EFFECT OF SMOKING ON INTERLEUKIN-6 AND CORRELATION BETWEEN IL-6 AND SERUM AMYLOID A-LOW DENSITY LIPOPROTEIN IN SMOKERS

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ABSTRACT

Objective: To investigate the effect of smoking on interleukin-6 and to find the correlation between serum amyloid A-low density lipoprotein (SAA-LDL) and IL-6 in smokers.

Methodology: The study was a randomized control trial, carried out in Army Medical College, Rawalpindi, from June 2014 to February 2015. Three hundred healthy males participated in the study and were divided into two groups. Group-I included non-smokers while group-II were smokers. Levels of SAA-LDL and IL-6 were determined using ELISA kit. Data were analyzed using t-test. Pearson correlation was used to find correlation between SAA-LDL and IL-6.

Results: IL-6 levels were high in the smokers than in non-smokers. The mean of IL-6 levels of group I and group II was 40.03 ±8.06 and 50.43 ±19.67 respectively. The difference was statistically significant ($p < 0.05$). Moderate positive association was found between SAA-LDL and IL-6 in smokers ($r = 0.651$, $n = 150$, $p < .05$).

Conclusion: Positive association was found between smoking and IL-6. Statistically significant moderate positive association between SAA-LDL and IL-6 in smokers shows that changes in one are associated with changes in other and vice versa.

Key Words: Cigarette smoking, Interleukin-6, Serum amyloid A-low density lipoprotein

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INTRODUCTION

Cigarette smoking is known for its deleterious effect on many systems and organs[1]. Smoking could lead to smoking-related medical conditions, increased risk of premature death and huge economic burden[2]; therefore there is a need to assess its toxicity.

Cigarette smoke (CS) not only contains reactive oxidants (ROS), but also elicits a marked activation of leukocytes which can contribute to the oxidative damage[3]. ROS are usually produced during aerobic metabolism. They cause cellular damage on lipid, protein, carbohydrate and nucleic acid molecules but are detoxified by the antioxidants present in the cells. ROS when produced in excess lead to oxidative stress. Oxidative stress is linked to inflammation, as it activates the nuclear factor kappa-beta signaling pathway to synthesize pro-inflammatory cytokines which promote inflammation[4].

Serum amyloid A-low density lipoprotein (SAA-LDL), an oxidative stress marker, is formed by oxidative modification of LDL[5]. Interleukin-6 (IL-6) is a multi-functional cytokine that participates in both physiological and pathological processes[6].

The study was designed to investigate the effect of smoking on IL-6, an inflammatory marker, and to determine the correlation between SAA-LDL and IL-6 in smokers. This will be of benefit to the health profession as SAA-LDL and IL-6 may be used as biomarkers for early diagnosis of smoke related disorders.

METHODOLOGY

The study was a randomized control trial, conducted at Army Medical College, Rawalpindi. The study was ap-

proved by Ethical Committee of Army Medical College. The study population consisted of 300 males; aged between 25 and 40 years. Participants were divided into two groups. Group I were non-smokers (n=150) and group II were smokers (n=150). Study participants were healthy with no past history of any known metabolic, cardiovascular or pulmonary disease. They also had no history of any drug or alcohol abuse. The non-smoker participants were classified as never smokers and smokers were current active smokers.

About 6-7 ml blood sample was collected from all study participants. Blood was taken in vacuum tubes containing clot activator. Serum obtained by centrifugation was stored at -80°C. SAA-LDL and IL-6 levels were determined using commercially available ELISA kits at CREAM, Army Medical College.

Study variables (SAA-LDL and IL-6) were analysed by SPSS version 17. The arithmetic mean and standard deviation of all observations were calculated. Pearson correlation test was used to find correlation between SAA-LDL and IL-6. Significant p value was <0.05.

RESULTS

The comparison of mean of IL-6 levels between two groups at the end of 12 weeks is shown in table 1. The mean IL-6 level was significantly increased in smokers than in non-smokers.

The correlation between mean of SAA-LDL and IL-6 levels in smokers is shown in table 2. There was a moderate positive correlation between SAA-LDL and IL-6 (r =.651, n=150, p <0.05).

DISCUSSION

Smoking is a risk factor of many diseases and contributes to the economic burden worldwide. Cigarette smoking kills more than 5 million people worldwide each year[7]. There is a need to assess its toxicity; however, toxic mechanisms underlying smoke related diseases are not yet completely understood.

IL-6 has long been considered a general marker of inflammation together with TNF-α and IL-1β, two other classical inflammatory cytokines as levels of IL-6 in serum have been found to be raised in a number of inflammatory diseases[8].

Oxidative stress and inflammation together form a vicious cycle that is responsible for the disease progression. Except few studies, most of the studies showed positive association between smoking and IL-6. Results of our study also showed that smokers have increased levels of IL-6 than that of non-smokers (p <0.05).

Wu et al[9] showed in his study that peripheral blood mononuclear cells of COPD mice produced more IL-6 and IL-8 stimulated by cigarette smoke extract. Cesar-Neto et al[10] showed that the levels of IL-6 were higher in smokers with periodontitis compared with controls (p<0.001). Herfs et[11] al showed in his study that smokers have higher expression of IL-6 in the respiratory epithelium as compared with the non-smokers. Arnson et al[12] also had similar results that smoking increases the production of IL-6. IL-6 levels were higher in smokers compared with non-smokers in a study by Moretti et al[13] and Helmersson[14] et al (p =0.01).

SAA-LDL is an oxidative stress marker used in this study. Few studies reported positive relationship between cigarette smoking and SAA-LDL. Wada et al[15] also showed association between serum levels of SAA-LDL and smoking as levels were significantly raised in smokers versus non-smokers. Kotani et al[16] documented, for the first time, in his study that serum SAA-LDL levels correlate positively with components metabolic syndrome. Another study published in 2009 showed positive correlation between SAA-LDL complex and serum triglyceride levels[17].

To the best of our knowledge, correlation between SAA-LDL and IL-6 in smokers has not yet been determined. In this study, we found a moderate positive correlation between SAA-LDL and IL-6 in smokers that is statistically significant (p <0.05). Our results tend to suggest that oxidative stress observed in smokers could be closely linked to inflammation. Further research will be needed to explore the mechanisms involved.

Table 1: Mean of IL-6 levels in group I and II

Mean ± SD values of both groups			
Variable	**Group I (n =150)**	**Group II (n =150)**	**P Value**
IL-6	40.03 ±8.06	50.43 ±19.67	<0.05

Table 2: Results of correlation between IL-6 and SAA-LDL in smokers

Variables	Mean ± SD	P Value	*r Value
IL-6	45.16 ±15.83	<0.05	0.651
SAA-LDL	2.94 ±0.66		

* r value is correlation coefficient or Pearson r

CONCLUSION

IL-6 and SAA-LDL are correlated in smokers as shown by the statistically significant moderate positive association found between IL-6 and SAA-LDL which indicates that changes in one variable are associated with the changes in other. Thus IL-6 and SAA-LDL may be involved in the pathophysiology of smoking related disorders.

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CONTRIBUTORS

AJ conceived the idea, planned the study, and drafted the manuscript. AR and AKN helped acquisition of data and did statistical analysis. MA critically revised the manuscript. All authors contributed significantly to the submitted manuscript.