Original Article

The Effect of Resistance Training Program with Citrulline-Malate on Blood Pressure, Nitric Oxide, and Vascular Endothelial Growth Factor in Postmenopausal Women with Prehypertension

Behpour N, Moradi F*, Tadibi V

Department of Sports Physiology, Faculty of Sport Sciences, Razi University, Kermanshah, Iran

Received: 02 Feb 2020 Accepted: 17 Mar 2020

Abstract

Background & Objective: Blood pressure generally increases after menopause. Training modalities with a supplement can influence blood pressure indices. The present study aims at investigating the effect of eight-week resistance training with citrulline-malate consumption on blood pressure, Nitric Oxide (NO), and Vascular Endothelial Growth Factor (VEGF) in postmenopausal women with prehypertension

Materials & Methods: The sample population is postmenopausal women with pre-hypertensive age ranging from 50 to 55 years old divided randomly into six groups, including "training + supplement", "training + placebo", "training", "no training + supplement", "supplement" and "placebo". Resistance training was held 3 sessions per week in which the training intensity was 45% to 55% IRM. The supplement included citrulline-malate (8 g) an hour before each training session. Blood pressure, NO, and VEGE were measured using a barometer and kit before and after the training sessions. Two-way analysis of variance test and Tukey's follow-up test were applied to analyze data.

Results: The findings demonstrated that training leads to a decrease in systolic and diastolic blood pressures while an increase in NO and VEGF. The results showed that an eight-week period of citrulline-malate supplementation has decreased systolic and diastolic blood pressure. Besides, it was revealed that eight weeks of citrulline-malate administration made NO and VEGF increase. Also, the results indicated that the "exercise + supplement" group has had the greatest effect on increasing NO and VEGF and reducing systolic and diastolic blood pressure. Moreover, the findings proved that resistance training with citrulline-malate made systolic and diastolic blood pressures in menopausal women with prehypertension reduce. These effects are accompanied by rising levels of NO and VEGF.

Conclusion: The findings revealed that the resistance training, which was applied in the present study, coupled with citrulline-malate supplementation, will improve blood pressure in postmenopausal women with hypertension.

Keywords: prehypertension, resistance training, menopausal women, citrulline malate, vascular function.

Introduction

Providing healthcare for older people has always been considered as a major concern of the international community. Being a problem of old age, the recognition of the factors contributing to the emergence of cardiovascular disease plays an important role in preventing the progress of the disease (1). Menopause is associated with a decrease in steroid hormones and an increase in body fat, especially abdominal fat. Hence, the risk of developing cardiovascular and metabolic diseases in postmenopausal women increases

***Corresponding Author: Moradi Fardin**, Department of Sports Physiology, Faculty of Sport Sciences, Razi University, Kermanshah, Iran. Email: fmoradi014@yahoo.com
https://orcid.org/0000-0001-9371-6654

(2). Generally, cardiovascular risk factors are exacerbated with age (3). Moreover, immobility and obesity can also put a person at risk for metabolic syndromes, including hypertension (1). Older women almost suffer from hypertension due to the decline in estrogen hormone production as a result of menopause, (2). In a study conducted on men and women in old age with the same Body Mass Index (BMI), it was found that postmenopausal women had a higher systolic blood pressure than men revealing an increase in systolic blood pressure after menopause (2). It is reported that over 90% of women after menopausal suffer from hypertension (3). Therefore, given the high risk of hypertension for older people, a new classification, called "prehypertension", was added to the classification of people with high blood pressure (2). Accordingly, people with the systolic blood pressure of 120 to 139 mmHg and diastolic blood pressure of 80 to 89 mmHg, fall into the category of people with prehypertension (4). Independent from other cardiovascular risk factors, high blood pressure also has a direct impact on endothelial function (3). The endothelium is a dynamic organ of the body that not only maintains vascular hemostasis through tone regulation but also protects them against atherogenesis. The vascular endothelium plays an important role in releasing vasomotor tone mediators (5). In this regard, endothelial function damage is not a primary level in atherosclerosis pathology, although it can develop mechanisms that contribute to the progression of vascular disease concerning a defective endothelial. Furthermore, Vascular Endothelial Growth Factor (VEGF) is identified as an important angiogenesis regulator, which has a mediating role in differentiation, proliferation, and migration of endothelial cells. However, not only does this factor inhibit cell apoptosis but also it is accompanied by increased Nitric Oxide (NO) and vascular permeability (6). According to previous studies (3), postmenopausal women have lower serum and circulating VEGF levels than pre-menopausal women, and therapeutic estrogen is accompanied by an increase in VEGF levels and a decrease in blood pressure among postmenopausal women (7). Besides, there is a positive relationship between serum levels of VEGF and gender, BMI, hypertension, and abdominal fat (8). Vascular endothelium has a critical and complex role in blood current regulation and chemical products such as NO, prostaticlinone, and endothelin. In addition to neural and humoral factors, vascular endothelium controls skin as well (9). Endothelium-induced NO provides the organs with better blood supply by creating continuous vascular contraction tone (10). Moreover, NO is an important factor in angiogenesis (11).

Nowadays, being recommended as a life-style modification for various patients, exercises are considered as an effective treatment for early control, as well as treatment, and hypertension control (12). Although the effects of exercises such as hormonal, vascular, neural and structural adaptations, reduced catecholamine and overall peripheral resistance, and changes in the levels of vasoconstrictors are pointed out as mechanisms to reduce blood pressure due to exercise, the exact mechanism of action are not clear (10). The type of exercise training in terms of the intensity and duration of exercise and the period of recovery after exercise have been considered as effective factors (9). The findings from Houston et al. (2014) revealed that NO supplementation has significantly made a 4 mmHg reduction in systolic rest and a significant decrease in 5 mmHg in diastolic. Besides, a statistically significant decrease in 6 mmHg in systolic and diastolic pressure was observed after 60 min. After half an hour a single dose, in vascular adaptation and after 4 hours, a significant improvement in endothelial function was observed (10). Moreover, there is a case about animals in which the impacts of resistance training on NO plasma level, vascular endothelial growth factor, and its receptor in healthy male rats are investigated (13). As far as the author knows, there have been no reports on human studies.

According to the above mentioned, it seems necessary to study an intervention which is able not only to provide a desirable level of NO, since it leads to vascular contraction and angiogenesis but also to reduce blood pressure level. Therefore, the researcher aims to find an intervention like citrulline-malate and L-Arginine to increase the NO level. The findings from previous studies have shown that citrulline-malate may reduce blood pressure levels (14). Citrulline-malate is an unnecessary alpha-amino acid that exists in some of the urea cycle proteins. Besides, it is a by-product of NO enzyme production reaction catalyzed by nitric oxide

synthase (15). Citrulline-malate increases intracellular NO, vasoconstriction, and blood current regulator (14).

According to the literature, there have not been studies on the long-term effects of citrulline supplementation with exercise on blood pressure and its indices. Besides, it is found that citrulline-malate increases blood supply for vessels, increases arginine plasma level, constricts vessels, makes arginine convert into NO and influences VEGF performance (7). Powers et al. showed that citrulline consumption for 3 weeks increases the arginine/ADMA ratio significantly in healthy obese women, improves vascular function and reduces blood pressure level (6). Investigating the effects of L-arginine consumption on blood pressure in 4 weeks, Dong et al. reported a significant reduction in systolic blood pressure as 5.39 mmHg and 2.66 mmHg reduction in diastolic blood pressure (5). Studying the effect of NO on blood pressure, Houston et al. stated that nitric-oxide consumption leads to a decrease in blood pressure, a significant improvement in vascular function, an enhancement in adaptation, and an improvement in endothelial performance in the patients with high blood pressure (10).

Menopausal is a physiologic event that emerges in the lives of all women leading to undesirable changes in endothelium performance. Menopausal women are a large part of the society who suffer from prehypertension while doing exercises, there have been limited studies on the effect of physical activity in this period. Previous studies were conducted on a limited number of patients with hypertension which were contrary to the results. Moreover, the reported studies have focused on the effect of training on NO and VEGF as well as L-arginine, although the effect of citrulline-malate on NO and VEGF in the human samples has not been reported. The current study aims at investigating the effect of resistance training having average intensity with citrulline-malate on the blood pressure during eight weeks, endothelial growth factor, and NO in women with prehypertension.

Materials & Methods

This study is an experimental one with a pretest, posttest and clinical trial design.

Subjects: The sample population includes 42 menopause women (50 to 55 years old) from Kermanshah with complete menstrual cycle stop for more than a year who participated in this study voluntarily and purposefully. The samples were randomly divided into six groups including training + supplement, training + placebo, training, no training + supplement, and supplement + placebo. Each group consisted of 7 persons.

Supplement protocol: citrulline-malate consumption in training + supplement groups and supplement group as a drink that includes 200 ml water, 8 g citrulline-malate, 20 ml lemon juice, and 10 g sugar an hour before training. For the control group (placebo), maltodextrin was used instead of 8 g citrulline-malate. Besides, the person who was not involved in the study was responsible to label the names of people on the supplement and placebo capsules randomly to ensure double-blind design (16).

Measurement tool: Promega kit (Promega Corp. UA) was used to measure NO level (NO2/NO3). Using this kit, the serum level of nitrite is measured as the main metabolite of NO. Systolic and diastolic blood pressures were evaluated by Biorr machine made in Germany with an accuracy of 0.1 mmHg. Moreover, Cusabio (made in China) with an analytical sensitivity of 0.8 picogram/ml based on the ELISA method was applied to measure VEGF.

Measurement of the research indices: Blood sampling was carried out in 2 stages to measure research indices: the first stage was before training while the second one was 48 hours after eight weeks of resistance training. Blood sampling was at 10:00 A.M. before starting the activities, so that subjects sat down for 15 minutes and then, a pretest blood sample was taken by the laboratory expert (10 cc) from the left antecubital vein of each subject while sitting down. At the end of the physical activity, 48 hours after the activity, blood sampling was repeated at 10:00 A.M. Blood samples were immediately poured into tubes containing EDTA. Then, they were rapidly transferred to the laboratory to measure the variables of interest. In the laboratory, the blood samples were poured into precooled tubes. Then, they were centrifuged for 10 minutes with 3001 rpm

at a temperature of 4 C which was tested after separating the resulted serum.

Resistance training protocol: The consent form was obtained from the subjects before training. Before starting the protocol, the prober forms of activities and the way to get the maximum repetition in each stop were explained by the researcher. Then, the maximum ability of subjects in front thigh, thighs, food press, chest press, seated cable row, and seated back extension were measured to control training intensity (5). The subjects in the resistance training group with average intensity exercise with 45-55% of a maximum repetition in three stages with 10-12 repetitions. The resting interval between each stage was two minutes and subjects rested for three minutes between each stop. Before training, the subjects did warm-up and stretching exercises. The procedure included foot press, chest press, seated cable row, back leg, seated back extension, and shoulder press. In all intervals, the procedure was the same as other intervals. A maximum repetition test was taken at the end of every two weeks to observe the principle of additional load, which determines the intensity of the next two weeks programs for each person (17, 18, 19).

Statistical method: Shapiro-Wilk test was applied both to evaluate normality and to investigate the effect of eight weeks of training and the supplement in response to resistance training, two-way analysis of variance with two factors of group and time. When necessary, Tukey's follow-up test was used to determine the difference between the groups. Moreover, dependent t-test was applied to compare the changes before and after 8 weeks of training. Meanwhile, all statistical operations were performed using SPSS 25 with a significance level of $P<0.05$.

Results

Before data analysis, the Shapiro-Wilk test was used to ensure the normal distribution of data. The findings revealed that the data were normal in all stages of the test. The results of investigating height, weight, BMI, and age are presented in Table 1.

The findings from variance analysis demonstrated that the effects of time, group, and interaction effect of time×group were significant on systolic blood pressure changes after eight weeks of resistance training ($p<0.05$). Also, the findings showed that the effects of time, group, and the interaction effect of time×group were significant on NO changes ($p<0.05$). In investigating VEGF changes, the effect of time, the effect of group, and the interaction effect of time×group were significant ($p<0.05$).

As table 2 shows, the findings from dependent t-test revealed that training + supplement consumption reduces systolic blood pressure and diastolic blood pressure, although they increase

Table 1. Characteristics of individual subjects (Mean ± SD)

Factors	placebo	supplement	control	Resistance	Resistance+ placebo	Resistance+ supplement
Age (years)	53.28±1.70	52.71±1.11	52.85±1.95	52.57±1.27	51.71±1.11	53.00±1.82
Height (cm)	160.28±4.02	158.71±1.49	159.00±2.88	158.85±2.67	158.57±2.63	158.00±1.41
Weight (kg)	76.85±3.84	73.85±4.18	73.14±5.08	72.42±3.15	72.14±3.97	73.42±4.07
BMI	29.964±2.13	29.31±1.41	28.92±1.68	28.72±1.59	28.71±1.99	29.42±1.85

NO and VEGF after eight weeks of training; the effect was significant (p=0.001, p=0.001, p=0.001, p=0.001, respectively). Furthermore, the results of this test for the mentioned factors in supplement group were p=0.003, p=0.047, p=0.001, p=0.001 and in training group were p=0.001, p=0.005, p=0.001, and p=0.001, respectively. In training + placebo group, similar results were obtained for reduced systolic and diastolic blood pressures and increased NO and VEGF changes after eight weeks. However, no significant difference was found in placebo (p=0.703, p=0.289, p=0.124, p=0.148) and control (p=0.766, p=0.103, p=0.227, p=0.866) groups after eight sessions.

As can be seen in Chart 1, the greatest effect on the reduction of systolic pressure was related to the exercise + supplement group. Similar results can be seen in the diastolic blood pressure decrease in Chart 2. Regarding the effect of exercise and the type of supplement considered in the present study on the level of nitric oxide,

Table 2. Results of t-test dependent on the rate of change of variables after eight weeks

	VEGF	NO	Diastolic pressure	Systolic pressure
	P-value	P-value	P-value	P-value
Resistance+ supplement	0.001*	0.001*	0.001*	0.001*
Resistance+ placebo	0.001*	0.001*	0.047*	0.003*
Resistance	0.001*	0.001*	0.005*	0.001*
control	0.866	0.227	0.103	0.766
supplement	0.001*	0.001*	0.001*	0.001*
placebo	0.148	0.124	0.289	0.703

* Significance level less than 0.05

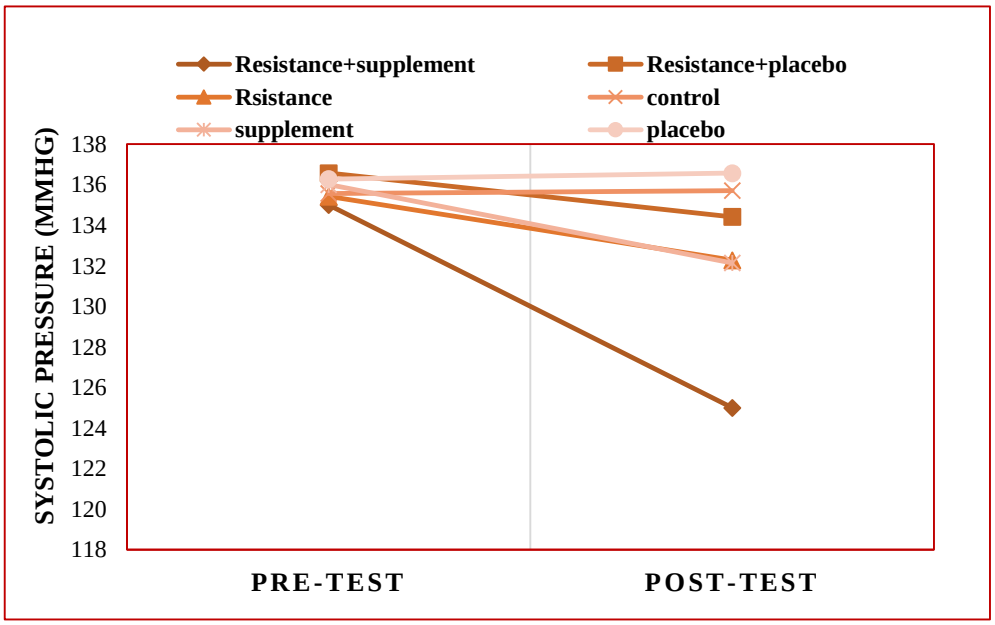

Chart 1. Systolic blood pressure in the pre-test to post-test groups. The results in the fig1 show that the greatest effect on the reduction of systolic blood pressure occurred in the exercise + supplement group.

as can be seen in Chart 3, the exercise + supplement group had the highest significant effect. The same results were obtained regarding the effect of the exercises and citrulline-malate supplementation used in this study presented in Chart 4.

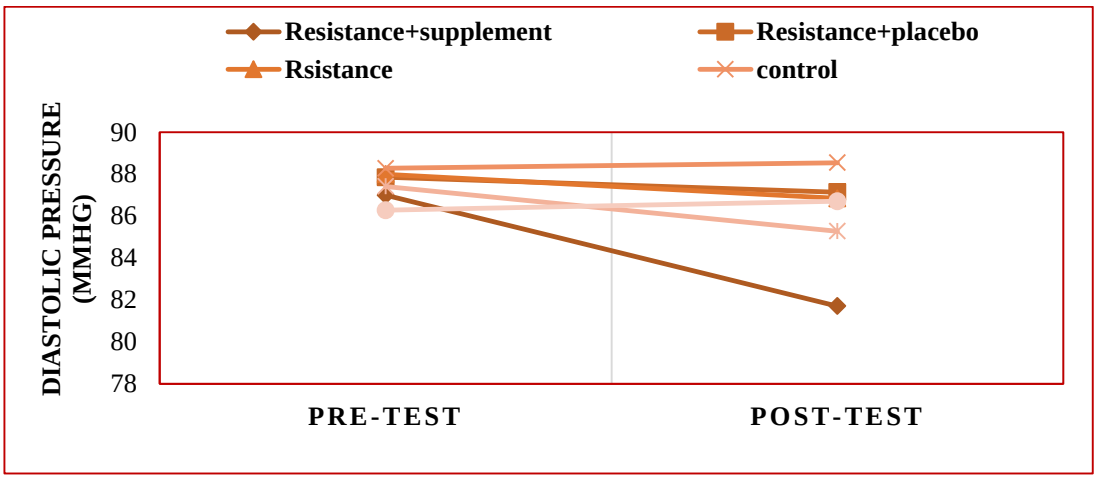

Chart 2. Diastolic blood pressure in the pre-test to post-test groups. The results in the fig2 show that the greatest effect on the reduction of diastolic blood pressure occurred in the exercise + supplement group

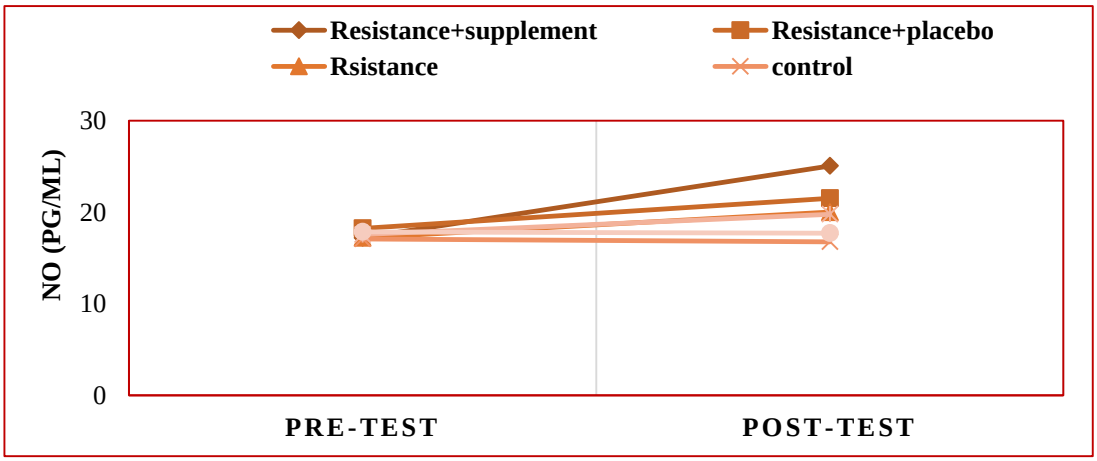

Chart 3. The amount of nitric oxide in the pre-test to post-test groups. The results in the fig3 show that the greatest effect on the increase of NO occurred in the exercise + supplement group**.**

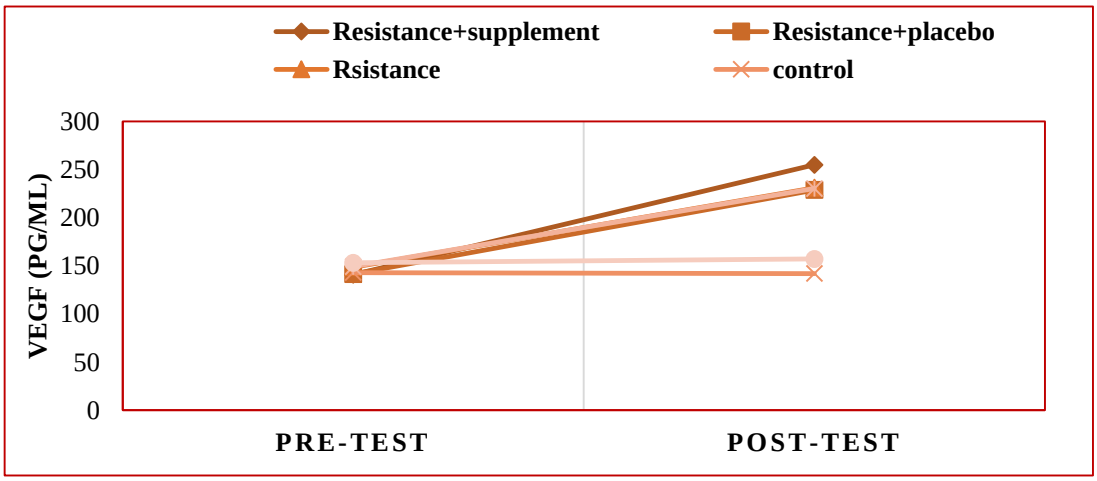

Chart 4. The amount of VEGF in the pre-test to post-test groups. The results in the fig4 show that the greatest effect on the increase of VEGF occurred in the exercise + supplement group.

Discussion

The findings of the present study showed that eight weeks of regular resistance training with continuous citrulline-malate consumption can lead to a decrease in systolic and diastolic blood pressures in menopausal women with prehypertension. Besides, these changes were accompanied by positive regulation of VEGF serum levels and NO increase in these people indicating the positive role of exercise and citrulline-malate in the improvement of hypertension through improving endothelial function. The results were consistent with the findings from the study by Wax et al. (20) in which they examined the effect of eating citrulline malate supplementation on low-trunk resistance training performance in male powerlifting athletes. The study population included 12 male Powerlifters. The findings showed that the exercise protocol combined with citrulline malate has increased the number of repetitions in all cases of resistance training compared to placebo. The results also revealed that blood lactate and heart rate were not significantly different between the two groups. The results also showed that there was no difference between the two groups in the changes in systolic and diastolic blood pressure. In conclusion, the results of this study showed that citrulline malate supplementation may be effective in improving athletic performance in low-body endurance training in male athletes. Moreover, the findings of this study are consistent with Minrovant et al. (18), and Mahboobi et al. (19) in terms of the effect of citrulline-malate on reduced blood pressure and vascular indices. Besides, the results are consistent with Shimio et al. (2) and Figura et al. (21) in terms of the long-term effects of resistance training on blood pressure and vascular indices. However, the results of this study are not consistent with Papadia et al. (22) and Troneksa (23) in terms of the effect of citrulline-malate on blood pressure and cardiovascular indices. Moreover, the results are not consistent with Bejamgard et al. (1) in terms of the effect of training on blood pressure and vascular indices. The conflicts can be related to intensity, duration, exercises, nutrition, initial readiness, individual differences, and the age of subjects. Besides, individual differences may be effective, because, in previous studies, it is stated that one of the factors that change the vascular reaction of women in the menopausal period is reduced estrogen hormone. Therefore, gender differences, despite no difference in age, physical conditions, and hypertension can lead to differences in research results. In the present study, the increased VEGF level in menopausal women as a result of exercise indicates the potential role of resistance training in moderating reduced VEGF levels resulted from menopausal and hypertension. Moreover, the improved blood pressure due to exercise can lead to an increase in VEGF through hypoxia induction and positive regulation of hypoxia induction. The findings from Gavin et al. (7) showed that 8 weeks of training is accompanied by an increase in VEGF mRNA in skeletal muscle of young and old people, independent from their training status (7). Another reason for the existence of conflicts in the findings can be related to the differences in training variables such as the difference in the performance of the exercise (traditional or circular methods), the intensity of the activity, numbers, repetitions, rests between sets, muscular groups involved in the activity, duration, and other factors such as age and physical conditions of the subjects. The results of the present study showed that reduced blood pressure, an increase in NO and VEGF level was observed after 8 weeks of resistance training in menopausal women with prehypertension. VEGF has high interaction effects with NO resulted from NO synthase. These results indicate that resistance training through increased blood current and shear press leads to the simulation of NO synthase making increased NO availability occur (13). Moreover, the development of endothelial NO availability leads to an increase in vascular dilation and a decrease in vascular resistance and blood pressure. So far, low blood pressure mechanism has not been fully understood due to physical activity, especially resistance training, although the results point to reduced cardiac output against reduced vascular resistance. The main reason for reduced blood pressure resulted from exercise is probably reduced cardiovascular sympathetic activity after participation in the training program (10). The findings from previous studies show that six months of training has influenced the metabolite levels of NO in women with hypertension. Moreover, it reveals that exercises have increased NO metabolites followed by reduced systolic and diastolic blood pressures (14). Therefore, 12 weeks of training on treadmill leads to a significant reduction in NO (9). The

results of previous studies show that regular exercise leads to a decrease in basic sympathetic activity in cardiovascular patients with normal blood pressure. However, a significant part of increased cardiovascular disease in menopausal women is due to undesirable changes in plasma lipoproteins which is due to a decrease in estrogen. Also, NO has different effects on the biological systems of the body. For example, in cardiovascular system functions, as a vascular constrictor, are derived from endothelium. Vascular endothelial cells have a key role in vascular control, localized hemostasis, vascular growth, and vascular wall proliferation process. These responses are regulated by different materials that are released from endothelium in response to physiological and mechanical simulations, such as prostacyclin, endothelin, and most importantly NO (11). About the effect of long-term consumption of citrulline-malate on the improvement of blood pressure in menopausal women with prehypertension, it can be said that citrulline-malate increases arginine level followed by increased NO and vasoconstriction (11). This effect of arginine on vasoconstriction can influence reduced blood pressure. Therefore, according to previous studies, the effect of citrulline-malate and its relationship with increased arginine, blood pressure, NO, and VEGF is addressed. Wax et al. (20) showed that citrulline-malate may improve vascular function (20). Also, Wax et al. (24) investigated the effect of citrulline-malate in lower body resistance training in male powerlifting athletes stating that citrulline-malate may improve blood pressure in lower body exercises (24). In investigating the effect of resistance training on blood pressure indices, Shimio et al. (2) showed that resistance training does not have any effect on plasma level of factors affecting angiogenesis including NO, vascular endothelial growth factor, and its receptor; the reasons such as duration, intensity, and sampling time can influence the results (2). Therefore, in a recent study, researchers investigated the effect of citrulline-malate consumption and resistance training in a long-term period. Conversion of citrulline into arginine is one of the most important roles of this amino-acid in the body that is carried out in kidneys through a relative urine cycle including argininosuccinate and argininosuccinase. Without metabolic adaptation, almost the whole arginine obtained from food is taken by the liver and only a small part of arginine becomes available for other organs. Moreover, since arginine is a positive regulator in urea formation, other amino-acids may decompose undesirably. However, Citrulline solves this problem. Since the liver cannot take citrulline from blood, it passes the liver as a coated form of arginine and decomposes into arginine in the kidneys (25- 27). Therefore, this arginine becomes available for other organs.

It should be said that the nutritional status of subjects was not controlled during exercise. Also, mental stress caused by performing tests which may be effective factors on blood pressure and measured factors in the present study is one of the weaknesses of the present study. One of the strengths of the present study is the level of physical fitness of the sample population. Moreover, mild hypertension of samples who did not receive drug treatment and finally the effect of exercise combination and Citrulline-Malate supplementation improved blood pressure levels and its related parameters.

Conclusions

According to the findings of this study, it can be said that citrulline-malate consumption can prevent problems since it is arginine production facilitation in the body. Besides, training for people with hypertension and people with prehypertension who are prohibited from doing resistance training can consume this supplement and take advantage of resistance training. In fact, their blood pressure level will not be a barrier against their sport exercises.

Acknowledgments

This article is taken from the Ph.D thesis of the Department of Sports Physiology. The authors express their gratitude to the participants in this study who had sincere and unwavering cooperation. Meanwhile, the present study has been approved by the ethics committee of Kermanshah University of Medical Sciences and has been approved with the ethical identification of IR.KUMS.REC.1398.058.

Conflict of Interests

The authors declare no conflicts of interest.

Reference

1. Bjarnegård N, Hedman K, Länne T. Vascular Adaptation to Indoor Cycling Exercise in Premenopausal Women. International journal of sports medicine. 2019;40(04):245-52.
2. Shimojo G. L, da Silva Dias D, Malfitano C, Sanches I.C, Llesuy S, Ulloa L, et al. Combined aerobic and resistance exercise training improve hypertension associated with menopause. Frontiers in physiology. 2018; 29(9):1471-88.
3. Tikhonoff V, Casiglia E, Gasparotti F, Spinella P. The uncertain effect of menopause on blood pressure. Journal of human hypertension. 2019; 33(6):421-8.
4. Haring B, Liu J, Salmoirago-Blotcher E, Hayden KM, Sarto G, Roussouw J, Kuller LH, et al. Blood pressure variability and brain morphology in elderly women without cardiovascular disease. Neurology. 2019; 92(12): 84-97.
5. Dong JY1, Qin LQ, Zhang Z, Zhao Y, Wang J, Arigoni F, et al. Effect of oral L-arginine supplementation on blood pressure: Ameta-analysis of randomized, double-blind, placebo-controlled trials article in american heart journal. 2011; 162(6): 959-965
6. Powers R, Weissgerber T.L, McGonigal S, Myerski A, Gallaher M, Speer P. D, et al. A. L-Citrulline administration increases the arginine/ADMA ratio, decreases blood pressure and improves vascular function in obese pregnant women. Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health. 2015; 5(1): 4-11.
7. Gavin TP, Robinson CB, Yeager RC, England JA, Nifong LW, Hickner RC. Angiogenesis growth factor response to acute systemic exercise in human skeletal muscle. J Appl Physiol, 2004; 96(1):19-24.
8. Pandey A. K, Singhi E. K, Arroyo J. P, Ikizler T. A, Gould E. R, Brown J, et al. Mechanisms of VEGF (Vascular Endothelial Growth Factor) inhibitor–associated hypertension and vascular disease. Hypertension. 2018;71(2): 1-8
9. Chiba T, Sakuma K, Komatsu T, Cao X, Aimoto M, Nagasawa Y, et al. Physiological role of nitric oxide for regulation of arterial stiffness in anesthetized rabbits. Journal of pharmacological sciences. 2019; 139(1):42-55.
10. Houston M, Hays L. Acute effects of an oral nitric oxide supplement on blood pressure, endothelial function, and vascular compliance in hypertensive patients. The Journal of Clinical Hypertension. 2014 Jul;16(7):524-9.
11. Mas-Capdevila A, Iglesias-Carres L, Arola-Arnal A, Aragonès G, Aleixandre A, Bravo F, et al. Evidence that Nitric Oxide is Involved in the Blood Pressure Lowering Effect of the Peptide AVFQHNCQE in Spontaneously Hypertensive Rats. Nutrients, 2019; 11(2): 225-236.
12. Casonatto J, Cavalari JV, Goessler KF, Christofaro DG, Polito MD, Enokida DM, et al. Citrulline malate supplementation might potentiate post-exercise hypotension in hypertensives: A 24-hour analysis. Science & Sports. 2019: 1;34(4):261-e1.
13. Shah AR, Van Horn AN, Verchinina L, Wichorek M, Su L, Markel D, et al. Blood Pressure Is Associated with Receiving Intravitreal Anti–Vascular Endothelial Growth Factor Treatment in Patients with Diabetes. Ophthalmology Retina. 2019; 3(5):410-26.
14. Barkhidarian B, Khorshidi M, Shab-Bidar S, Hashemi B. Effects of L-citrulline supplementation on blood pressure: A systematic review and meta-analysis. Avicenna journal of phytomedicine. 2019; 9(1):10.
15. Kaore SN, Amane HS, Kaore NM. Citrulline: pharmacological perspectives and its role as an emerging biomarker in future. Fundamental & clinical pharmacology. 2013 Feb;27(1):35-50
16. Douglas K. da Silva, Jeferson L. Jacinto, Walquiria B. de Andrade, Mirela C, et al. Aguiar. Citrulline Malate Does Not Improve Muscle Recovery after Resistance Exercise in Untrained Young Adult Men. Nutrients, 2017; 9(10): 1132.
17. Figueroa A, Okamoto T, Jaime SJ, Fahs CA. Impact of high-and low-intensity resistance training on arterial stiffness and blood pressure in adults across the lifespan: a review. Pflügers Archiv-European Journal of Physiology. 2019; 7(3):467-78.
18. Mirenayat MS, Moradi S, Mohammadi H, Rouhani MH. Effect of L-Citrulline supplementation on blood pressure: a systematic review and meta-analysis of clinical trials. Current hypertension reports. 2018; 20(11):98-110.
19. Mahboobi S, Tsang C, Rezaei S, Jafarnejad S. Effect of L-citrulline supplementation on blood pressure: a systematic review and meta-analysis of randomized controlled trials. Journal of human hypertension, 2019; 33(1):10-21.

20. Wax B, Kavazis A., Luckett W. Effects of supplemental citrulline-malate ingestion on blood lactate, cardiovascular dynamics, and resistance exercise performance in trained males. Journal of dietary supplements. 2016;13(3):269-282.
21. Figueroa A, Wong A, Jaime S.J,Gonzales J.U. Influence of L-citrulline and watermelon supplementation on vascular function and exercise performance. Current opinion in clinical nutrition and metabolic care. 2017; 20(1):92-98.
22. Papadia C, Osowska S, Cynober L, Forbes A. Citrulline in health and disease. Review on human studies. Clinical Nutrition. 2018; 37(6 Pt A):1823-1828.
23. Troncoso L.J. The Effects of Supplemental Citrulline Malate on Arterial Elasticity, Aerobic Performance, Blood Pressure, and Heart Rate . International Journal of Exercise Science: Conference Proceedings. 2017; 2(9): 78-88.
24. Wax B, Kavazis AN, Weldon K, Sperlak J. Effects of supplemental citrulline malate ingestion during repeated bouts of lower-body exercise in advanced weightlifters. J Strength Cond Res. 2015; 29(3):786-792.
25. Botchlett R, Lawler JM, Wu G. L-Arginine and l-citrulline in sports nutrition and health. In Nutrition and enhanced sports performance. J sport since and health. 2019; 1(2): 645-652. Academic Press.
26. Sureda A, Pons A. Arginine and citrulline supplementation in sports and exercise: ergogenic nutrients? In Acute Topics in Sport Nutrition. Med Sport Sci. 2012; 59(7):18-28.
27. Takeda K, Takemasa T. An Overview of Ornithine, Arginine, and Citrulline in Exercise and Sports Nutrition. In Nutrition and Enhanced Sports Performance. J Exercise Science. 2019 Jan 1 (pp. 627-636). Academic Press.

مقاله پژوهشی

اثر یک دوره تمرین مقاومتی همراه با مصرف مکمل سیترولین مالات بر فشار خون، نیتریک اکساید(NO) و فاکتور رشد اندوتلیال عروقی(VEGF) در زنان یائسه دچار پیش پرفشاری خون

ناصر بهپور، فردین مرادی*، وحید تأدیبی

گروه ورزشی، دانشکده علوم ورزشی دانشگاه رازی، کرمانشاه، ایران

تاریخ دریافت مقاله: ۱۳۹۸/۱۱/۱۳ تاریخ پذیرش مقاله: ۱۳۹۸/۱۲/۲۷

چکیده

زمینه و هدف: فشارخون بعد از یائسگی عموماً افزایش مییابد. روشهای تمرینی همراه با مکمل میتوانند بر شاخصهای فشارخون تأثیر بگذارند، هدف از مطالعه حاضر بررسی تأثیر هشت هفته تمرین مقاومتی با مصرف سیترولین-مالات بر فشارخون، نیتریک اکسید(NO) و فاکتور رشد اندوتلیال عروقی (VEGF)در زنان یائسه با پیشپرفشارخونی بود.

مواد و روش ها: جامعه آماری شامل زنان یائسه دچار پیشپرفشارخونی ۵۰ تا ۵۵ ساله بود که بهطور تصادفی به شش گروه تقسیم شدند: تمرین+مکمل، تمرین+مکمل، تمرین، کنترل، مکمل و دارونما. تمرین مقاومتی ۳ جلسه در هفته با شدت ۴۵ تا ۵۵ درصد IRM بود. مکمل شامل سیترولین-مالات (۸ گرم) یک ساعت قبل از هر جلسه تمرینی بود. فشارخون، NO و VEGE با استفاده از فشارسنج و کیت قبل و بعد از جلسات تمرینی اندازهگیری شد. برای تحلیل دادهها از تحلیل واریانس دوراهه و آزمون تعقیبی توکی استفاده شد.

نتایج: نتایج نشان داد که تمرین مقاومتی منجربه کاهش فشارخون سیستولیک و دیاستولیک و افزایش NO و VEGF میشود. همچنین مصرف سیترولین-مالات سبب کاهش فشارخون سیستولیک و دیاستولیک میشود. علاوه بر این، مشخص شد که هشت هفته مصرف سیترولین-مالات سبب افزایش NO و VEGF شد. نتایج نشان داد که گروه تمرین+مکمل بیشترین تأثیر را در افزایش VEGF،NO و کاهش فشارخون داشته است. نتایج نشان داد که تمرینات مقاومتی با مصرف سیترولین-مالات سبب کاهش فشارخون در زنان یائسه دچار پیشپرفشارخونی میشوند. این تأثیرات با افزایش سطح NO و VEGF همراه است.

نتیجه گیری: یافته های پژوهش حاضر نشان داد که تمرین مقاومتی به همراه مکمل سیترولین-مالات سبب بهبود فشارخون در زنان یائسه دچار پیشپرفشارخونی میشود.

کلمات کلیدی: پیش پرفشارخونی، تمرین مقاومتی، زنان یائسه، سیترولین مالات، عملکرد عروقی

***نویسنده مسئول: فردین مرادی،** گروه ورزشی، دانشکده علوم ورزشی دانشگاه رازی، کرمانشاه، ایران.
Email: fmoradi014@yahoo.com
https://orcid.org/0000-0001-9371-6654