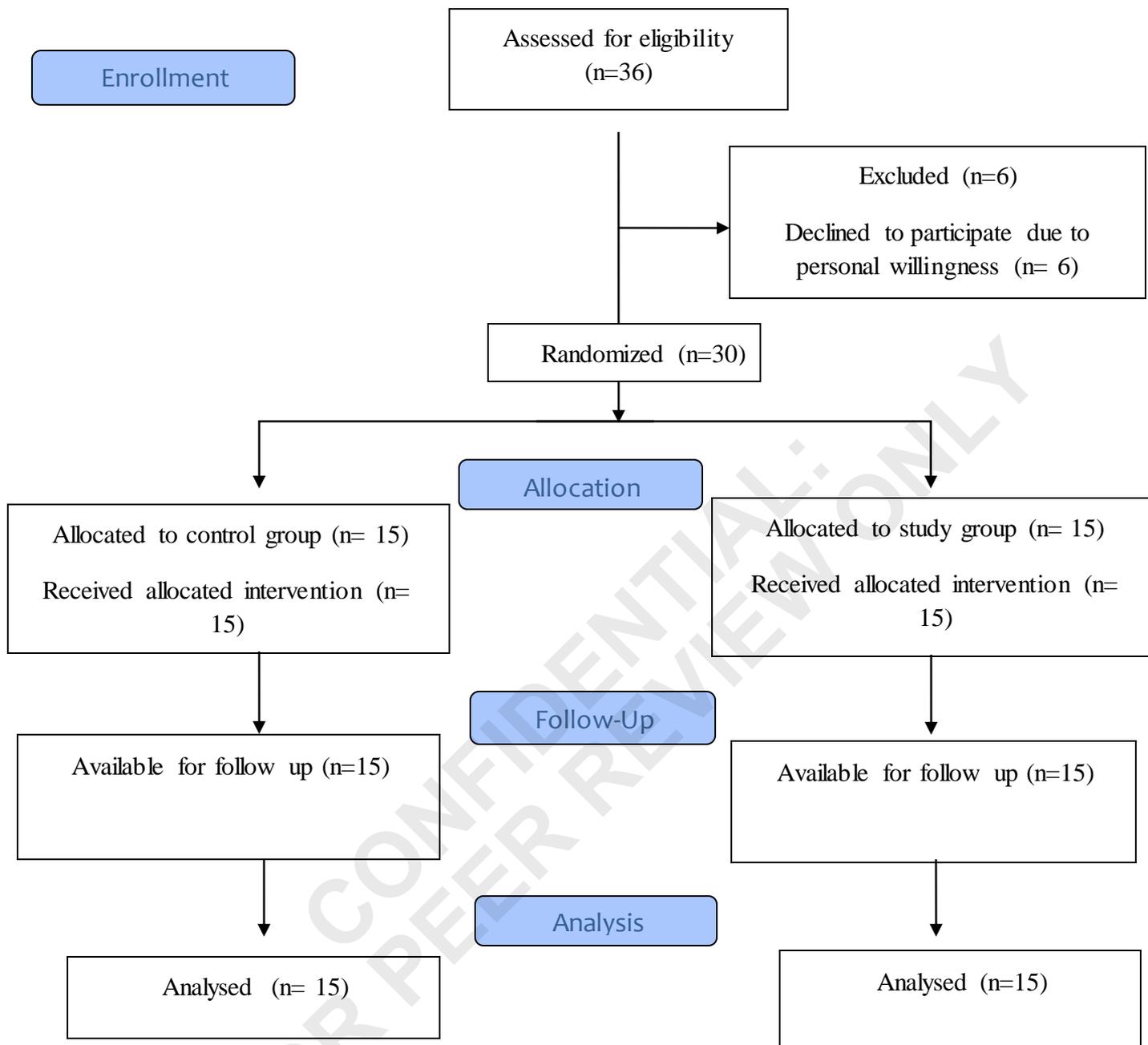


Fig (1): Flow chart of the study.

Table (1): Personal characteristics of patients in both groups

Items	Group A	Group B	Comparison		Significance
	$\bar{x} \pm SD$	$\bar{x} \pm SD$	t-value	P-value	
Age (years)	51.66±5.21	53.29±5.31	-0.915	0.367	NS
Body mass (kg)	84±14.9	84.05±11.28	-0.013	0.99	NS
Height (cm)	157.22±5.05	157.7±3.49	-0.327	0.746	NS

* \bar{x} : Mean, SD: standard deviation, P: probability, S: significance, NS: non-significant.

Mixed design MANOVA investigated thirty patients allocated into two identical groups in numbers. It showed a significant within-subject effect ($F = 124.358$, $p = .0001$) and treatment * time effect ($F = 35.942$, $p = .0001$); on the other hand, there was significance in the between-subject effect ($F = 12.289$, $p = .0001$). Table (2) present descriptive statistics (mean \pm SD) and multiple pairwise comparison tests for the measured variables. Additionally, regarding the within-subject effect, the multiple pairwise comparison tests uncovered significant increase ($p < .05$) in vitamin D levels and quality of life scores after treatment in comparison with before treatment means for both groups. Calculations of the between-subject effects using multiple pairwise comparisons revealed significant increase ($p < .05$) in both vitamin D and quality of life more in group A than in group B.

Table (2): Descriptive statistics and multiple pairwise comparison tests for the all dependent variables for both groups at different measuring periods

Variables	Group A		Group B	
	Pre	Post	Pre	Post
Vitamin D	20.5±1.91	32.77 ±5.34	19.22 ±1.88	22.08±2.55
Quality of life	44.35±4.28	57.05 ±5.44	41.68 ±3.99	46.25±5.02
<i>Within groups (Pre Vs. post)</i>				
p-value	Vitamin D		Quality of life	
Group A	.0001*		.0001*	
Group B	.001*		.0001*	
<i>Between groups (group A Vs. group B)</i>				
	Vitamin D		Quality of life	
Pre treatment	.064		.075	
Post treatment	.0001*		.0001*	

*Significant at the alpha level ($p < .05$).

DISCUSSION

It has been found that musculoskeletal disorders account for 14-30% of disorders affecting postmenopausal women resulting in functional deterioration, increase in the requirement for support in the achievement of routine activities, and poor quality of life [16]. The main cause of such limitations is the decline in estrogen levels leading to progressive drop in levels of growth hormone (GH) and insulin-like growth factor1 (IGF1). The associated decline in androgen production is accounted for the onset of sarcopenia [17]. The risk of sarcopenia in postmenopausal women has been reported to be doubled when concentrations of 25(OH)D drop lower than 10 ng/ml. Vitamin D deficiency is generally silent and usually women exhibit no clear symptoms, even though some amounts of muscle weakness and pain might be present and possibly lead to further reduction in the woman's quality of life [18]. In the present study, results revealed significant rise in vitamin D level and enhancement in the quality of life questionnaire scores in both post intervention groups when compared to pre intervention scores; however significant higher scores of vitamin D level and quality of life in subjects treated with UV radiation were recorded after treatment when compared to controls. Such observations agree with others [19], who reported that vitamin D deficiency is a frequently encountered clinically in post menopause and was linked to reduced intensity and duration of exposure to ultraviolet by 80-90% and other 10-20% by low dietary vitamin D intake. Each of these two sources was accused to provide sufficient supply, but if one of them is lost, the other source can easily become insufficient. In a multinational European study, occurrence of vitamin D deficiency reached 32.1% [20], while others published higher rates [14].

In this study, remarkable improvements were recorded in the ultraviolet radiation group. Such observation may be attributable to that the main source of vitamin D is the synthesis in the skin facilitated by the ultraviolet radiation effect on the 7-dehydrocholesterol, the vitamin D precursor. UVB has been accounted for the fabrication of vitamin D in the skin, and may reach 1,000 IUs for each minute of irradiation. In addition, any vitamin D deficiency can be caused by factors affecting the UVB photons to penetrate the skin. Dietary intake is a documented alternative source of vitamin D; on the other hand, contemporary diets lack sufficient amounts of vitamin D, even in fortified diets containing high levels of dairy and/or cereal products. Thus, the human body relies highly on skin production of vitamin D otherwise deficiency is inevitable [21]. The observed increase in vitamin D in this study is supported by other

248 authors [22], who reported increase in vitamin D levels even 24 hours post UV light
249 exposure.

250 In the same context, the conclusions of the present study are in agreement with others
251 regarding improvement observed in the quality of life [16], who studied the added value
252 of vitamin D on regular physical activity on 77 sarcopenic postmenopausal women.
253 Adding Vitamin D supplements to gentle exercise was found useful in addressing
254 catabolic mediators, inflammatory mediators such as C-reactive protein (CRP), and
255 consequently refining some anabolic markers and thus increased the production of
256 muscle proteins. These associated changes led to increase in fat-free mass and muscle
257 strength, demonstrating effectiveness in management of sarcopenia with additional
258 enhancements in functional markers and quality of life. The improvements recorded in
259 the present study can be accounted for possible subsequent genomic and nongenomic
260 actions leading to adequate muscle function. Genomic cascade are facilitated by nuclear
261 vitamin D receptors that influence transport of calcium in the muscles and other related
262 metabolisms [23]. Normal serum calcium level, enabled by suitable vitamin D levels,
263 can be regarded as crucial for ordinary muscle functioning. Nongenomic actions were
264 found to take place through vitamin D receptors existing on cell membranes. This
265 binding triggers a series of pathways that were found to convey signals to the
266 cytoplasm. Such mechanisms are also believed to regulate calcium inside the muscle
267 cells [24]. Another possible explanation could be the initiation of mitogen-activated
268 protein kinase signaling paths that were highly correlated with myogenesis regulation,
269 cell proliferation, differentiation, and apoptosis. Taking these mechanisms altogether,
270 it can be deduced that vitamin D can produce stimulation of muscle cell proliferation
271 and growth. Additionally, potential protein synthesis observed can be the result of
272 vitamin D binding protein that is linked to adenosine triphosphate (ATP) uptake in the
273 skeletal muscle reticulum [25]. Four doses of vitamin D supplementation were found
274 effective in enhancing physical and mental components of SF-36 [26]. In another study
275 [27], community dwelling women were evaluated for physical performance according
276 to vitamin D status and concluded that serum vitamin D was significantly associated
277 with muscle strength and physical function scores recorded by SF-36 in
278 postmenopausal women. These findings were confirmed in other studies performed in
279 elderly women [28]. Aerobic exercises exhibited significant improvement in quality of
280 life. This improvement is attributable to that regular physical activity is safe for
281 postmenopausal women and the risks of developing major systemic or musculoskeletal

283 disorders are reduced by regular physical activity with various identified modes and
284 intensities [29]. The results agree with others [30], who recommended that
285 postmenopausal women could benefit from the positive effects of physical activity
286 through performing modest but regular physical activity. However, a combination of
287 various modes of training, particularly resistance and endurance training has been
288 claimed to be more beneficial than using one mode of exercising individually. Such
289 variation in the training modes was claimed to contribute to improved quality of life
290 among postmenopausal women with moderate deficits or frailty.

291 **LIMITATIONS**

292 Possible limitations in this study might be the psychological, physiological and
293 potential cultural issues.

294 **CONCLUSION**

295 At the end, it can be concluded that, in postmenopausal women, 12-week program of
296 ultraviolet radiation in addition to aerobic exercises yielded significant improvement in
297 vitamin D, and improved the score of SF-36 quality of life score when matched to
298 aerobic exercises only.

299 **ACKNOWLEDGEMENTS**

300 Authors would like to acknowledge to all participants involved in this study.

301 **CONFLICT OF INTEREST**

302 Authors state no conflict of interest

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