HIGH SENSITIVE C – REACTIVE PROTEIN (HSCRP) IN YOUNG MEN UNDERGOING AEROBIC EXERCISE AND ITS RELATION TO LIPID PARAMETERS

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ABSTRACT

BACKGROUND

Increased hsCRP levels is known to be associated with increased risk of myocardial infarction, thromboembolic attacks and peripheral vascular disease. Moderate intensity physical activities like aerobic exercise training, may reduce the inflammatory process in the arteries causing a reduction in the hsCRP levels.

AIM AND OBJECTIVES

To assess the serum hsCRP levels, BMI (Body Mass Index) and lipid status of individuals undergoing aerobic exercise and to study the correlation of hsCRP levels with BMI and the lipid parameters.

MATERIALS AND METHODS

An analysis was conducted among 40 young adult men who had underwent aerobic exercise for more than 6 months and 40 non- exercising men. Serum hsCRP & lipid parameters analysed using semiautoanalyzer.

STATISTICAL ANALYSIS

The statistical analysis was done using SPSS version 16. The parameters were compared among the 2 groups using Independent t test and correlations between hsCRP and other parameters were done.

RESULTS

Serum hsCRP levels were significantly high (p=0.007) in non-exercising men of group 2(2.66±1.51 mg/L) compared to the exercising group 1 (1.77±0.84 mg/L). The serum Triglycerides (p=0.005) & BMI (p=0.014) were increased in the non-exercising men from that of the exercising group. Serum HDL levels were significantly high in the exercising group (p=0.000). Serum hsCRP was positively correlated with BMI and triglycerides and negatively correlated with HDL levels.

CONCLUSION

Aerobic exercise training may cause a reduction in hsCRP levels, thereby reducing the risk of cardiovascular mortality and morbidity.

KEYWORDS

hsCRP, CRP, Aerobic exercise, BMI, Obesity, Physical activity.

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INTRODUCTION: Sedentary lifestyle is a problem faced by both developed and developing countries all over the world. This type of lifestyle has resulted in increased incidence of obesity, a known CVD (cardiovascular disease) risk factor. Lack of exercise and obesity along with other risk factors has led to an epidemic of cardiovascular disorders, with increasing incidence of premature mortality and morbidity. Physical activity has been known to have a favourable impact on the traditional risk factors, decreasing the risk of CVD, by different mechanisms.

High sensitive C-reactive protein (hsCRP) is a non-specific marker of inflammation, which is moderately elevated in obesity, metabolic syndrome, type 2 diabetes and coronary artery disease. C-reactive protein (CRP) is an acute phase protein whose increase results in an increase in coronary artery disease by 2 to 5 times. C-reactive protein (CRP), an inflammatory marker, appears to take part in the pathogenesis of various stages of atherogenesis, where a state of low grade inflammation persists.[1] Hence increase in hsCRP levels could predict the occurrence of cardiovascular events.[2,3]

Obese individuals have significantly higher hsCRP levels compared to the non-obese subjects.[4] Adipose tissue can

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induce a state of chronic low grade inflammation by producing many inflammatory cytokines, including IL-6, TNF-α & CRP. Obesity can be defined by increased Body Mass Index (BMI) and many studies indicate a strong correlation between hsCRP levels & BMI.[5] Obese persons with a higher BMI have been found to have higher hsCRP concentrations than those with a lower BMI.[6]

Moderate intensity exercise training may reduce the inflammatory process in the arteries and hence cause reduction in the hsCRP levels, by multiple mechanisms.[7,8] Lifestyle changes by increasing physical activity and reducing obesity/BMI, may lower the hsCRP levels and hence reduce the risk of cardiovascular disorders.[9,10]

So we have chosen one form of physical activity- Aerobic exercise training underwent by young healthy males for more than 6 months and tried to analyse its effects on BMI, hsCRP and other lipid parameters. We have also tried to assess the correlation between these parameters.

MATERIALS AND METHODS: Study Design: Our study had been conducted in a Fitness Gym, Salem over a period of 3 months.

It is a cross-sectional study conducted in 80 healthy young men in the age group of 25-40 years. They were divided into 2 groups.

Group 1: 40 healthy adult males (25-40 years) who did not take part in any form of exercise program and formed the control group.

Group 2: 40 healthy adult males (25-40 years), who underwent some form of aerobic exercise (workouts in treadmill /elliptical/ cycling) in the fitness centre, forming the study group. All the members of this group had exercised regularly for 30 minutes to 1 hour a day, for a minimum of 5 days a week. They had regularly followed this schedule for more than 6 months.

Written consent was obtained from all the subjects, after clearly explaining to them the about our study protocol. This study was approved by the ethical committee of Vinayaka Missions' Kirupananda Variyar Medical College, Salem.

Subjects with diabetes, hypertension, cardiac/renal disease, chronic infections, systemic illness, endocrine disorders, malignancy or neuropsychiatric illness were excluded from the study. The participants were neither alcoholics nor smokers. All the relevant demographic data were collected and the subjects were age and sex matched. Anthropometric measurements including height, weight, waist, hip circumference were measured to calculate BMI & waist hip ratio.

SAMPLE COLLECTION: Fasting blood samples were collected from all the subjects-both the study and control groups 1 & 2. Blood was allowed to clot and serum separated after centrifuging the samples. The sera were used for analysis of biochemical lipid parameters like total cholesterol, triglycerides, HDL cholesterol (high density lipoprotein), and hsCRP (high sensitive C - reactive protein).

BIOCHEMICAL METHODS:

1. HsCRP: Standard clinical assays for CRP typically have a lower detection limit of 3 to 8 mg/L.[11] Thus, these assays lack sensitivity within the low-normal range and cannot be used effectively for vascular risk prediction.
   In the present study we have determined the levels of CRP by using a highly sensitive method: hs-CRP, with a detection limit 0.25mg/L.[11] hsCRP is effective in low normal range vascular risk prediction.[12] Serum hsCRP levels were estimated by Latex-turbidimetric assay, in semi autoanalyzer.[11]
   The relation between hsCRP levels and cardiovascular risk[1] is as follows.

Sl. No.	hsCRP levels	CVS risk status
1	<1 mg/dl (normal range)	no cardiovascular risk
2	1 to 3 mg/dl (moderately increased)	slightly increased risk of cardiovascular events
3	> 3 mg/L (high values)	increased risk of cardiovascular events

2. Serum Total Cholesterol and Triglycerides were analyzed by endpoint methods & HDL cholesterol by direct enzymatic methods, in semi-autoanalyzer.
3. LDL was calculated using Friedewalds' equation: LDL= Total cholesterol-HDL-TGL/5.[13]
4. BMI, an index of obesity was calculated using formula BMI=Weight in kilograms/(height in meters).[2]
5. Waist/Hip ratio (WHR) was calculated using the measurements.

STATISTICAL ANALYSIS: Statistical analysis was done using the software SPSS version 16 and data expressed as mean ± 2SD. Differences in mean between the 2 groups were analyzed using independent t test. Correlations between hsCRP, lipid parameters & BMI were done.

RESULTS: The lipid parameters and hsCRP levels were analyzed in 40 exercising and 40 non-exercising healthy young males. The mean and standard deviations of hsCRP, lipid parameters, BMI & waist/hip ratio are depicted in Table 1.

There was a significant increase in the hsCRP levels (2.66±1.51 mg/L) in non-exercising young men of group 1 (p=0.007), compared to the exercising men (1.77±0.84 mg/L) in group 2. Serum HDL levels were high in group 2 men (58±11.5mg/dl) than those in group 1 (40±6.5mg/dl) with p=0.000. Serum Triglycerides were found to be high in non-exercising men (205±122.6 mg/dl) than that of the exercising group (134±52.1mg/dl) with p=0.005. But there was no significant change in the total cholesterol and LDL-cholesterol levels among the 2 groups. BMI was found to be high in the sedentary men (group 1) than the exercising men (p=0.014), while no change was observed in the waist/hip ratio.

Table 2 showed the correlations of hsCRP levels with BMI, Triglyceride and HDL levels. The hsCRP levels showed a significant positive correlation with BMI (p=0.045) and serum Triglyceride levels (p=0.002). There was also a significant negative correlation between hsCRP and HDL levels (p=-0.390).

Parameters	Group 1 (non-exercising men)	Group 2 (exercising men)	Unpaired t test Sig (2-tailed) p-value
hsCRP* (mg/L)	2.66±1.51	1.77±0.84	0.007
T. Cholesterol NS (mg/dl)	149±32.1	160±29.8	0.180
LDLNS (mg/dl)	72±33.6	75±28.7	0.703
HDL* (mg/dl)	40±6.5	58±11.5	0.000
TGL* (mg/dl)	205±122.6	134±52.1	0.005
BMI* (kg/m2)	23.8±4.26	26.7±4.64	0.014
WHRNS	0.92±0.05	0.93±0.06	0.74

Table 1: Means & Standard Deviation for hsCRP, BMI & lipid parameters among non-exercising (group1) and exercising (group2) young men

(NS-Non significant; * P <0.01)

		Correlation coefficient (r)	Sig. (2-tailed)
hsCRP	BMI	0.259*	0.045
	TGL	0.396**	0.002
	HDL	-0.390**	0.002

Table 2: Correlations of hsCRP with BMI, Triglycerides and HDL Cholesterol

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

DISCUSSION: We have conducted our study among young healthy adult males in the age group of 25-40 years. We divided them into 2 groups, group 1 comprising of non-exercising men and group 2 of men who had undergone aerobic exercise regularly for more than 6 months.

In our study, serum hsCRP levels is significantly low in healthy young men (group 2) undergoing aerobic exercise training as compared to the non-exercising men (group1) who led a sedentary lifestyle. Lower levels of inflammatory markers like CRP have been associated with regular participation of individuals in some form of exercise/ physical activity.[14,15,16] While some studies have admitted an inverse association between physical activity and hsCRP levels,[17,18,19] a few couldn't find any significant correlation.[20,21]

Physically active men, once they become inactive, their CRP levels have been found to become similar to that of non-exercising men and vice versa. Continuous physical activity is necessary to maintain its effect on the CRP levels.[22]

CRP being an inflammatory cytokine is produced in response to vascular inflammation and results in atherogenic changes in the vessel walls. Endothelium produces the relaxing factor nitric oxide (NO), which causes vasodilatation, thereby protecting the arterial wall from development of atherosclerosis and thrombosis. CRP is known to potentially downregulate the endothelial NO synthase gene transcription, resulting in a decreased release of NO, thereby accelerating the atherogenic process.[23] CRP also binds to lipoproteins (LDL & VLDL), promotes oxidative modification of LDL, induces expression of plasminogen activator inhibitor-1 and acts as a powerful activator of the complement system.[23] By all the above mechanisms it can mediate the progression of atherosclerosis.[24]

CRP is synthesized mainly in the liver in response to cytokines like IL-6, IL-1β & TNF-α. Among these IL-6 is the main inflammatory cytokine regulating the hepatic production of CRP. Recently CRP gene has been found to be expressed in adipose tissue, indicating its synthesis from adipose tissue also. So adipose tissue is also a direct source of CRP production, along with liver.[25] Adipose tissue can induce chronic low grade inflammation by producing pro-inflammatory cytokines such as interleukin-6, which enhances CRP production in liver as well as adipose tissue.[26,27] Hence the hsCRP levels might be increased in obese individuals compared to lean ones. Hence there is increased CRP production in inflammatory states as in obesity, and the high CRP levels in turn could cause vascular changes, activating the atherosclerotic process.

Physical activities, like aerobic exercise, have the tendency to reduce obesity and BMI, which might lead to a reduction in CRP levels. In our study both BMI and hsCRP levels were high in the non-exercising men while both these parameters were low, in men undergoing regular aerobic exercise. We have also found a positive correlation between hsCRP levels and BMI.

The low circulating hsCRP levels in group 2 individuals undergoing aerobic exercise, may be attributed to reduction in the adipose tissue mass. Aerobic exercise may also attenuate the production of inflammatory cytokines by the mononuclear cells.[28] All these effects of physical activity could create an anti-inflammatory state, with reduced hsCRP levels.

This decrease in hsCRP levels may in turn reduce oxidative stress, cause increased production of nitric oxide by the endothelial cells, thereby reducing progression of vascular inflammation. Hence moderate physical activity over a long period of time has protective effects, from CVD complications.

We have also found a significant increase in serum triglyceride levels in the non-exercising men (group1) compared to their exercising counterparts. In obese individuals, with greater BMI, increased adipocyte mass might cause an increased production of IL-6, resulting in increased hepatic triglyceride secretion.[29] This may be the cause of hypertriglyceridemia noticed in non-exercising men with higher BMI. We have also observed a positive correlation of hsCRP with triglyceride levels.

Physical activity has been found to have beneficial effects on many cardiovascular disease risk factors, including total and HDL cholesterol.[30] But, we did not observe any

significant change in the LDL-cholesterol and Total cholesterol levels among the 2 groups. We have found an increase in serum HDL levels in the exercising group 2 and HDL is negatively correlated with hsCRP levels.

In our study, the mean hsCRP levels in the exercising group is 1.77±0.84mg/L (lower limit of moderate cardiovascular risk) and that of the non- exercising individuals is 2.66±1.51mg/L (upper limit of moderate cardiovascular risk). By prospective studies in larger populations, the change in hsCRP levels after a specified time duration of aerobic exercise training can be assessed.

CONCLUSION: We have observed low hsCRP levels in healthy young adult men, who have undergone aerobic exercise training for more than 6 months, compared to men who did not take part in any form of exercise. ↑hsCRP levels could be one of the important predictive markers, that can be used in the risk assessment of coronary artery disease. Aerobic exercise training may reduce the hsCRP levels both by reducing obesity and by its anti-inflammatory effects. Our study emphasises the importance of aerobic exercise training at a younger age, causing a reduction in circulating hsCRP levels and thereby preventing the occurrence of cardiovascular diseases in future. An awareness should be created among the public, educating them about the beneficial effects of regular physical exercise, in health care maintenance. Further long-term prospective studies could be carried out in larger populations for assessing the usefulness of hsCRP as a predictive marker of cardiovascular events.

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