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# The Effect of Aerobic Exercise and Nicotine Exposure on CRP Levels

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**Abstract:** *Objective: The aim of this study was to investigate the effect of aerobic exercise for 3 months on serum levels of CRP in low-activity smoker and non-smoker males. Materials and Methods: For this purpose, 26 adult male volunteers were chosen randomly to participate in the study in two groups: smokers (number = 13) and non-smokers (number = 13). Both research groups participated in a three-month aerobic exercise program of 3 sessions ranging from 45 to 60 minutes. Exercise intensity was considered 60 to 80 percent of the maximum heart rate during the exercise program. Independent t-test and t-correlated test were used to analyze the data. Results: findings showed that there is a significant difference between CRP levels, body weight, body mass index, and body fat percentage in adult male smokers and non-smokers. The results also indicated that 12 weeks of aerobic training and nicotine treatments improved serum CRP levels, body weight, body mass index, and body fat percentage in adult male smokers. Conclusion: The findings of the present study showed that inactive smoker males have higher levels of CRP as inflammatory cytokines in compare to non-smokers, which confirms a number of previous studies. On the other hand, the intervention of aerobic training for 12 weeks leads to a decrease in CRP in both smokers and non-smokers. However, the improvement in the smokers group is much more than the non-smokers group.*

**Keywords:** *Aerobic Exercise, Nicotine, Cigarette, CRP.*

## INTRODUCTION

Smoking cigarette is rising rapidly around the world. It is considered one of the most important factors in the prevalence of chronic diseases including diabetes and respiratory diseases such as chronic obstructive pulmonary disease (COPD) (Dilyara et al., 2007). Smoking cigarette causes heart diseases, stroke, cataracts, chronic pulmonary diseases, emphysema, as well as lung, blood, mouth, glucose, pancreas, neck and bladder cancer. In addition to systemic inflammation, smoking is also associated with inflammation of the respiratory tract (Tanni et al., 2010). Tobacco consumption is shown to cause the spread of atopic and asthmatic diseases, which is associated with hyperactivity of macrophages and dendritic cells (Arnson et al., 2010). Some recent studies have indicated a direct correlation between smoking and increased inflammatory biomarkers such as C Reactive Protein, fibrinogen, and increased white blood cell count (Virginia et al., 2011; Mendall et al., 2000). Although higher levels of CRP are reported in smokers in comparison to non-smokers, it is unclear whether nicotine of the cigarette affects the expression of CRP in macrophages. In this regard, laboratory studies on mice show that nicotine consumption leads to increased levels of protein and expression in macrophages (Mao et al., 2012). Several studies have shown that CRP levels increase in response to smoking, which is associated with the outbreak of cardiovascular diseases (Karadag et al., 2008; Groenewegen et al., 2008). As mentioned by

a number of studies, CRP levels remain at high levels even 10 to 20 years after quitting (Dilyara et al., 2007). Most studies have reported that the increase in the levels of inflammatory markers such as CRP is the effective factor in reducing adiponectin in smokers (Ikonomidis et al., 2005; Miller et al., 2003). Scientific resources have supported the role of sports activity as an effective factor in preventing or reducing the severity of inflammation in healthy or sick populations. However, a number of studies have also indicated that exercise does not have any effects on these variables.

Despite the numerous studies indicating the impact of different types of exercise programs with different methods on the systemic levels of inflammatory and anti-inflammatory mediators in healthy and sick populations, the findings of smokers are limited (Hammett et al., 2006). For example, results indicate that a long-term aerobic training course did not lead to a significant change in CRP in smokers (Behboudi et al., 2014). While other studies reported a significant reduction in CRP following a long-term exercise (Jorge et al., 2011). In another study, 12 weeks of aerobic exercise program was conducted on smoking women. Despite the improvement in their athletic performance, there were no significant changes in the levels of inflammatory indices such as CRP and white blood cell count (Hammett et al., 2006). Regarding the lack of information on the effect of different exercise methods on CRP levels, the aim of this study was to investigate the effect of 3 months of aerobic exercise on serum CRP levels in low-activity male smokers and non-smokers.

## Materials and Methods

This quasi-experimental study was conducted in the laboratory on the adult smoker and non-smoker males in the city of Islamshahr. For this purpose, 26 adult males were randomly volunteered into two groups: smokers (n = 13) and non-smokers (n = 13). The subjects were non-athletes, did not attend any regular exercise program at least during the past year, and had no history of chronic diseases such as cardiovascular disease, diabetes, any types of cancers, and kidney and digestive disorders. After being informed about the study objectives, all subjects completed the consent form for participation in the study. Those people who consumed at least 10 cigarettes a day in the last 5 years ago were considered as smokers (Ghoddousi et al., 2006).

Aerobic exercises were performed in 3 sessions of 45 to 60 minutes for three months. Both groups of smokers and non-smokers participated in the training sessions. Training sessions included warming up and running on a plain surface (main training), then aerobic group exercise activities and eventually cooling off. Training sessions started with 5 to 10 minutes of warming up. The intensity and duration of the training increased gradually within the training sessions. So that the first sessions were held with the least intensity, and gradually it was added to the intensity and volume of the training. The target heart rate and the intensity of the workout were measured and recorded by Pollard's pulse rate. Exercise intensity during the exercise program was considered 60 to 80 percent of the maximum heart rate. The maximum heart rate was determined using the formula (age - 220) for each person. The distribution of exercise intensity during running activity in the training program is represented in Table 1.

**Table 1**: Distribution of exercise intensity during running activity

| Training period | Exercise intensity (%HRmax) | Time in each training session | Inactive rest between sets |
|---|---|---|---|
| first week | Intensity≤60% | Three sets of 5 minutes | 3 minutes |
| second week | 60%≤ Intensity ≤ 65% | Three sets of 6 minutes | 3 minutes |
| third week | 65%≤ Intensity ≤ 70% | Three sets of 8 minutes | 3 minutes |
| forth week | 65%≤ Intensity ≤ 70% | Two sets of 12 minutes | 5 minutes |
| Fifth week | 65%≤ Intensity ≤ 70% | Two sets of 14 minutes | 5 minutes |
| Sixth week | 70%≤ Intensity ≤ 75% | Two sets of 16 minutes | 5 minutes |
| Seventh and eighth weeks | 70%≤ Intensity ≤ 75% | Two sets of 18 minutes | 5 minutes |
| ninth, tenth, eleventh and twelfth Weeks | 75%≤ Intensity ≤ 80% | Two sets of 20 minutes | 5 minutes |

Blood samples were taken in both pre-test and 48 hours after the last exercise session (post-test) to measure serum CRP in all subjects. After 10 to 12 hours of fasting, all subjects admitted to the laboratory between 7:00 and 8:00 AM, and after 10 minutes of rest, blood samples were taken from the cephalic vein (5 cc). All subjects were advised to stop performing any heavy physical activity 48 hours before blood sampling. Samples were centrifuged immediately to isolate the serum and were frozen at the temperature of 80 ° C until measuring. The serum CRP was measured using the Eliza method by commercially available human CRP kit (High Sensitivity C-Reactive Protein (Hs-CRP) kit , Diagnostics Biochem Inc., Canada). Internal and external coefficient of in-test, and sensitivity of serum CRP measurement were 15.2, 9.9 and 10 ng / ml, respectively. Anthropometric indices including height, weight, BMI and body fat percentage were measured before and after the training program in both groups.
Statistical comparisons were performed in SPSS software version 16. The Kolmogorov-Smirnov test was used to ensure the normal distribution of the data. Independent t-test was used to compare the intra-group, and t-test was used for determining the level of intra-group changes level.

## Results

The results of the normal distribution of data using the Kolmogorov-Smirnov test for each of the dependent variables are summarized in Table 2.

**Table 2:** The results of normal distribution of data using Kolmogorov-Smirnov test

| Training period | Exercise intensity (%HRmax) | K-S | p-value |
|---|---|---|---|
| Weight (kg) | Smokers | 0.518 | 0.952 |
| | non-smokers | 0.745 | 0.636 |
| BMI (Kg/m$^2$) | Smokers | 0.558 | 0.880 |
| | non-smokers | 0.425 | 0.994 |
| Body fat percentage | Smokers | 0.567 | 0.904 |
| | non-smokers | 0.597 | 0.869 |
| CRP (ng/ml) | Smokers | 0.767 | 0.599 |
| | non-smokers | 0.594 | 0.872 |

The mean and standard deviation of anthropometric indices in pre-test stage between the two groups are presented. Based on findings from independent t-test, there was no significant difference in the anthropometric indices between the two groups of smokers and non-smokers in pre-test stage ($p>0.05$) (Table 3).

**Table 3:** Mean and standard deviation of anthropometric indices in pre-test stage between the two groups

| Variable | smokers group | Non-smokers group | p-value |
|---|---|---|---|
| Age (year) | 42 ± 2.61 | 41.9 ± 2.48 | 0.978 |
| Height (cm) | 175 ± 2.52 | 174.1 ± 3.33 | 0.433 |
| Weight(kg) | 94.7 ± 3.93 | 94.6 ± 5.37 | .751 |
| Body fat percentage | 31.01 ± 1.56 | 30.76 ± 1.5 | .732 |
| BMI (Kg/m2) | 30.93 ± 1.67 | 31.09 ± 1.71 | .810 |

In addition, to determine the significance level of intra-group changes in each anthropometric index between pre-test and post-test stages in each group, t-test was used, which is shown in Table 4. The findings showed that levels of body weight, body mass index and body fat percentage were significantly different between the two pre-test and post-test groups in both smoker and non-smoker groups (Table 4). In other words, 12 weeks of aerobic training was associated with a significant decrease in each of these indices in both groups ($p <0.05$).

**Table 4:** Mean and standard deviation of anthropometric indices in the pre-test and post-test stages

| Variable | smokers group | | | Non-smokers group | | |
|---|---|---|---|---|---|---|
| | pre-test | post-test | p-value | pre-test | post-test | p-value |
| Weight (kg) | 94.7 ± 3.93 | 90 ± 3.68 | ≤0.001 | 94.6 ± 5.37 | 90.85 ± 5.61 | ≤0.001 |
| Body fat percentage | 31.01 ± 1.56 | 28.37 ± 1.39 | ≤0.001 | 30.76 ± 1.5 | 29.13 ± 1.58 | ≤0.001 |
| BMI ($Kg/m^2$) | 30.93 ± 1.67 | 29.4 ± 1.59 | ≤0.001 | 31.09 ± 1.71 | 30.05 ± 1.65 | ≤0.001 |

The results of the t-correlated test showed a significant difference in serum CRP levels between pre-test and post-test stages in both smoker and non-smoker groups (Table 5). In other words, 12 weeks of aerobic training resulted in a significant decrease in serum CRP in both smokers (p = 0.000) and non-smokers (p = 0.000). On the other hand, although aerobic exercise led to a significant reduction in serum CRP in both groups. when the CRP delta (pre-test and post-test difference) was compared between the two groups by independent t-test, a significant difference was seen in the delta CRP between the two groups, which refers to the greater effect of aerobic exercise on CRP in the smokers group. In other words, the amount of reduction in CRP in the smokers group was far more than the non-smokers group (Table 5).

**Table 5:** Results of intra-group and between-group serum CRP analysis in the study groups

| Variable | group | stage | Mean ± standard deviation | intra-group | Between groups | |
|---|---|---|---|---|---|---|
| CRP (ng/ml) | smokers | pre-test | 4576 ± 1312 | 0.001 | -3.022 | 0.006 |
| | | post-test | 3014 ± 1282 | | | |
| | Non-smokers | pre-test | 3142 ± 792 | ≤0.001 | | |
| | | post-test | 2724 ± 660 | | | |

## Discussion

One of the findings of the research is that there is a significant difference in CRP between adult smoker and non-smoker males. The findings of this study showed that smokers have higher levels of CRP than non-smokers. Along with the findings of this study, some other studies supported the increase in CRP levels as an inflammatory marker in smokers (Panagiotakos et al., 2004; Das, 1985, Danesh et al., 2000). Cigarette smoking increases the binding of carbon monoxide to hemoglobin in red blood cells, which results in a reduction in the circulation of oxygen through red blood cells (Wasserman, 1973). The consequence of the harmful effects of nicotine, nitrogen oxides, and other oxidants caused by smoking on tissues of the body, especially the central nervous system, is the inflammation of the respiratory tract (Valença et al., 2009). Inflammatory markers such as CRP and TNF-a play a major role in regulating inflammatory responses. Although the structure of CRP is distinct from immunoglobulins, it contributes to immunoglobulins in many biological activities. For example, CRP contributes to the production of increasing inflammatory cytokines (Du Clos et al., 2000). Therefore, it is measured as a determinant of inflammation and tissue necrosis (Merghani et al., 2012). It has been shown that male smokers who are continuously taking tobacco or cigarettes have higher levels of CRP than non-smokers, which suggests an increase in inflammatory processes in these individuals (Merghani et al., 2012). On the other hand, consistent to the findings of this study, some previous studies reported an insignificant increase in plasma CRP in smokers than non-smokers (Boshtam et al., 2006). It is unclear whether these contradictory results are due to differences in genetic factors, environments, changes associated with half-life of CRP (Merghani et al., 2012) or they are due to other intervening factors. Other research finding shows that 12 weeks of aerobic exercise and nicotine consumption alter the serum levels of CRP in adult male smokers. So far, several studies

are conducted to determine the effect of different training methods on the levels of inflammatory mediators in healthy or sick people. In this regard, the findings of this study showed that 12 weeks of aerobic training leads to a significant reduction of CRP as an inflammatory cytokine in smokers. It should be noted that the studied subjects had a passive lifestyle in before participating the study. Significant decrease of CRP was observed in the smoker group while aerobic exercise was associated with a significant decrease in CRP in the non-smoker group. In other words, independent from the type of studied population regarding smokers or non-smokers, an aerobic training period for 12 weeks leads to a decrease in serum CRP in inactive patients. Regardless of smoking cigarettes or not, several studies have pointed to the pharmacological effects of sports exercises with an emphasis on the reduction of inflammatory cytokines. These effects include a reduction in serum CRP levels. For example, during two studies, 24 exercise programs in form of fast walking for 5 sessions per week (Di Raimondo et al., 2013), and 3 and 6 months of aerobic and severe resistance exercise (Stavropoulos et al., 2013) led to a significant reduction in serum CRP levels and risk factors of fat profile in MS patients and patients with rheumatoid arthritis, respectively. However, another study included three months of long-term exercise, and it did not show any changes in inflammatory markers such as CRP in chronic heart disease patients (Ahmad et al., 2014). Another study was based on six months of aerobic exercise, which did not show any significant changes in levels of inflammatory markers such as CRP, IL-6 and TNF-α in obese or overweight postmenopausal women (Cavagnolli et al., 2014). As a conclusion, the response or adaptation of CRP to the training methods seems to be somehow contradictory. This contradiction can be attributed to the type of exercise program in terms of severity, duration and repetition of training sessions, as well as the type of studied population and other unknown factors. On the other hand, although aerobic exercise was associated with a decrease in the levels of CRP in both smokers and non-smokers in the present study, the level of improvement in the smoker group was more than the non-smoker group based on statistical tests comparing the delta (pre-test and post-test difference) between the two groups. Consistent with most of the previous studies (Danesh et al., 2000; Wasserman, 1973; Valença et al., 2009), the findings of the present study showed that smokers had higher CRP levels in compare to non-smokers at the beginning of the study. On the other hand, the effect of training intervention shows the pharmacological effects of aerobic exercises, regardless of smoking or non-smoking. These higher levels of improvement in inflammatory profile in smoking males (in response to aerobic exercise even in the presence of continued smoking (nicotine consumption)) may be attributed to the disruption of the levels of these cytokines at the beginning of the study. In other words, smoking males had higher levels of CRP compared to the smoker group at the beginning of the study. This imbalance can be attributed to other hormone or metabolic components in response to smoke cigarettes (Ikonomidis et al., 2005; Miller et al., 2003). In general, it can be concluded that consistent with the findings of some previous studies, the results of the present study indicate that inactive smokers have higher levels of CRP as inflammatory cytokines in comparison to non-smokers. On the other hand, although the intervention of aerobic training for 12 weeks reduces CRP in both smoker and non-smoker groups, the improvement in the smoker group is far more than the non-smoker group. This improvement can be attributed to the inflammatory profile disorder in smokers at the beginning of the study, which more reflects the response to aerobic training in these individuals in comparison to non-smokers.

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