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RESEARCH ARTICLE

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The effect of zinc supplementation on fatigue among elderly community dwellers: A parallel clinical trial

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Abstract

Background and Aims: Fatigue is one of the most common complaints of the elderly. This study was conducted to assess the effect of zinc supplements on fatigue among the elderly.

Methods: This randomized clinical trial was conducted on 150 elderly aged ≥60 years who were recruited from the health centers (Kashan, Iran) with a convenience sampling method. Participants were allocated to intervention and control groups by block randomization. Participants in the intervention group received a daily dose of 30 mg of zinc supplement for 70 days; meanwhile, in the control group, no intervention was performed. The level of fatigue was measured by the multidimensional fatigue inventory before and after the intervention. Both groups were homogeneous in terms of demographic variables, fatigue, and serum zinc level before the intervention. The significance level was considered as 0.05 in all tests.

Results: Zinc supplementation significantly reduced fatigue (mean difference: −10.41 vs 1.37, $P < .001$) and increased serum zinc level (mean difference: 14.22, vs −0.57, $P < .001$) compared to the control group.

Conclusion: Consumption of zinc supplements for the elderly is recommended to overcome fatigue.

KEYWORDS
aging, fatigue, geriatric nursing, zinc

1 | INTRODUCTION

Fatigue is defined as a feeling of disability and weakness that leads to a reduction in the capacity of individuals to do their function and daily activities.[1] And it is associated with disease conditions and impacts health status and quality of life,[2] which conversely affects job performance, the activity of daily life, and social relationships. The prevalence of fatigue is estimated to be 21.9% in the general population[3]; however, it exceeds in the elderly populations, and 40% to 74% of them experience it.[4] Fatigue is a common complaint among elder community dwellers[5] and it can be attributed to decreased muscle strength, physical activity, motor neuron performance, and the level of steroid hormone production, as well as to nutritional problems and micronutrient deficiencies.[6] In fact, malnutrition in the elderly or those who adhere to a specific and restricted diet is invoked as one of the mechanisms underlying fatigue.[2] Vitamins and minerals are essential in a variety of basic metabolic pathways that support basic cellular functions in humans. Their deficiency, in turn, has effects on the

cognitive and psychological process and causes problems such as mental and physical fatigue.[7] On the other hand, chronic fatigue syndrome is associated with zinc deficiency.[8] It is supposed that more than 2 billion people around the world are suffering from one or more micronutrient deficiencies referred to as "hidden hunger."[9] Zinc, as an intracellular signaling molecule, plays an important role in various physiological processes such as deoxyribonucleic acid (DNA) repair, cellular proliferation, immune system regulation, anti-inflammatory reactions, adenosine triphosphate (ATP) functioning, and regulation of some enzymatic structures.[10] Zinc provides the energy needed for metabolism, and reduced serum zinc levels debilitate the functional capacity of muscles.[11]

Serum zinc concentration decreases with aging.[12] It has been shown that about 35% to 45% of the elderly over 60 have zinc levels below the normal range.[13] In this regard, the results of a study in Iran showed serum zinc level was lower than the normal range at 40.8% of the elderly subjects.[14] With aging populations, age-related health problems will prevail in societies in the near future. Nutritional interventions and effective drug supplements that are used to reduce fatigue in patients and groups are listed as Creatine electrolyte, vitamin B, and a combination of arginine, valine, and serine.[15-17]

Surprisingly, fatigue in the elderly usually remains untreated and overlooked.[18] To the best of our knowledge, there has been no study that directly measures the effect of zinc supplements on fatigue among elderly community dwellers. Therefore, this study was conducted to investigate the effect of zinc supplement on fatigue among elderly subjects in the community.

2 | METHODS

2.1 | Study design and setting

This study was conducted as a parallel randomized clinical trial registered in the Iranian Registry of Clinical Trials with the registration code of IRCT2017080635110N2. The study was conducted in the health centers of Kashan, Isfahan province, Iran.

2.2 | Sample and sampling method

The inclusion criteria included were being elderly aged 60 years and above, with no record of taking zinc supplements, and no intestinal or hepatic disorders, and being able to speak the Persian language. Moreover, we recruited subjects with good cognitive functions with the mini-mental state examination (MMSE) score of 25 or above among the literate participants[19] and abbreviated mental test (AMTS) score equal to seven or above among the illiterate participants.[20] The exclusion criteria were consumption of any form of zinc supplements before to the study, withdrawal from the study for any reason, and the recent incidence of any severe stressful condition (such as hospitalization or death of a close relative).

The sample size was determined based on a study by Reference 21. By choosing a significant level of 95%, type 2 error equal to 20%, a mean difference between the two groups was −13.72, the sample size was calculated as 120 (60 participants in each group). For higher precision and prediction of 25% loss to follow up, the final sample size was considered 150 with 75 participants in each group. By convenience sampling method, the elderly were invited to participate in the study in four selected health centers randomly from 32 health centers in Kashan, Iran. Participants were randomly assigned to the intervention and control groups by using block randomization with a block size equal to four blocks. The statistician of the research team planned and performed randomization. The participants were assigned to control or intervention groups according to the group names in the sealed envelopes.

2.3 | Data collection tools

The instruments used for data collection included a demographic questionnaire and the multidimensional fatigue inventory (MFI). The demographic questionnaire was used to record participants' age, sex, marital status, education, and income level. The MFI was first developed by Smets et al[22] and was used to assess levels of fatigue in the elderly. This inventory contained 20 items, organized in five dimensions including general, physical, and mental fatigue, decrease in physical activity, and lack of motivation. Each item of the inventory was scored based on a 5-point Likert scale from 1 to 5 with the lowest and highest obtainable scores being 20 and 100, respectively. A higher score indicated more severe fatigue. The Cronbach's alpha coefficients were greater than 0.80 for general, physical, and mental fatigue dimensions.[22] For the decrease in physical activity and lack of motivation, the Cronbach's alpha coefficient was 0.65.[22] Hafezi et al validated the Persian version of this inventory. Furthermore, a panel of experts including 10 experts who had a clinical understanding of the fatigue process and had expertise in psychometrics approved the content validity of the inventory. Moreover, the reliability of the inventory was verified by Cronbach's alpha coefficient of 0.85.[23]

2.4 | The measurement of serum zinc level

The serum zinc level was determined after venous blood sampling using a specific ELISA kit (Audit Diagnostics Laboratory Kit, Ireland) and applying the OLYMPUS AU400 autoanalyzer (Japan). The normal serum zinc levels were considered 72.6 to 127μg/dL for males and 70 to 114μg/dL for females.[24]

2.5 | Intervention

Prior to the commencement of zinc supplementation, the aims and process of the study were explained to the eligible elderly. Based on the sealed envelopes, the participants were randomly allocated to

either the intervention or the control group. The demographic questionnaire and MFI were completed via face-to-face interviews with participants. The venous blood samples (5 mL) were collected from the elderly in both intervention and control groups and were sent to the laboratory for measuring serum zinc level before and after the intervention. Five milliliters of blood were taken from each participant for measuring serum zinc level at baseline.

Zinc supplements containing 30 mg zinc[25] were administered daily for 10 weeks to subjects in the intervention group.[26] Prior to the administration of a full dose of zinc supplement, in order to prevent possible side effects of the zinc, seven pills (equal to a total dose of 210 mg) were administered to the elderly in the intervention group. At the end of the first week and after ensuring no side effects (according to available references, a list of possible side effects of zinc supplements was prepared and all participants were asked about these complications.), the remaining pills were administered to the elderly in the intervention group. To ensure regular and continuous consumption of zinc supplements, the participants were given a checklist for checking scheduled and daily consumption of zinc supplements. The participants in the intervention group were instructed to use the zinc supplements (30 mg pills produced by Nature-Med Company) along with a glass of tap water 30 minutes after lunch on a daily basis for 10 weeks. At the end of the 10-week period, the MFI was completed for both intervention and control groups (Figure 1). In order to comply with ethical principles, if an elderly individual in each of the groups had severe fatigue after 70 days, as measured by MFI, relaxation exercises were taught. Moreover, in case of any abnormal value of serum zinc, the participants in each group were recommended to visit their family doctor and receive the therapeutic dose of zinc supplement.

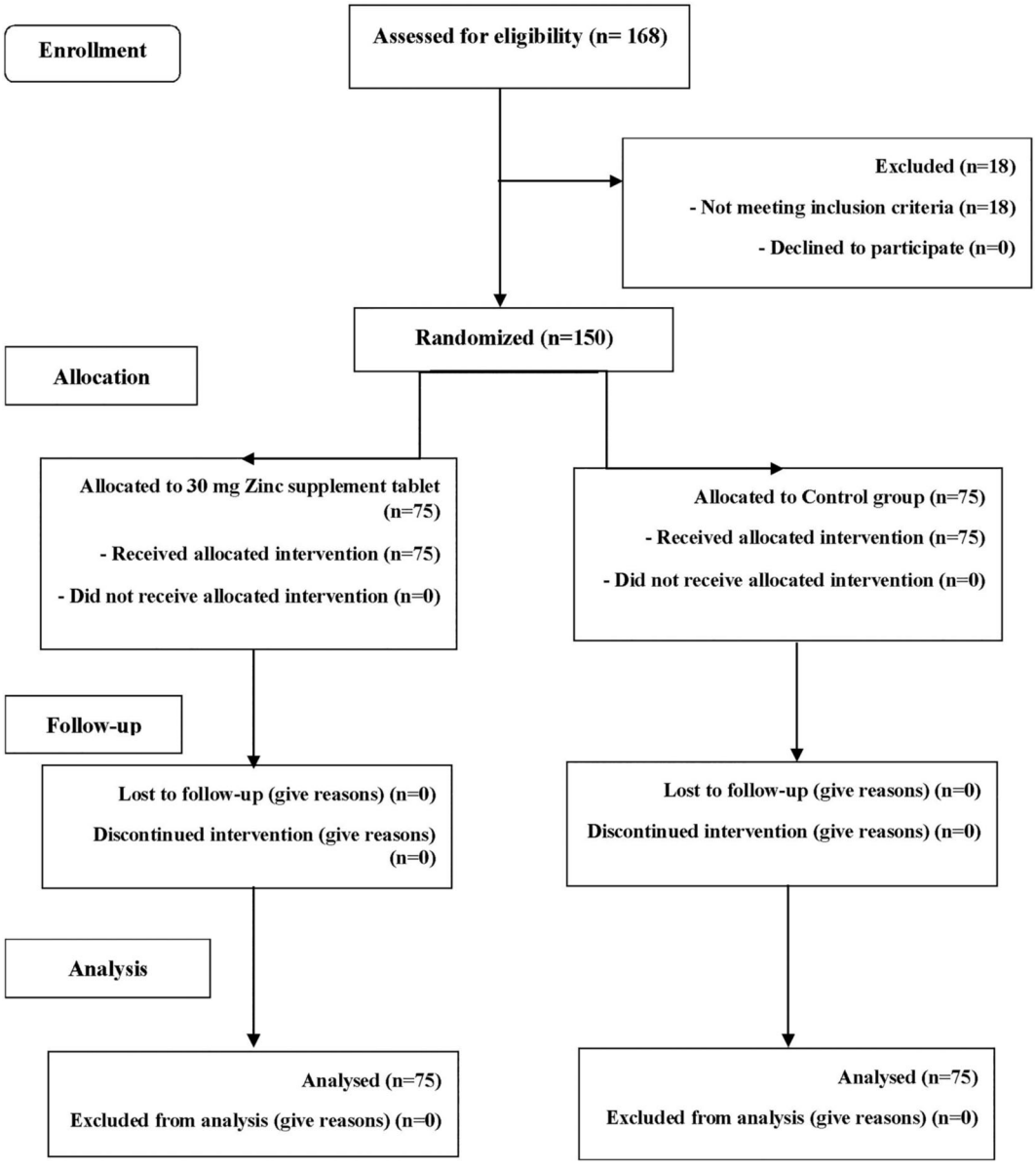

FIGURE 1 CONSORT flow diagram of the study

2.6 | Data analysis

In order to categorize and summarize the findings, descriptive statistics including mean, SD, absolute, and relative frequencies were applied. Besides, Chi-square or Fisher's exact test (if appropriate) was used to assess the homogeneity of demographic variables in the two groups. The independent sample *t* test, one-way ANOVA and, ANCOVA were used to compare the mean values of fatigue score and other quantitative variables between the control and intervention groups. The significance level was considered .05 in all tests.

2.7 | Ethical considerations

The objectives of the study were explained to the eligible volunteer subjects who accepted to participate in this study. Written informed consent was obtained from each eligible subject before entering the study. The participants were informed that they could withdraw from the study at any time. This study was approved by the Ethics Committee of Shahroud University of Medical Sciences (ethical code: IR.SHMU.REC.1396.80).

3 | RESULTS

In statistical analysis, the normality of variables was assessed and confirmed by using the Kolmogorov-Smirnov test. Most of the subjects were female (68.65%) also 61.3% (n = 46) and 76% (n = 57) of the elderly in the intervention and control groups were married, respectively. There were no significant differences between the two groups in terms of the demographic variables (gender, educational level, marital status, and source of income) before the intervention, ensuring the homogeneity of the two groups. The demographic data of this study are summarized in Table 1.

The baseline serum zinc levels were lower than the normal range in 62.70% and 48% of the subjects in the intervention and control groups, respectively. However, 80.00% and 46.40% of the subjects in the intervention and control groups had serum zinc levels within the normal range after the intervention, respectively (Table 2).

There was no significant difference in the mean fatigue scores between the two groups before the intervention. However, the mean fatigue scores were significantly lower in the intervention group compared to the control group after the intervention. Also, a significant difference was observed in the mean difference of fatigue scores before and after intervention in both groups (Table 3). Moreover, based on the ANCOVA test, variables such as serum zinc and gender had a significant effect on fatigue scores after the intervention, so that fatigue scores decreased with increasing serum zinc levels ($P = .001$) and male gender ($P = .001$).

Based on the Pearson correlation coefficient test, there was no significant correlation between fatigue score and serum zinc level before intervention; however, a significant and negative correlation was observed between fatigue score and serum zinc level after intervention in two groups (Table 4).

TABLE 1 The demographic characteristics of study participants

Variable		Intervention N (%)	Control N (%)	*P*
Age	60-75	65 (86.7)	69 (92.0)	0.290
	>76	10 (13.3)	6 (8.0)	
Level of education	Primary and secondary school	69 (92.0)	68 (90.7)	0.765
	High school	5 (6.7)	7 (9.3)	
	Academic degree	1 (1.3)	0 (0)	
Marital status	Married	61 (81.3)	65 (86.7)	0.373
	Single	14 (18.7)	10 (13.3)	
Source of income	Dependence on spouse	29 (38.7)	38 (50.7)	0.139
	Independence	46 (61.3)	37 (49.3)	

Abbreviations: *P*, *P*-value; SD, standard deviation; N: number; %, percent.

TABLE 2 Frequency distribution of serum zinc levels in two groups before and after the intervention

	Before the intervention			After the intervention		
Serum zinc level	Less than normal range (%)[a]	Total (%)[a]	Significance level[b]	Less than normal range (%)[a]	Total (%)[a]	Significance level[b]
Intervention	47 (62.7)	75 (100)	$P = 0.07$	15 (20)	75 (100)	$P < 0.001$
Control	36 (48.0)	75 (100)		40 (53.3)	75 (100)	

[a]Number (percentage).
[b]Fisher's exact test.

TABLE 3 Mean and mean difference of fatigue scores in both groups before and after the intervention

Mean scores	Groups		Significance level[a]
	Intervention[b]	Control[b]	
Baseline	54 ± 16.16	58.64 ± 17.31	$P = 0.09$
After the intervention	43.58 ± 14.83	60.01 ± 17.26	$P < 0.001$
Mean difference scores	−10.41 ± 17.15	1.37 ± 1.30	$P < 0.001$

[a]Independent sample *t* test.
[b]Mean ± SD.

TABLE 4 The correlation between the fatigue score and serum zinc level in the elderly before and after the intervention

	Serum zinc level	
	Before the intervention	After the intervention
Fatigue score	$R = -0.07$[a] $P = 0.36$	$R = -0.24$[a] $P = 0.002$

[a]Pearson correlation coefficient.

4 | DISCUSSION

The findings of the present study indicated that the serum zinc levels were below the normal range in most of the subjects in both groups before the intervention. In this regard, it should be considered, zinc deficiency in the body is characterized by symptoms such as immune system defects and growth retardation that can be reversed and improved by taking zinc supplements.[27,28]

Furthermore, as a result of zinc supplementation, serum zinc levels in the intervention group increased significantly, which was consistent with most previous studies.[29,30] Karagozoglu et al study aimed to determine the effect of zinc supplementation on serum zinc concentrations in the elderly. They concluded that serum zinc levels increased in the elderly of the intervention group after a 3-month period of taking 30 mg zinc supplementation.[31] In Sharif et al's study, the effect of taking zinc supplements during 12 weeks was assessed on genomic stability biomarkers, antioxidant activity, and zinc transporter genes among an elderly Australian population with low serum zinc level. They found that zinc serum levels increased among the elderly of the intervention group,[32] and the results of the present study were consistent with the two last studies.

There is growing literature on the importance of serum zinc level and its association with fatigue among elderly community dwellers. Most of the elderly subjects were suffered from levels of fatigue before the intervention. In Karagozoglu et al's study that aimed to investigate the levels of fatigue in the elderly living in nursing homes, the mean fatigue scores (range 0-10) were reported 5.83 ± 2.63 and 5.08 ± 2.20, respectively.[31,33]

Another finding of the current study was that taking zinc supplements and increasing the serum zinc level in the intervention group decreased the severity of fatigue among the subjects in the intervention group. Moreover, there was a significant reverse correlation between serum zinc level and fatigue severity. This finding is in accordance with a previous study indicating that serum zinc levels were directly correlated to functional status and physical performance in the elderly.[34] Maes et al found that the zinc level in patients with chronic fatigue syndrome was significantly lower than in healthy subjects.[35] Similarly, Ribeiro showed that zinc supplementation prevented fatigue and maintained the quality of life of patients with colorectal cancer. Moreover, in a study among patients who underwent chemotherapy, fatigue levels increased in the control group during chemotherapy, but in the intervention group (zinc supplement), the mean score of fatigue was not significantly different compared to the pre-chemotherapy period.[36] This result is consistent with our study, indicating that the fatigue levels in the group receiving zinc supplements were lower than the control group.

Consistent with the results of the present study, the study by Yosaee et al showed that zinc supplementation, vitamin D, or in combination for 12 weeks significant effects on decrease depression scores in obese or overweight patients.[37] Also, results of the Jafari et al study revealed that zinc supplementation for 12 weeks among women with the premenstrual syndrome had a positive effect on physical and psychological symptoms of premenstrual syndrome.[38] Previous studies have shown that oxidative stress was increased in chronic fatigue syndrome; since zinc has antioxidant properties, people with fatigue should use certain types of antioxidants such as zinc supplements.[39]

Despite the limitation of our study is the lack of a placebo group, the results of this study added a new perspective to the issue of fatigue among elderly people. As such, in both groups, subjects with a higher zinc level reported less fatigue after the intervention. Also, some factors (level of physical activity or chronic physical illness) that may affect fatigue in the elderly were not assessed in the present study. Other researchers are recommended to extend the period of intervention to assess the longer period efficacy of the zinc supplement. Since fatigue levels vary with season, it is recommended to ascertain fatigue and its related factors in all seasons of the year in future studies. Moreover, other important outcomes for zinc supplement such as improved cognition can be investigated. The present study showed that the use of zinc supplements can significantly improve fatigue in the elderly. Thus, we recommend considering zinc supplements as a complementary strategy to prevent and alleviate fatigue among the elderly.

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CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

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All authors have reviewed and approved the final version of this manuscript.

Hossein Ebrahimi had full access to all of the data in the study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

TRANSPARENCY STATEMENT

Hossein Ebrahimi affirms that this manuscript is an honest, accurate, and transparent account of the study being reported and all aspects of the study have been reported.

DATA AVAILABILITY STATEMENT

If interested in obtaining the data from this study, please contact ebrahimi@shmu.ac.ir.

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