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Research Article

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The effect of eight weeks of walking exercise and folate supplementation on plasma homocysteine levels in elderly non-athletes

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Information Articel	***ABSTRACT***
Submit: 19– 03 – 2021	*aims / objectives of the research: The increase in cardiovascular diseases among the elderly is one of the world's leading causes of death, and aerobic exercise is one way to prevent these conditions. Aim and Objective: This study aimed to determine the effect of 8 weeks of walking and folate consumption on plasma homocysteine levels in non-athletic older women. Materials and Methods: In this experimental study, 20 non-athletic older women aged 50 to 60 volunteered to participate and were randomly assigned to one of two groups: exercise+folic acid (10 persons) or exercise+placebo (10 persons). Both groups completed a walking program of eight weeks (3 sessions per week, each lasting 60 minutes). Following the conclusion of the exercise program, blood samples were collected and analyzed using independent and dependent t-statistics. After completing the walking exercise program for eight weeks, the plasma homocysteine levels fell considerably in both the exercise+supplement (P=0.002) and exercise+placebo (P=0.005) groups. Results: After completing the walking exercise program for eight weeks, the plasma homocysteine levels fell considerably in both the exercise+supplement (P=0.002) and exercise+placebo (P=0.005) groups.Conclusion: According to the present study's findings, elderly individuals should engage in walking exercises and take supplemental folate to lower plasma homocysteine and prevent cardiovascular risks.* ***Keywords**: Aerobic Exercise, Folate supplement, Homocysteine*

INTRODUCTION

Cardiovascular diseases rank among the leading causes of death in the world today, accounting for 46% of fatalities in Iraq (Mohammed et al., 2022). According to the World Health Organization (M. A. Khan et al., 2020), coronary heart disease will be the leading cause of disability worldwide by 2020. The risk factors for coronary artery disease are usually unknown to patients. (Forsythe, Brownrigg, & Hinchliffe, 2015). The illnesses listed above can be divided into two groups, each of which has a variety of risk factors. The first group of risk factors includes elements that have been thoroughly researched over time, including hyperlipidemia, diabetes, smoking, and a family history of heart disease. The second group of variables includes, among others, substances like homocysteine, fibrinogen, and lipoprotein that have only lately come to light (Duncan et al., 2004).

A sulfur-containing amino acid called homocysteine is produced during the metabolism of methionine (Blachier, Andriamihaja, & Blais, 2020). Researches show that the increase of homocysteine from the desired level causes an increase in cardiovascular diseases, and its decrease causes a decrease in the risk of heart attacks)Okura et al., 2006(. In other words, because the serum level of homocysteine is recognized as a cardiovascular risk factor, each micromole of homocysteine increases the risk of coronary problems by 28% (Tian, Ogura, Little, Xu, & Sawamura, 2019). An increase in homocysteine through mechanisms including disruption of endothelial function, increase in the growth rate of vascular smooth muscle cells, increase in platelet adhesion, and increase in oxidation of LDL and its deposition in the artery wall causes atherosclerosis (Tian et al., 2019).

External factors like physical activity, lifestyle, and diets like alcohol use, smoking, and a lack of vitamins B9 and B12 affect homocysteine levels in addition to factors like age, genetics, gender, and so on (Delport et al., 2014). Homocysteine positively correlates with age and rises with age among these variables (Xu et al., 2020). On the other hand, a change in body composition with advancing age increases body fat. At the same time, a simultaneous decrease in fat-free mass appears to enhance cardiovascular risks in the elderly and expose the individual to disease (Després, 2012). On the other hand, a change in body composition with advancing age increases body fat. At the same time, a simultaneous decrease in fat-free mass appears to enhance cardiovascular risks in the elderly and expose the individual to disease.

Sports activities are one way to prevent changes in body composition and cardiovascular risk factors, ensuring that the benefits of physical activity and exercise for the primary and secondary prevention of cardiovascular diseases have been adequately demonstrated (Hossain, Sayfaddin, Ghanbari, & Mahmmod, 2019). Additionally, increasing physical activity can improve health and help middle-aged people lose excess weight (Cava, Yeat, & Mittendorfer, 2017). Physical activity and exercise are related to leading a healthy lifestyle (Chrysant & Chrysant, 2018). Additionally, evidence indicates that physical activity reduces homocysteine levels in the blood (Alghadir, Gabr, Anwer, & Li, 2021). Exercise lowers homocysteine, which can help reduce the risk of cardiovascular diseases by decreasing body fat mass, improving vitamin absorption, or modifying homocysteine concentration (Hejazi et al., 2013).

Folic acid, often known as folate or vitamin B9, is necessary for many bodily functions, including the brain system, blood, and cell health. (Del Mondo, Smerilli, Sané, Sansone, & Brunet, 2020). This vitamin helps to protect the body from heart disease, congenital disabilities, osteoporosis, and certain cancers. (Ratajczak et al., 2021). Folate and vitamin B12 deficiency raises serum homocysteine levels because they are inversely related (Shahbazian, Jafari, & Haghnia, 2016). Athletes' blood homocysteine levels have been demonstrated to decrease in certain prior studies as a result of participating in sports (Deminice, Ribeiro, & Frajacomo, 2016). The impact of vitamins and supplements on regulating blood homocysteine levels has been studied independently in other studies, but the combined use of exercise and folate consumption has received less attention (Lai et al., 2018).

It appears that taking folate supplements and exercising can assist the elderly, based on what has been mentioned regarding the impact of exercise and folic acid supplementation in lowering homocysteine levels (N. N. Khan, Boyle, Lang, & Harrison, 2019). Due to their unique cardiovascular needs and the fact that they frequently suffer from many health issues, seniors cannot engage in numerous athletic activities (Ahmadinejad, Alijani, Mansori, & Ziaee, 2014). However, since most seniors utilize specific drugs, they cannot consume any diet or athletic supplements (Finger et al., 2015). The elderly can use this type of exercise, like walking, to improve their cardiovascular health because they cannot engage in sustained, strenuous sports activities. Still, on the other hand, they are constantly exposed to cardiac dangers as they age (Devereux-Fitzgerald, Powell, Dewhurst, & French, 2016). The current study aims to determine whether taking folate tablets for 8 weeks while also walking can lower plasma homocysteine levels in women in their 50s and 60s and lower their risk of cardiovascular disease.

METHODS

Twenty non-athletic older women (50-60) in good physical health volunteered to participate in this study. This study's statistical sample was randomly divided into two groups: exercise + folate supplement (10 people) and exercise + placebo (10 people). According to the individuals' doctors, they were all in excellent physical and mental health, with no history of cardiovascular disease or other physical issues that would have affected their homocysteine levels (including high blood pressure, blood sugar, and lipids). They also did not take any medications in the previous six months that could have impacted their homocysteine levels, such as: (folate, statin, estrogen, etc.). They did not engage in any regular physical activity. These individuals agreed to participate in the study by signing a signed consent form.

EXOERIMENTAL DESIGN

Before starting the training protocol, the subjects' height was measured without shoes, and their weight was also measured without shoes and with light clothes (Table 1). The subjects' body mass index was calculated using the following formula.

$$(Weight/kg)/(〖height〗^2/m)$$

The training program consisted of 8 weeks of walking (3 sessions per week) performed on even days of the week at 9 am. The subjects walked for 60 minutes at 45–65% of their maximal oxygen intake (Herzig et al., 2014). The subjects' VO2MAX was calculated indirectly using Bruce's test)Buttar, Saboo, & Kacker, 2019(.

Table 1. Anthropometric and physical characteristics of the participants

GROUP		AGE	HEIGHT	WEIGHT	BMI
FOLATE	Mean	55±2.84	162.12±4.54	74.125±6.33	28.20±3.48
	N	10	10	10	10
PLACIBO	Mean	56±3.34	159.37±5.12	76.137±5.67	29.97±5.23
	N	10	10	10	10

SUPPLEMENTATION

During the study, subjects were asked to refrain from taking other supplements and changing their dietary patterns. Participants were randomly assigned to receive folic acid supplementation or a placebo in a double-blind fashion. Supplements were provided to participants in identical, unmarked, sealed containers by (Matchland Pty Ltd, t/a New Products Development –ABN57052101176, Brisbane, Australia). The subjects of the exercise+supplement group received a 5 mg tablet of the folic acid supplement every day for 8 weeks (Asemi, Karamali, & Esmaillzadeh, 2014), and the subjects of the exercise+placebo group also received a 5 mg tablet of placebo every day for 8 weeks. It was recommended that Tablets should be taken with meals and enough water.

BLOOD SAMPLING AND BIOCHEMICAL ANALYSIS

One day before the exercise and food protocol implementation, a blood sample was taken to determine the baseline level of homocysteine in the amount of 5 ccs from the brachial vein and after 10 hours of fasting in a sitting position. Immediately after completing the 8-week training and oral protocol, 5 ccs of blood were collected from the brachial vein in a sitting position. The concentration of plasma homocysteine was measured using a special kit from (Bioassay Technology Laboratory, made in China), using the link immunoassay ELISA method, based on the instructions of the manufacturer of the kit. (The sensitivity of plasma homocysteine kit is 1 micromole/liter).

STATISTICAL ANALYSIS

Data values are expressed as the mean ± standard deviation of the mean. Kolmogorov Smirnov test was used to see the normal data distribution in each group. A dependent t-test was used to compare the changes in variables before and after training in each group, and an independent t-test was used to compare two groups in the studied indicators. All analyzes were performed using SPSS version 26.0 (SPSS Inc., Chicago, Ill., USA) and GraphPad Prism 8.4 software programs (GraphPad Software Inc., San Diego, CA, USA). The statistical significance level was set at ($P \leq 0.05$).

RESULTS AND DISCUSSION

The physical and anthropometric characteristics of the participants are presented in (Table 2). No significant difference was observed between the average of the folic acid supplement and placebo groups in any of the mentioned indicators.

Table.2- Subject characteristics

GROUP		AGE	HEIGHT	WEIGHT	BMI
FOLATE	Mean	55.00	162.12	74.125	28.20
	Std. Deviation	2.84	4.54	6.33	3.48
PLACIBO	Mean	56.00	159.37	76.137	29.97
	Std. Deviation	3.34	5.12	5.67	5.23
TOTAL	Mean	55.50	160.745	75.131	29.085
	Std. Deviation	3.09	4.830	6	4.355

The effect of exercise+folate supplement on the reduction of blood serum homocysteine levels

The dependent t-test was used to observe intra-group changes in each group's pre-test and post-test phases, and the independent t-test with an alpha adjustment of 0.0125 was used to examine inter-group changes in the pre-test and post-test phases. The mean and standard deviation of the changes in serum homocysteine blood levels of the subjects in 2 stages of the test: pre-test (before taking the supplement and exercise protocol) and post-test (immediately after the supplement and exercise protocol) were examined.

The average level of plasma homocysteine decreased by (-33.30%) in the post-test stage compared to the pre-test stage following 8 weeks of walking training and taking folate supplements. These changes were statistically significant ($p \leq 0.05$; see Table 3, Figure 1).

Table.3- Plasma homocysteine concentration of older women in the exercise+folate supplement group

Group	Test stage	Mean±Std. Deviation	P
Exercise+Folate	Pre-Test	47.26±12.45	0.002
	Post-Test	31.52±14.92	

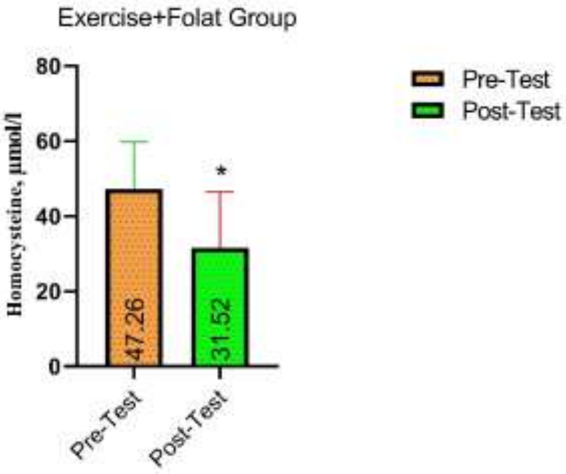

Figure 1. The effect of exercise+folate supplementation on reducing blood serum homocysteine levels
Data are represented as mean ± SD.
dependent t-test : *vs Pre-Test (P<0.05).

The effect of exercise + placebo on the reduction of blood serum homocysteine levels

The results of the dependent t-test showed that after 8 weeks of walking training and taking a placebo, the average level of plasma homocysteine decreased by (-16.88%) in the post-test stage compared to the pre-test stage, and these changes were statistically significant (p≤0.05; see Table 4, Figure 2).

Table.4- Plasma homocysteine concentration of older women in exercise+placebo group

Group	Test stage	Mean±Std. Deviation	P
Exercise+placebo	Pre-Test	45.13±17.64	0.005
	Post-Test	37.51±11.38	

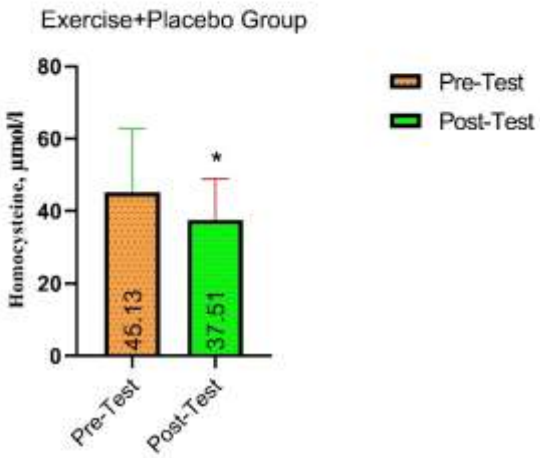

Figure 2. The effect of exercise+placebo on the reduction of blood serum homocysteine levels
Data are represented as mean ± SD.
dependent t-test : *vs Pre-Test (P<0.05).

The effect of folate supplement on the reduction of blood serum homocysteine levels

The independent t-test showed that after 8 weeks of folate supplementation, the average inter-group changes in plasma homocysteine level in the post-test phase of the exercise group + folate supplement decreased by (-15.97%) compared to the post-test phase of the exercise + placebo group. And these changes were statistically significant (p<0.05; see Figure 3).

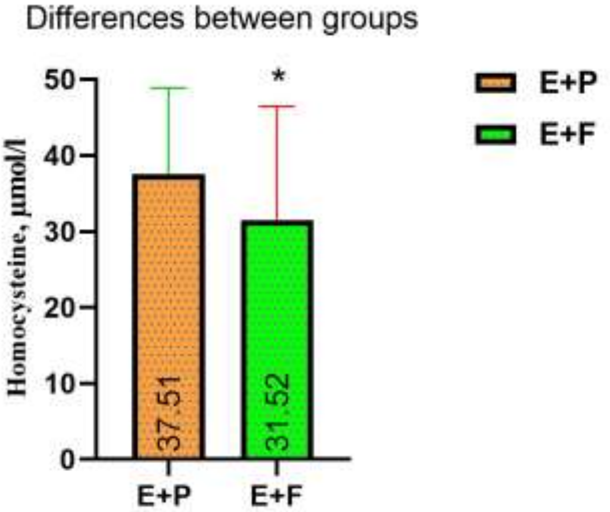

Figure 3. The effect of folate supplement on the reduction of blood serum homocysteine levels
Data are represented as mean ± SD.
Abbreviation: E, exercise. P, placebo. F, folat
Independent t-test : *vs Exercise+Plasebo (P<0.05).

The present study showed that walking for 8 weeks could significantly reduce plasma homocysteine. Vicente et al.)Vincent, Braith, Bottiglieri, Vincent, & Lowenthal, 2003(showed a significant decrease in total homocysteine in 62 to 70-year-olds following resistance exercises, which is consistent with the results of the present study. Similar results have been shown by Okura et al.(Okura et al., 2006), Castellano et al. (Castellano et al., 2017), and Randeva et al.(Randeva et al., 2002) following different sports exercises. Aerobic and mild activities may lower homocysteine and convert it into methionine and cysteine by boosting vitamin absorption, especially B vitamins, in the elderly's intestines (whose absorption of vitamins from their intestines is reduced) (Ghahramani, Karbalaeifar, & Zokaei, 2019). Aerobic and light sports prevent the accumulation of homocysteine in the blood and prevent cardiovascular diseases (Szczepańska, Białek-Dratwa, Janota, & Kowalski, 2022). Also, light aerobic exercises reduce other cardiovascular risk factors such as low-density lipoprotein, body mass index, weight, total cholesterol, and triglycerides (Liang, Pan, Zhong, Zeng, & Cheng, 2021). It seems that exercises performed at a higher intensity cannot affect reducing homocysteine, so Donsan et al. (Duncan et al., 2004) investigated the effect of intense resistance exercises on serum homocysteine levels in adult men and observed a slight increase in this index, while Dehghan et al. (Papandreou, Malindretos, Arvanitidou, Makedou, & Rousso, 2010) investigated the effect of low-pressure aerobic exercise on plasma homocysteine concentration of non-athlete elderly women, and the results showed a significant decrease.

During its metabolism, methionine turns into homocysteine. The produced homocysteine has three primary fates: 1) It turns into methionine during reactions with betaine consumption, 2) It turns into methionine during the remethylation pathway in which folic acid and vitamin B12 participate as cofactors, and 3) It turns into the amino acid cysteine during the transsulfuration pathway reactions (Dalto & Matte, 2017). During the transsulfuration pathway, vitamin B6 is necessary as a cofactor (Herrmann, Herrmann, & Obeid, 2007). During intense exercise, muscle glycogen reserves are significantly reduced. As a result, the need for reactions dependent on vitamin B6 increases. In these reactions, vitamin B6 is required as a coenzyme for the function of glycogen phosphorylase. Because of this, vitamin B6 is not readily available under these circumstances to carry out transsulfuration reactions (Herrmann et al., 2007). This is one of the reasons for an increase in the amount of homocysteine. It is not seen during low-intensity sports (Asadi, Sharifi, Abedi, & Fatolahi, 2020).

It appears that taking folate supplements along with walking exercise has a positive impact on the reduction of plasma homocysteine in women because the training + folate group's subjects experienced a more significant decrease in plasma homocysteine concentration (-33.30%) compared to the training + placebo group's subjects (-16.88%). 50 to 60-year-olds are inactive, which is in line with the research of Rakek et al. (Racek, Rusnakova, Trefil, & Siala, 2005).

Folic acid, one of the compounds related to group B vitamins, plays an essential role in homocysteine metabolism cycles and prevents the conversion of methionine to homocysteine (Abbasi et al., 2018). Several types of research have been conducted on using folic acid supplements or food fortification in reducing serum homocysteine levels. Based on the results, the role of the mentioned compound in reducing the level of homocysteine has been determined, and cases of hyperhomocysteine when folic acid deficiency are also seen (Barnabé et al., 2015). Tamadon et al. (2011) observed a significant decrease in serum homocysteine in adults after taking folic acid (Tamadon et al., 2011). Folic acid seems to be a safe and effective supplement to reduce blood pressure and homocysteine (Singh et al., 2019).

CONCLUSION

According to the current study's findings, walking exercise in 50–60-year-old women can lower plasma homocysteine and the risk of cardiovascular illnesses. This can be asserted for older persons looking for an alternative to medication. Exercise moderately and take folate supplements to lower your risk of cardiovascular disease.

WEAKNESSES AND RECOMMENDATIONS

The following are some of the research's weaknesses and essential recommendations:

- The report only cites the effect on plasma homocysteine levels, potentially ignoring other potentially significant consequences. Including additional measurements or indications pertinent to the intervention might be helpful, such as cardiovascular health, cognitive function, or quality of life.
- Limited time for intervention: Eight weeks might not be long enough to see significant improvements in plasma homocysteine levels. Stronger outcomes and a clearer knowledge of long-term consequences might come through a longer intervention or several follow-up examinations.
- Limited generalizability: By concentrating on non-athletes, the study may not offer insight into the larger population or athletes. The results may only be applicable outside of the particular study group.

AUTHOR'S STATEMENT

We guarantee that this article has never been submitted to or published in any other magazine.

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