Effect of 12 weeks aerobic exercise on coronary heart diseases' markers of inflammation in middle-aged women

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Original Article

Abstract

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Introduction: This study aims at analyzing the effect of 12 weeks physical exercise (30 minutes for three days a week: 70-85% of the maximum heart rate) on variations of inflammation markers in middle-aged women's Coronary Heart diseases (CHDs).

Methods: In this study a total of 40 subjects including 40-55 years old women were selected purposively and were divided into two experimental and control groups. The experimental group members were asked to follow a certain physical exercise program including 12 weeks physical exercise (30 minutes, three days a week with 70-85% of maximum heart rate using a treadmill); whereas subjects in the control group were asked to follow their normal lifestyle and do not change their activities and food habits. Levels of factors that can affect coronary heart risks including fibrinogen, C-reactive protein (CRP), and white blood cells (WBCs) were measured before and after exercises. Independent and paired t-tests were used to analyze data.

Results: The results of this study indicated a significant decrease in fibrinogen, CRP, and WBC levels after 12 weeks physical exercise in the experimental group (P≤0.05); whereas no significant change was seen in the control group (P>0.05).

Conclusion: Regarding the results of this study we can conclude that performing physical exercise (30 minutes, three days a week with 70-85% of maximum heart rate) can play an effective role in reducing risk factors of coronary heart disease (CHD) and hence in preventing coronary heart disease in 40-55 years old women with the similar properties of patients examined in this study.

Key words: Risk Factors – Fibrinogen – C-Reactive Protein (CRP)

Introduction:

Despite the decreasing trend of coronary heart diseases occurrence within the past several decades, it still is considered as the leading cause of death among men and women living in the modern industrial world and it is expected the highest rate of CHD is recoded in 2020 (1). In the United States 250,000 people die from sudden cardiac death

(SCD), which accounts for 50 percent of total deaths caused by CHDs, every year. Similarly, 39% of deaths in Canadian women are due to CHDs, which is more than deaths caused by various sorts of cancers (3,10,11). Although diagnosing coronary heart disease increases considerably the mortality risk, more than half of victims of SCD are not diagnosed for having coronary heart disease before death (4,9,13,14).

Therefore, identification of risk factors that result in CHDs can play a key role in preventing the disease progression.

A sedentary lifestyle brings about the most risks for development of CHD and death in general; there is a relationship between performing regular physical activities and the reduced rate of many chronic diseases including CHD. Regular physical activity, even at moderate levels, reduces considerably the risk of CHDs, diabetes, brain attacks, obesity and death in general (1,11,23).

Since, as the result of hormonal changes, after menopause period women face the risk of CHDs (10), determining the effect of type, intensity and duration of exercises on risk factors for heart diseases in such people can play a key role in preventing the progression of the disease. For this reason, estimating the risk of CHD seems necessary to enhance the health index of Iranian women, to avoid wasting high costs of treatment, and to take preventive measures against the mentioned disease (1,10). Inflammation markers have been recognized as the key predictive factors of CHDs. General inflammation markers play a key role in development and progression of atherosclerosis. Certain inflammation markers such as CRP and fibrinogen in contrast to blood lipids are considered as strong predictor of coronary hearth diseases by the researchers (1,21,26,27). Physical exercises cam reduce risks of CHDs. Declining CRP sensitivity is an effective mechanism in this regard (10). Thanks to its bondage with the damaged cells' phospholipids, activating complements and increasing attraction of the damaged cells by macrophages, CRP plays several roles (6,7). Aronson et al. (2004) reported a reverse and significant relationship between cardiorespiratory fitness and CRP levels in 894 middle-aged men and women (3).

Fibrinogen is among the coagulation factors which are produced by liver. The increased levels of fibrinogen enhanced that blood viscosity and coagulation, emboli and cardiovascular traumas (1). Studies have shown that people who perform high levels of regular physical exercises in contrast to people who perform lower activities have less fibrinogen level (12,23,25). Recent studies reported high level of fibrinogen in prediction of CHDs (24,25). Verdit et al. (2004) did not find any relationship between physical exercise and variation in CRP and fibrinogen levels in 809 men (39). On the one hand, the increased level of WBCs is treated as an important factor in diagnosing CHD and type II diabetes (16). Recent studies indicate that reactors of acute phase of inflammation such as fibrinogen, CRP, IL-6 and WBC have a reverse relationship with cardiovascular fitness ($VO2_{max}$) and any activity that declines such markers will decline coronary heart accidents, too (10,16,17).

No decisive findings have been found about compatibilities of coagulation factors, inflammation markers and aerobic exercises in sedentary middle-aged people in which the risk of CHDs is high yet (1,4,8,10,21,22). Since, (high levels of) fibrinogen and CRP are among very important risk factors of CHDs and sedentary middle-aged people face CHDs more than other populations, this study tried to analyze the effect of 12 weeks aerobic exercises on inflammation markers of coronary heart disease in the middle-aged women.

Methods:

The quasi-experimental method was used in this study.

The statistical population of the study consisted of 4-55 years old women. 40 subjects were selected casually and were divided into two groups: experimental group (n=20) and control group (n=20). The inclusion criteria were having no regular physical exercise and CHDs, peripheral vascular diseases, musculoskeletal diseases, pulmonary diseases, diabetes and hypertension. Postmenopausal women (who had not menstruation within past 12 months), women who used hormone therapy and women whose blood pressure BMI were higher than 140.90 mmhg and higher than 30, respectively, were excluded.

Before the first week of exercise and at the end of 12th week, blood samples were prepared. 10 ml venous blood was collected using the sterile tubes containing EDTA by lab experts. All subjected fasted since 14 hours before blood sampling. Within an hour the collected samples were transferred to the lab, where experts analyzed them. The blood variables in this study were fibrinogen, WBCs, and C-reactive protein (CRP). WBCs were counted automatically with Hycel parametrical cell counter, model celly. ELISA method was used to analyze CRP. It is necessary to note that subjects were provided with necessary information about the study and considerations that they need to meet before blood sampling. Meanwhile, they were asked to record their menstrual cycle date; it helped researchers to perform blood sampling exactly before and after the practical course at the same menstrual phase.

Before starting the exercise program, initially the maximum heart rate was measured using the Karvonen Formula (age-220) and its 70-85% was determined. The exercise intensity was controlled with stethoscope belt. The exercise program (2,18) for experimental group was 12 weeks running (30 minutes, 3 days a week, 70-85% maximum heart rate) on a treadmill (Techno gym, made in Italy) which was carried out in the Javan Gym. Program of a single exercise session included 15 minutes warming up with stretching, warm-up and running. Then running with a stable trend and 70-85% of maximum heart rate of subjects was conducted. In the first session, the running time was 15 minutes and then after each two session one minute was added to the running time until it reached 30 minutes and this duration was kept until the last

exercise session (the end of 12th week). At the end of each session, the body was cooled down by jogging, stretching, etc. for 10 minutes. The control group members were asked to maintain their normal lifestyle and do not change their activities and food habits, otherwise the researcher should be informed.

The descriptive statistics were used to describe data and to determine central tendency and dispersion. Kolmogorov-Smirnov normality test was used to make sure of normal distribution of data. The inter-group difference before and after 12 weeks exercise was assessed using independent t-test. The intra-group difference was assessed using paired t-test through comparing results of pretest and posttest. The inter-group change was measured through reducing pretest results from posttest results and comparing differences of such data between the two groups using independent t-test. SPSS 16 was employed to conduct statistical calculations. $P < 0.05$ was considered significant.

Results:

The results of our study represent a significant decrease in fibrinogen, WBC, CRP levels after 12 weeks physical activity in posttest of experimental group in contrast to its pretest ($P=0.002$, $P=0.001$, and $P=0.02$, respectively); whereas no significant variation was seen in the control group ($P < 0.05$); likewise a significant difference was seen between pretest and posttest value of experimental and control groups ($P=0.02$, $P=0.01$, $P= 0.02$, respectively).

Table 1. Personal data of subjects (data are suggested as M±SD)

Variable	Experimental		Control	
	Pretest	Posttest	Pretest	Posttest
Age (year)	46.25 ± 1.61		46 ± 1.55	
Height (m)	1.62 (0.04)		1.60 (0.03)	
Weight (kg)	72.65±7.88	67.4±7.49	70.33±8.12	69.53±8.26

Table 2. Comparing intra-group and inter-group variations of fibrinogen, WBC, CRP of subjects in pretest and posttest phases

Variable	Experimental group			Control group			Intergroup P value
	Pretest	Posttest	Intra-group P value	Pretest	Posttest	Intra-group P value	
Fibrinogen (mg/dl)	287.9 ± 35.5	254.9 ± 21.9	0.002	295.4 ± 35.5	293.9 ± 21.9	0.2	0.02
WBCs (Cu/mm)	8.08 ± 1.66	6.16 ± 1.2	0.001	7.11 ± 2.36	6.9 ± 2.2	0.1	0.01
CRP (mg/dl)	1.34 ± 0.48	0.94 ± 0.28	0.02	1.25 ± 0.41	1.16 ± 0.28	0.1	0.02

Conclusion:

The results represent a significant decrease in fibrinogen level of experimental group in contrast to the control group in terms of comparing pretest and posttest, which it was compatible with Nikbakht et al. (2007). They reported the significant decrease in serum level of fibrinogen in active men and women in contrast to that in inactive men and women in both health and CAD patient groups (23).

However, it was inconsistent with Borier et al. (2001), Bijeh et al., who did not report significant variations (4). Likewise, Nikbakht et al. (2007) reported that exercises and physical activity had not significant effect on fibrinogen levels and values of such risk factors in three groups of active, inactive and CAD were not different significantly. Similarly, there was not a significant correlation between $VO2_{max}$ amount and fibrinogen concentration in various groups (23). Bizheh et al. reported a significant increase of inflammation markers and coagulation factors levels in postmenopausal women after 15 weeks endurance training; they suggested that possible the increased release in catecholamines and local ischemia are due to exercises which in turn increases fibrinogen level and vascular thrombogenesis potential (4).

Possibly, the physical activity cannot solely be effective in reducing serum level of fibrinogen; because people's health condition, especially lack of certain factors such as smoking, hypertension, obesity, especially abdominal obesity, diabetes, aging, inheritance, etc. can affect the fibrinogen's concentration (2-4, 23).

Fibrinogen is not only an inflammation marker, but also is a key role in determining the plasma viscosity. A reverse significant relationship was found between $VO2_{max}$ and plasma viscosity. The significant reverse relationship between fibrinogen and $VO2_{max}$ indicates the role of systemic inflammation marker, fibrinogen, in blood (10,23).

The significant decrease in CRP level was reached in experimental group in contrast o the control group in terms of comparing pretest and posttest results. However, certain factors such as BMI, weight loss, estrogen, smoking, aging, gender, iteration, duration and intensity of exercises, etc. can affect the exercise response to CRP (4,10,25). Possibly, the decreased level of CRP can be interpreted as a sort of compatibility due to endurance training and strengthening heart and vessels of subjects. This process directly will improve the endothelial function and will increase the antioxidant factors through increasing nitric oxide resulted from endothelial, which in turn reduces systemic and local inflammation and production of inflammatory cytokinins from smooth muscles of endothelia wall and finally will decrease production of CRP from liver (8,10,14,19,26).

On the other hand, strengthening cardiovascular system by endurance training, metabolism improvements and strengthening lipolysis process will result in decreasing lipid level, as one of the major producers of inflammatory cytokines, and this will result in direct or indirect reduction of CRP production in liver (6,9). Body changes including variation in BMI and obesity affect CRP variations, as Diaxon et al. (2012) reported the significant increase and decrease in CRP level of obese and thin 45-64 years old men a week after ceasing activities (9).

On the other hand, the different fitness level of subjects participated in the long-term exercises can be the result of why there are some contradiction between finings of different studies (17,20). The increased inflammation in certain activities such as a session of triathlon including 2.4 miles swimming, 112 miles biking and 62.2 miles running would be due to over training process (14).

In the same direction, type of subject and cross-sectional nature of study and self-reporting would

be other reasons for why the findings are contradicted (11).

In this study, number of white blood cells of the experimental group in contrast to that in the control group in terms of comparing pretest results with posttest results decreased significantly. Bijeh et al. (2011) reported the increased number of WBCs [4]; while Hamednia et al. (2009) reported the decreased level of CRP and WBC after 13 weeks aerobic exercise in fat men (13). Likewise, Charch et al. reported a direct relationship between WBCs and fibrinogen and obesity and a reverse relationship between them and cardiorespiratory fitness (5).

Johansson et al. (2011) reported a significant decrease in number of WBCs and their subclasses within 6 months exercises with 12 kcal/kg per week; which it had a relationship with reduced level of IL-6 and waist circumference (16).

What is important here is type of exercise. Type of exercise can be mentioned as a reason for why the exercise had not a significant effect on the inflammation markers. Researcher studied the effect of various exercises on inflammation markers and aerobic exercises were selected and they concluded that such exercises have a significant effect on inflammation markers (20,24,25).

However, a number of researchers have referred to exercise intensity in terms of the maximum oxygen intake to produce significant effects on inflammation markers (15,26,27).

With regard to results of this study, conducting physical activity (30 minutes, 3 days a week, 70-85% of maximum heart rate) can play a key role in reducing CHD risk factors and preventing coronary heart diseases in 4-55 years old women with the same properties of women studied in this study.

Acknowledgement:

References:

1. American Heart association. Heart disease and stroke statistics. Updati Dallas, Tex. The dangerous tall of cardiovascular disease (heart disease and stroke) in the United State.

2. Angeli F, Angeli E, Ambrosio G, Mazzotta G, Reboldi G, Verdecchia P. Neutrophil count for the identification of postmenopausal hypertensive women at increased cardiovascular risk. *Obstet Gynecol*. 2010;115:695-703.

3. Aronson D, Sheikh-Ahmad M, Avizohar O. C-Reactive protein is inversely related to physical fitness in middle-aged subjects. *Atherosclerosis*. 2004;176:173-179.

4. Bizheh N, Rashidlamir A, Zabihi A, Jaafari M. The acute effects of strength training on inflammatory markers predicting atherosclerosis: a study on inactive middle-aged men. *Tehran University of Medical Sciences Journal*. 2011;69:204-209.

5. Church TS, Earnest CP, Skinner JS, Blair SN. Effects of different doses of physical activity on cardiorespiratory fitness among sedentary, overweight or obese postmenopausal women with elevated blood pressure: a randomized controlled trial. *JAMA*. 2007;297:2081-2091.

6. Davise ME, Edwards DG, Brubafer PH, Phillips I. Lipid profiles and plasma C-reactive protein levels in patients entering cardiac rehabilitation: *Med Sci Sports Exerc*. 2002;34:180-185.

7. De Ferranti S, Rifai N. C-reactive protein and cardiovascular disease: a review of risk prediction and interventions: *Clin Chim Acta*. 2002;317:1-15.

8. De Gonzalo-Calvo D, Fernandez-Garcia B, de Luxan-Delgado B, Rodriguez- Gonzalez S, Garcia-Macia M, Suarez FM, et al. Long-term training induces a healthy inflammatory and endocrine emergent biomarker profile in elderly men. *Age*. 2012;34:761-771.

9. Dixon NC, Hurst TL, Talbot D, Tyrrell RM, Thompson D. Effect of short-term reduced physical activity on cardiovascular risk factors in active lean and overweight middle-aged men. *Metabolism*. 2013;62:361-368.

10. Falah omran S, Zeyaie N, Ravasi AA. Relationship between inflammatory markers of cardiovascular disease and VO2peak in asymptomatic females. *J Sports Med Phys Fitness*. 2013;53:198-202.

11. Ford ES. Does exercise reduce inflammation? Physical activity and C-reactive protein among U.S. adults. *Epidemiology*. 2002;13:561-568.

12. Hambrecht R. Effect of exercise on coronary endothelial function in patients with coronary artery disease. *N Engl J Med*. 2000;342:454-460.

13. Hamedinia MR, Haghighi AH, Ravasi AA. The effect of aerobic training on inflammatory markers of cardiovascular disease risk in obese men. *Word J Sport Sci*. 2009;2:7-12.

14. Hilier D. C- Reactine protein Levels before and after endurance exercise. *Med Sci Sports Exerc*. 2003;35:121.

15. Kullo J, Khaleghi M, Hensrud DD. Markers of inflammation are inversely associated with VO2max in asymptomatic men. *J Appl Physiol*. 2007;102:1374-1379.

16. Johannsen NM, Priest EL, Dixit VD, Earnest CP, Blair SN. Association of white blood cell subfraction concentration with fitness and fatness. *Br J Sports Med*. 2010;44:588-593.

17. Kim H, Lee Ho, Kim CK. Biomakers of muscle and cartilage damage and inflammation during a 200 km. *Eur Appl Physiol*. 2007;99:443-447.

18. Margolis KL, Manson JE, Greenland P, Rodabough RJ, Bray PF, Safford M, et al. Leukocyte count as a predictor of cardiovascular events and mortality in postmenopausal women: the Women's Health Initiative Observational Study. *Arch Intern Med*. 2005;165:500-508.

19. Mattusch F, Dufaux B, Heine O, Mertens I, Rost R. Reduction of the plasma concentration of C- reactive protein following nine months of endurance training. *Int J Sports Med*. 2000;21:21-24.

20. Michishita R, Shono N, Inoue T, Tsuruta T, Node K. Effect of exercise therapy on monocyte and neutrophil counts in overweight women. *Am J Med Sci*. 2010;339:152-156.

21. Mora S, Lee IM, Buring JE, Ridker PM. Association of physical activity and body mass index with novel and traditional cardiovascular biomarkers in women. *JAMA*. 2006;22:295:1412-1419.

22. Morss GM, Jordan AN, Skinner JS, Dunn AL, Church TS. Dose Response to Exercise in Women aged 45–75 yr (DREW): design and rationale. *Med Sci Sports Exerc*. 2004;36:336-344.

23. Nikbakht HA, Amirtash AM, Gharouni H, Zafari A. Correlation of physical activity with serum fibrinogen and homocysteine concentration in active, sedentary and with CAD males. *Olympic*. 2007;38:71-80.

24. Pitsavos C, Chrysohoou C, Panagiotakos DB. Association of leisure-time physical activity on inflammation markers (C-reactive protein, white cell blood count, serum amyloid A, and fibrinogen) in healthy subjects (from the ATTICA study). *Am J Cardiol*. 2003;91:368-370.

25. Pitsavos C, Panagiotakos DB, Chrysohoou C, Kavouras S, Stefanadis C. The associations between physical activity, inflammation, and coagulation markers, in people with metabolic syndrome: the ATTICA study. *Eur J Cardiovasc Prev Rehabil*. 2005;12:151-18.

26. Stauffer BL, Hoetzer GL, Smith DT, Desouza CA. Plasma C – reactive Protein is not elevated in Physically active postmenopausal women taking hormone replacement therapy. *J Appl Physiol*. 2004;96:143-148.

27. Stewart LK, Flynn MG, Campbell WW, CRAIG BA, Robinson JP, Timmerman KL, et al. The Influence of Exercise Training on Inflammatory Cytokines and C -reactive protein. *Med Sci Sports Exerc*. 2007;39:1714-1719.

تأثیر ۱۲ هفته فعالیت ورزشی هوازی بر شاخص‌های التهابی بیماری‌های قلبی – عروقی زنان میانسال

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چکیده

مقدمه: هدف از تحقیق حاضر، بررسی تأثیر دوازده هفته فعالیت بدنی (۳۰ دقیقه، سه روز در هفته، شدت: ۸۵–۷۰ درصد حداکثر ضربان قلب) بر تغییرات شاخص‌های التهابی بیماری‌های قلبی – عروقی زنان میانسال بود.

روش کار: بدین منظور ۴۰ آزمودنی از بین زنان ۵۵–۴۰ سال به صورت هدف‌دار انتخاب و به دو گروه تمرین و کنترل تقسیم شدند. برنامهٔ گروه تمرین فعالیت بدنی شامل دوازده هفته فعالیت بدنی به مدت ۳۰ دقیقه، سه روز در هفته، با شدت ۸۵–۷۰ درصد حداکثر ضربان قلب روی دستگاه تردمیل بود و از آزمودنی‌های گروه کنترل خواسته شد تا شیوهٔ طبیعی زندگی خود را حفظ کنند و میزان فعالیت و عادات غذایی‌شان را تغییر ندهند. مقادیر عوامل تأثیرگذار بر خطر قلبی – عروقی شامل: فیبرینوژن، پروتئین واکنش دهنده C (CRP) و گلبول‌های سفید خون قبل و بعد از انجام برنامهٔ تمرینی اندازه‌گیری شد. برای تجزیه و تحلیل اطلاعات از آزمون t مستقل و t زوجی استفاده شد.

نتایج: نتایج این پژوهش نشان دهنده کاهش معنی‌داری در فیبرینوژن، پروتئین واکنش دهنده C (CRP) و گلبول‌های سفید خون پس از دوازده هفته فعالیت بدنی در گروه تمرین بود ($P \leq ۰/۰۵$)، در حالی که تغییر معنی‌داری در گروه کنترل مشاهده نشد ($P > ۰/۰۵$).

نتیجه‌گیری: با توجه به نتایج تحقیق حاضر، انجام فعالیت بدنی (۳۰ دقیقه، ۳ روز در هفته، شدت: ۸۵–۷۰ درصد حداکثر ضربان قلب) می‌تواند نقش مؤثری در کاهش عوامل خطر قلبی – عروقی (CHD) و متعاقب آن پیشگیری از بیماری‌های قلبی عروقی در زنان ۵۵–۴۰ سال با ویژگی‌های مشابه افراد مورد مطالعه در این پژوهش داشته باشد.

کلیدواژه‌ها: عوامل خطر – فیبرینوژن – پروتئین واکنش دهنده C (CRP)

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