Correlation of Physical Activity with Serum Fibrinogen, Homocysteine (HCY) and C-reactive Protein (CRP) Concentration in Active, Sedentary and with Coronary Heart Disease (CAD) Females

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Abstract: The aim of this cross-sectional study was compare of serum concentration of Fibrinogen, Homocysteine and C-reactive protein in active, sedentary and with CAD women. Sixty individuals participated in this study voluntarily which divided in three groups based on National Health Interweave Surveys (NHIS) and Physical Activity Rating questionnaire (PA-R) questionnaire. Blood samples were taken for measuring serum concentration of fibrinogen, homocysteine and CRP. Data analysis by using ANOVA-one post hoc Tukey test results ($p \leq 0.05$). ANOVA-one way analysis of variance indicated that serum fibrinogen concentration in the CAD (396.75 ±35.20) was significantly higher than fibrinogen levels of active and sedentary groups (327.55 ± 60.69 and 297.5 ± 47.77, respectively) (F=21.57, P=0.001) whereas, the homocysteine levels did show significant difference among groups (F=26.67, P=0.003). Moreover, CRP concentrations for different groups were significantly different (F=6.88, P=0.002). This cross-sectional study has shown significantly higher CRP, homocysteine and fibrinogen levels in patients with CAD as compared to active and sedentary subjects. These newer parameters were also correlated with BMI and Vo2max values. Thus, these can probably be used as surrogate markers for the prediction of cardiovascular dysfunction. Undoubted, a prospective study is needed to identify the risk factors and their predicative value better.

Key words: Fibrinogen · Homocysteine · CRP · CAD and Physical Activity

INTRODUCTION

It is well known that established risk factors contribute to the cardiovascular disease (CVD), but they fail to predict all cardiovascular events [1]. On the other hand, recent analysis have shown that some newer risk factors are also important in the pathophysiology of the vascular events [2] and this critical role has made them a pivotal target for the therapeutic strategies. Plasma CRP levels is an important marker of subclinical chronic vascular inflammation, being considered a strong predictor of cardiovascular events because it contributes to the development and progression of atherosclerosis [3, 4]. The plasma levels of another marker, homocysteine correlate with the CAD, stroke and peripheral arterial disease [5]. Recent data from the Framingham Heart trial data showed a strong association between homocysteine

concentrations and the risk for CVD in both men and women with no prior history of CAD [6]. Fibrinogen, a molecule produced in the liver, is concerned that has a central role in the fibrin thrombus formation and increase of plasma viscosity [7] and also correlate positively with hypertension and cholesterol levels [8].

Because many studies have indicated that exercise training, particularly regular exercise is a best way and non-pharmacological therapeutic modality that can prevent and improve chronic diseases, especially coronary artery disease, atherosclerosis and lipid disorders in men and women with different ages [9, 10], Therefore, we aimed to compare the relationship between level of physical activity as an indicator of training with serum fibrinogen, homocysteine and CRP concentration in active, sedentary and with established cardiovascular disease women.

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MATERIALS AND METHODS

This cross section study was conducted on sixty middle-aged women with different statuses of conditioning to compare their concentration of homocysteine, fibrinogen and CRP levels. The criteria to determine study groups was based on NHIS, PA-R scores and the American College of Sports Medicine (ACSM) standard at the level of physical activity questionnaire and patients group were selected from subjects who had established CAD. Then, they divided in three groups as follow: Active (N=20), Sedentary (N=20) and CAD (N=20). At beginning of the project written consent was taken from all subjects. After that, fasting blood sample was taken of each subject for measuring serum concentration of fibrinogen with chronometric method, homocysteine with ELISA method and CRP with serologic method. The Normality of distribution and homogeneity of variance were calculated by used Kolmogorov- Smirnov and Levine tests, respectively. Data were described using mean ± standard deviation (SD). In statistical analysis of the study results, the groups were compared by using One-way ANOVA post hoc Tukey test results. All analyses were performed by using SPSS version 16.0 software. A p value less than 0.05 was considered significant.

RESULTS

There was a total of 60 subjects in our study. Table 1 indicate descriptive characteristic of the subjects in each group. There were not significant differences between age and height between three groups but it was seen that the CAD group had significantly higher levels of weight ($F_{(2,57)}$= 2.836, p= 0.003) and BMI ($F_{(2,57)}$= 4.935, p = 0.002) in compare to Active and Sedentary groups.

The study parameters in the three groups are shown in Table 2. It was seen that in the CAD group, differences of serum of fibrinogen ($F_{(2,57)}$ = 21.57, p= 0.001) and homocysteine ($F_{(2,57)}$ = 26.67, p= 0.001) are significantly higher than other groups and the CRP levels of CAD group also was statistically significant than Active and Sedentary groups ($F_{(2,57)}$= 21.57, p= 0.001).

Table 1: shows descriptive characteristic of the subjects of study groups

parameter	Active	Sedentary	CAD
Age (yrs)	44.1±8.25	41.55±6.22	51.35±5.01
Weight (kg)	66.45±10.34	65.95±5.88	68.55±4.94
Height (m)	1.62±0.04	1.63±0.03	1.61±1.03
BMI (kg/m^2)	24.24±4.17	24.54±2.51	26.25±2.3

Table 2: study parameters in the three groups

parameter	Active	Sedentary	CAD
Fibrinogen	327.55±60.69	297.5±47.77	396.75±35.2
Homocysteine	13.10±1.6	15.94±2.49	17.45±1.46
CRP	1.92±0.137	2±0.184	2.11±0.196

Since VO_2max is the best marker for level of physical activity, we correlate study parameters with this marker. Therefore, in Table 3 the correlation of the CRP, fibrinogen and homocysteine levels have been made with the estimated VO_2max as a marker for level of physical activity among all groups who were included in the study. The correlation between fibrinogen and VO_2max was shown although there was not a meaningful relationship between VO_2max & fibrinogen in all groups, a direct but incomplete relationship was observed in active (r = 0.051, p =0.415), CAD (r = 0.045, p = 0.365) and indirect and incomplete relationship in sedentary group (r = -0.32, p = 0.052). Moreover, the VO_2max levels correlated with homocysteine values only with sedentary group (r=-0.378, p=0.028). Whereas, it was not seen for active (r = -0.378, p = 0.051) and CAD (r = 0.12, p = 0.181). The correlation between CRP and VO_2max in active group was not meaningful and very weak (r = 0.003, p = 0.99) but for sedentary group (r = 0.361, p = 0.118) and CAD group (r = 0.121, p = 0.612) was positive however it was not significant.

DISCUSSION

In our cross sectional study, we compere some of the selected of noble risk factors for cardiovascular disease in different population based on their health condition and physical activity. The main target of this study was to investigate any probable relationship

Table 3: correlation between study parameter and VO_2max in all groups

Correlation	Active	sedentary	CAD
fibrinogen	r = 0.051, p =0.415	r = -0.32, p = 0.052	r = 0.045, p = 0.365
homocysteine	r = -0.378, p = 0.051	r = -0.304, p = 0.028	r = 0.12, p = 0.181
CRP	r = 0.003, p = 0.99	r = 0.361, p = 0.118	r = 0.121, p = 0.612

between fibrinogen, homocyteine and CRP in study groups. According to results we found significantly higher levels of fibrinogen, homocyteine and CRP in CAD group more than active and sedentary groups.

The role of fibrinogen have been confirmed by large studies to be associated with increased cardiovascular disease [11, 13]. The factors which are associated with increasing fibrinogen levels involved health conditions, especially in the presence of factors such as smoking, hypertension, obesity (especially abdominal obesity), diabetes, aging and heredity and serum concentration of fibrinogen. Therefore, many of investigation reported effect of physical activity on changing levels of fibrinogen but the results have been controversial. The results of Nissen *et al* (22), Schneider *et al* (16) and Heit Kamp *et al*. (23) showed that regular physical activity may not reduce serum levels of these risk factors, whereas, Hejazi *et al*(12), Furukawa *et al* (14), Myint *et al* (15), Mora (24), Fallah Mohammadi (25) and Jae (26) indicated that physical activity could improve fibrinogen levels. The results of mentioned studies are different that might be due to exercise protocols, training status, body weight, BMI, age and sex of the study subjects. Nevertheless, several mechanisms could explain the fluctuation of fibrinogen levels in these studies. It is believed that exercise training might decrease catecholamine stimulations and increasing blood flow to muscles, this could result in reduce IL-6 which is built in adipose tissue and since IL-6 is a stimulator in synthesis of fibrinogen, its reduction results in decreased fibrinogen [17].

Besides, the other results of present study were higher levels of homocyteine and CRP levels in CAD group more than active and sedentary groups. In the primary prevention Women's Health Study, women with the highest baseline CRP levels had a 5-fold higher risk of suffering from vascular events than women with low CRP levels [19]. In the Physicians' Health Study, subjects with high baseline levels of CRP had a 2-fold increase in the risk of cardiovascular disease with p with low CRP levels [18]. Higher CRP level is likely due to part of IL-6 which stimulates CRP production which is accumulated in adipose tissue. It is believed that obesity is associated with elevated CRP [19]. In this study, the weight and BMI of CAD group also were higher than the other groups that could be mediated with elevated CRP levels. In addition, it has been reported that homocysteine levels increase with aging, male gender and in the presence of CVD [20]. On the other hand, the levels of homocysteine are associated with decreasing of body

mass [21] and there is a relationship between elevated homocysteine and lipids [12]. Since performing exercise has some beneficial effects on reducing fat mass therefore, it seems that physical activity is a practical strategy which has been caused our active and sedentary groups had lower levels of this parameter in compare to CAD group. However, our study was cross sectional and more studies are required to clarify these risk factors of CAD.

CONCLUSION

The results of this study indicated that CAD group does not have desirable levels of homocysteine, fibrinogen and CRP concentration. Based on correlations between physical activity rating and VO2max with homocysteine, fibrinogen and CRP concentration, it seemed that performing physical activity is a significant way for controlling these parameters. However, more studies especially prospective study are needed.

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REFERENCES

1. Khot, U.N., M.B. Khot, C.T. Bajzer, *et al*., 2003. Prevalence of conventional risk factors in patients with coronary heart disease. JAMA, 290: 898-904.

2. Rudrajit Paul, Pradip K. Sinha, Avishek Saha, Ramtanu Bandyopadhyay and Amit K. Banerjee, 2011. A study on the blood levels of homocysteine, fibrinogen and hsCRP in diabetic patients with ischaemic stroke from eastern India. Journal of Clinical and Diagnostic Research. November (Suppl-2), 5(7): 1389-1392.

3. Theuma, P. and V.A. Fonseca, 2003. Inflammation and emerging risk factors in diabetes mellitus and atherosclerosis. Curr Diab Rep., 3: 248-54.

4. American Diabetes Association, 2010. Diagnosis and classification of diabetes mellitus. Diabetes Care, 33 Suppl, 1: S62-9.

5. Graham, I.M., L.E. Daly, H.M. Refsum, *et al*. 1997. Plasma homocysteine as a risk factor for vascular disease: the European Concerted Action Project. JAMA; 277: 1775-81.

6. Vasan, R.S., A. Beiser, R.B. D'Agostino, *et al*. 2003. Plasma homocysteine and risk for congestive heart failure in adults without prior myocardial infarction. JAMA; 289: 1251-7.

7. Reinhart, W.H., 2003. Fibrinogen-marker or mediator of vascular disease? Vascular Medicine; 8: 211-216.

8. Haffner, S.M., 2006. The metabolic syndrome: inflammation, diabetes mellitus and cardiovascular disease. Am J Cardiol; 97: 3A-11A.

9. Mora, S., Lee, I. Min and J.E. Buring, 2006. *JAMA*. Chicago: Mar, 295(12): 1412-20.

10. Thomas, D.E., E.J. Elliott and G.A. Naughton, 2006. Cochrane Database of Systematic Reviews, Issue 3.Art. No: CD002968. DOI: 10.1002/14651858. CD002968. pub2.

11. Resch, K.L., E. Ernst, A. Matrai and H.F. Paulsen, 1992. Fibrinogen and viscosity as risk factors for subsequent cardiovascular events in stroke survivors. Ann Intern Med; 117: 371-5.

12. Hejazi, S.M., A. Rashidlamir, A. Jebelli, S. Nornematolahi, S.M. Ghazavi and M. Soltani 2013. The effects of 8 weeks aerobic exercise on levels of homocysteine, HS-CRP serum and plasma fibrinogen in type II diabetic women. Life Science Journal; 10: 1s.

13. Tayebi, S.M., P. Hanachi, A.G. Niaki, P. Nazar and F. Ali, 2010. Ghorban-alizadeh. Ramadan Fasting and Weight-Lifting Training on Vascular Volumes and Hematological profiles in young male weight-lifters. Global J. Health Sci., 2(1): 160-166.

14. Furukawa, F., K. Kazuma, M. Kojima and R. Kusukawa, 2008. Effects of an off-site walking program on fibrinogen and exercise energy expenditure in women. Asian Nursing Res., 2(1): 35-45.

15. Myint, P.K., R.N. Luben, N.J. Wareham, A.A. Welch, S.A. Bingham and K.T. Khaw, 2008. Physical activity and fibrinogen concentrations in 23,201 men and women in the EPIC-Norfolk population-based study. Atherosclerosis; 198(2): 419-25.

16. Schneider, S.H., Hugh C. Kim and Avedis K. Khachadurian, 2004. Impaired fibrinolytic response to exercise in type II diabetes: Effects of exercise and physical training. University of Medicine and Dentistry of New Jersey, Robert Wood. Johnson Medical School, New Brunswick, NJ, USA.

17. Hoffner, L., J.N. Jens, L. Henning and H. Ylva, 2003. Exercise but not prostanoids enhance levels of vascular endothelial growth factor and other proliferative agents in human skeletal muscle interstitium. J Physiol, 5: 217-225.

18. Ridker, P.M., M. Cushman, M.J. Stampfer, R.P. Tracy and C.H. Hennekens, 1997. Inflammation, aspirin and the risk of cardiovascular disease in apparently healthy men. N Engl J Med; 336: 973-9.

19. Papazafiropoulou, A., N. Katsilambros and N. Tentolouris, 2008, Novel Risk Factors for Atherosclerosis. The Open Biomarkers Journal, 1: 36-47.

20. Gauthier, G.M., J.G. Keevil and P.E. McBride, 2003. The association of homocysteine and coronary artery disease. Clin Cardiol; 26: 563-8.

21. Zafari, A., H. Nikbakht, A.M. Amirtash and M. Gharooni, 2012. Correlation of VO2max with Serum Concentrations of Fibrinogen and Homocysteine. Pelagia Research Library. European Journal of Experimental Biology, 2(5): 1593-1597.

22. Nissen, Steven, E. and Schoenhagen, Paul, 2002. Lipid Management, 6: 4.

23. Heit Kamp, H.C., S. Wegler and U. Brehme, 2008. J Sports Med Phys Fitness; Mar, 48: 113-119.

24. Mora, S., Lee, I. Min and J.E. Buring, 2006. *JAMA*. Chicago: Mar, 295(12): 1412-20.

25. Fallah Mohammadi, Z. and M. Poor Amir, 2006. Jour of Sports Sciences, 2(3): 13.

26. Jae, S.Y., K.S. Heffernan and M.K. Lee, 2008. Amer Jour of Cardio, NY: Sep 15, 102(6): 700.