ORIGINAL ARTICLE

Effect of Chronic Cigarette Smoking on Plasma Fibrinogen and Haematocrit

ABDULLAH ABBASSI[1], HABIBULLAH QURESHI[2], SEEMEEN GHAFOOR[3], *SHAHEENA[4], ABDUL WAHAB SHAIKH[5]*

ABSTRACT

Aim: To observe the effects of chronic cigarette smoking on plasma fibrinogen levels and heamatocrit, along with hemoglobin, total leukocyte count and erythrocyte counts.

Methods: A total of 102, apparently healthy subjects, of the age ranging from 25-35 years were included in the study. 72 smokers (36 heavy and 36 moderate smokers) and 30 non smokers with similar dietary habits and socioeconomic conditions were investigated for the above mentioned parameters.

Results: All the parameters were significantly increased ($p< 0.0001$) in smokers as compared to non-smokers. Significant rise was also seen in values of all parameters of heavy smokers when compared to moderate smokers, plasma fibrinogen $p= <0.05$; haematocrit and haemoglobin $p =<0.001$. total erythrocyte and total leucocytes $p = <0.001$.

Conclusion: Cigarette smoking has deleterious effects on the properties of blood flow by raising plasma viscosity more in heavy smokers than moderate smokers.

Keywords: Cigarette smoking, fibrinogen, haematocrit, ischemic heart disease.

INTRODUCTION

Cigarette smoking is one of the largest causes of preventable death worldwide. It is the leading cause of coronary artery disease (CAD), 2-4 times higher in smokers than in non smokers. Cigarette smoking and other forms of tobacco consumption kill four million people per year, with the majority of these deaths already occurring in developing countries[1]. National Health Survey of Pakistan indicates that smoking is a major problem in Pakistan. Smoking is more common in males than females. It has been estimated that 54% of men and 20% of women use some form of tobacco on regular basis[2].

Smoking has been reported to exert a significant effect on almost all the hematological parameters including heamatocrit, plasma fibrinogen, hemoglobin, red blood cell (RBC) count and white blood cell (WBC) count[3]. Cigarette smoking has several deleterious effects on the properties of blood flow and these are quickly reversible or partly so, once smoking has been stopped. Hemoglobin, heamatocrit and fibrinogen along with carboxyhemoglobin and plasma viscosity are raised by smoking, and cardiac output is decreased with raised heamatocrit. Smoking is the strongest known determinant of fibrinogen levels in healthy persons. This relationship is dose dependant and reversible after smoking cessation[4,5].

The study of Harrison et al, has suggested that a high heamatocrit may be associated with the risk of carotid thrombosis. High heamatocrit and fibrinogen have been observed in these patients and higher they are worse is the prognosis[6]. Smoking is strongly related to plasma fibrinogen concentration. Smoking is the strongest known determinant of fibrinogen levels in healthy persons. This relationship is dose dependant and reversible after smoking cessation[4,5]. Elevated plasma fibrinogen concentrations are reported in smokers as compared to nonsmokers, and implicated as risk factor for stroke and myocardial infarction[9,10,11].

The association between smoking and high leukocyte and erythrocyte count has been demonstrated in many studies[12,13]. Heamatological variables deteriorate in parallel with a rise in cigarette consumption, highest in current smokers, particularly with high consumption of cigarettes and lowest in never smokers[14,15]. Leukocytes play a major role in inflammatory processes. The circulating WBC count has been proposed as one of a few biomarkers of potential current utility for cardiovascular risk prediction[7]. Although a role as a biomarker of cardiovascular risk has been suggested for total WBC, the relative ability of specific WBC subtypes to

[1]*Associate Professor Physiology, Liaquat University of Health Sciences Jamshoro.*
[2]*Professor and Head of Biochemistry Department, Shaheed Mohtarma Benazir Bhutto Medical College, Karachi.*
[3]*Associate Professor Biochemistry Department, Yusra Medical and Dental College Islamabad*
[4]*Assistant professor Biochemistry, Shaheed Mohtarma Benazir Bhutto Medical College, Karachi.*
[5]*Assistant Professor Department of Physiology Chandka Medical College SMBBMU, Larkana*
Correspondence to Dr. Habibullah Qureshi. Tele:03332659725

predict cardiovascular risk in asymptomatic individuals remain largely unexamined[18]. Early detection of atherosclerosis may help to prevent complications of the disease or slow its progress, which is difficult to predict by standard risk factors alone[8]. Systemic inflammation involving activated polymorphonuclear neutrophils is clearly associated with unstable condition of coronary artery disease and an increased number of circulating neutrophils is a well known risk indicator of future cardiovascular outcomes[29]. The neutrophil/lymphocyte ratio has recently been described as a predictor of mortality due to cardiovascular diseases[28,30].

MATERIAL AND METHODS

This study was carried out in the department of Physiology, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi. A total of 102(72 smokers, with a smoking history of not less than 10 years, and 30 non smokers) apparently healthy, male subjects of age ranging between 25 -35 years, were randomly selected from the general population of Karachi.

Subjects were grouped as smokers: test group (72 further sub grouped according to number of cigarettes smoked per day,

Moderate smokers (36) smoking > 20 cigarettes per day Heavy smokers (36) smoking <20 cigarettes per day

Exclusion criteria: Subjects excluded from the study were those suffering from any acute or chronic diseases like, respiratory diseases, gastrointestinal and liver diseases, ischemic heart diseases, endocrine diseases, hypertension, anemia and had history of blood donation or blood loss from the body in last six months.

Haematocrit values were estimated by microhaematocrit method on microheamatocrit machine (Harmle, Germany). Quantitative determination of plasma fibrinogen level was done the clotting method using kit, Cat. No. 00609 supplied by Diagnostic Stago, France. Blood hemoglobin level was estimated by Cayanmet hemoglobin method by using kit, Cat.No.950051, supplied by Labsystems Pakistan (Pvt) Ltd. Counting of white blood cells was done by counting chamber method. Counting of red blood cells was done by counting chamber method.

RESULTS

A total of 102 apparently healthy male subjects of age ranging between 25-35 years, with similar dietary habits and socio-economic conditions were recruited into the study. Subjects were grouped according to the smoking habits into non-smokers (n=30) and smokers (n=72). Smokers were further subdivided depending upon number of cigarettes smoked per day as moderate smokers (n=36) and heavy smokers (n=36). The results are given in tables I to III.

Table I shows comparisons of mean (±SEM) of age, body mass index (BMI), pulse rate, systolic blood pressure, and diastolic blood pressure in non-smokers (Control) and smokers. No significant differences were found in these parameters when smokers compared to non-smokers.,

Table II represents comparative analysis of plasma fibrinogen, haematocrit, WBC count, RBC count and hemoglobin levels in non- smokers (Control) and smokers. The mean (±SEM) levels of plasma fibrinogen, haematocrit, WBC count, RBC count and hemoglobin levels were found significantly ($P < 0.001$) high in smokers as compared to control.

Table I: Physical parameters and anthropometric measurements of control and smokers

Parameters	**Controls (n=30)**	**Smokers (n=72)**
Age (Years)	29.90 ± 0.55	29.97 ± 0.32
BMI (Kg/m²)	22.08 ± 0.20	21.88 ± 0.11
Pulse Rate (per minute)	71.87 ± 0.39	71.92 ± 0.23
Systolic BP (mmHg)	117.60 ± 0.76	117.06±0.71
Diastolic BP(mmHg)	77.07 ± 0.80	76.19 ± 0.61

Values are given as mean ± SEM.
All the values are non significant as compared to control.

Table II: Plasma fibrinogen, hematocrit, WBC count, RBC count and haemoglobin in controls and smokers

Parameters	**Controls (n = 30)**	**Smokers (n = 72)**
Plasma Fibrinogen (mg/dL)	263.7±8.65	353.72±7.84*
Haematocrit (%age)	42.10±0.24	47.79± 0.22*
WBC Count (thousands/mm□)	6.98±0.15	8.37 0.09*
RBC Count (millions/mm□)	5.06±0.03	5.21±0.02
Haemoglobin (g/dL)	14.53± 0.12	16.07±0.10

Values are given as mean ± SEM.
P < 0.001 as compared to control

Table III represents the comparative analysis of various hematological parameters in non-smokers (control), moderate smokers and heavy smokers. The mean (±SEM) values of plasma fibrinogen, heamatocrit, WBC count, RBC count and hemoglobin level were found highest in heavy smokers, lowest in non-smokers (control) and moderate smokers had intermediate values. The differences were highly significant (P< 0,001) for heamatocrit, WBC and hemoglobin, when different groups were compared to each other. RBC count showed significant change when moderate smokers group was compared with control group (P<0.05) and heavy smokers group (P<0.01). However, highly significant difference

(P<0.001) was observed when control group was compared with heavy smokers group.

The differences in plasma fibrinogen levels were found significant (P<0.05), when moderate smokers group was compared with heavy smokers group but highly significant differences were noted when control group was compared with moderate smokers and heavy smokers (P<0.001).

Table III: Plasma fibrinogen, hematocrit, WBC count, RBC count and haemoglobin in controls, moderate smokers and heavy smokers

Parameters	Controls (n = 30)	Moderate smokers (n = 36)	Heavy smokers (n = 36)
Plasma Fibrinogen (mg/dL)	263.7 ± 8.65	336.58 ±9.79**	370.86 ±11.69†§
Haematocrit (%age)	42.10 ± 0.24	46.44 ±0.26**	49.14±0.15†§§§
WBC Count (thousands/mm□)	6.98 ± 0.15	7.79 ±0.09**	8.95±0.09†§§
RBC Count (millions/mm□)	5.06 ± 0.03	5.161 ±0.03*	5.266±0.01†§§
Haemoglobin (g/dL)	14.53 ± 0.12	15.51 ±0.12**	16.63±0.10†§§§

*P < 0.05 * P < 0.001 as compared to control P < 0.0001 as compared to controls*
P < 0.05, §§ P < .01, §§§ P < 0.001 when heavy smokers compared with non smokers

DISCUSSION

Long- term smoking is associated with an increased risk of cardiovascular diseases, several cancers and many chronic inflammatory diseases[16]. Cigarette smoke contains a large number of toxic chemicals that cause oxidant-antioxidant imbalance including oxidative stress[17] and produce unfavorable changes in various hematological parameters[3].

This study was designed to assess the effects of chronic cigarette smoking on various hematological parameters (plasma fibrinogen, hematocrit, WBC count, RBC count and hemoglobin).

Raised fibrinogen in smokers reported here are in agreement with Wilhelmsen *et al.*[9], Galea and Davidson[4] and Rigotti and Pasternak[11]. In another study carried out by D.O. Gordan *et al.* fibrin D-dimer (a marker of fibrin turnover) was found to be associated with a stronger predictor of coronary risk than inflammatory markers, perhaps due to its ability to stimulate monocyte release of interleukin-6 (a cytokine in the process of inflammation[27]. Fibrinogen also showed a dose dependent relationship with smoking. This finding is compatible with previous workers[25,13,10].

In the present study a significant positive relationship was observed between heamatocrit and smoking. This favors the studies of many authors[4,12,15,18,]. The increase in heamatocrit concentration with the increase in number of cigarettes was also observed in the present study. This finding is compatible with previous workers[13,19].

The effect of smoking on leukocytes has been studied by many workers[12,13,15,21] and the results of all of these studies are consistent with results of our study. All are agreed on the fact that smoking significantly increases the number of leukocytes. This response is closely related with the number of cigarettes smoked per day. The mechanism by which smoking may increase WBC count are unknown. One of the postulates is that nicotine induces release of catecholamines that can raise the WBC count. Another is that there is an irritant effect of cigarette smoke on the respiratory tree with resultant inflammation[23]. It is reported that WBC count increases during infection and inflammatory illnesses and has been shown to predict coronary heart diseases, independent of traditional cardiovascular risk factors[26]. Some studies found that leukocyte count is associated with aortic arch plaque thickness, progress of aortic atheroma in patients with stroke or increased risk of stroke and vascular death in patients with systemic intracranial atherosclerotic disease[31].

Findings of the present work showed marked effect of smoking on RBC count as the smokers had higher number of RBCs when compared to non-smokers. Similar results were reported by Helmen and Rubenstein[12]. The possible explanation for elevated hemoglobin, heamatocrit and RBC count in the blood is that the change is possibly due to carbon monoxide (CO), another toxic substance present in the cigarette smoke. Carbon monoxide reacts with hemoglobin forming carboxyhemoglobin, which interferes with the oxygen transport and utilization leading to hypoxyia[20]. Carbon monoxide induced hypoxia produces a demand for more erythrocytes. This may lead to increased levels of hemoglobin, heamatocrit and erythrocyte count.

Hemoglobin level was found elevated in smokers and the response was dependent on the number of cigarettes smoked per day. Similar observations were documented by other investigators.

The results showed significantly higher values of plasma fibrinogen, heamatocrit, WBC count, RBC count and hemoglobin in smokers. It is concluded that there may be a positive association between the increased levels of these hematological parameters and the number of cigarettes smoked per day. A

larger scale study is desired to establish a reference range in our population.

REFERENCES

1. Taylor AL. and Bettcher DW. (2000). WHO framework convention on tobacco control; a global good for public health. Bulletin of the WHO , 78(7):920-929.
2. National Health Survey of Pakistan (1990-1994): Health profile of the people of Pakistan. Initial report (1998).
3. McGill HC. (1988). The cardiovascular pathology. Am Heart J, 115:250-257.
4. Galea G and Davidson (1985). Hematological and hemorrhological changes associated with cigarette smoking. J Clin Pathol, 38:978-984.
5. Papazafiropoulou A, Katsilambros N. (2008). Novel risk factors for atherosclerosis. The Open Biomarkers J, 1: 36-47.
6. Harrison MJG, Kendal IBE, Pollock S, Marshal IJ. (1981). Effects of heamatocrit on carotid stenosis and cerebral infarct. Lancet, ii:114-115.
7. Home BD, Anderson JL *et al* . (2005). Which white bloob cell subtypes predict increased cardiovascular risk. J Am Coll Cardiol,, 45(10): 1638-1643.
8. Feng Cheng, Keeley EC. (2012). Molecular prediction for atherogenic risks across different cell types of leukocytes. BMC Medical Genomics, 5:2. http// www.biomedcentral.com/1755-8794/5/2.
9. Wilhelmsen L, Svardudd K, Bengsten KK, Larrson B, Welin L, Tibblin G. (1984). Fibrinogen as a risk factor for stroke and myocardial infarction. N Eng J Med, 311:501-505.
10. Tauheed S, Shoaib S and Naeemul Haq. (1999). Plasma fibrinogen a coronary risk factor. J CPSP Vol. 9(2): 91-93.
11. Rigotti NA and Pasternak RC. (1996). Cigarette smoking and coronary heart disease: risks and management. Cardiol Clin, 14(1):51-68.
12. Helman N and Rubenstien LS. (1975). The effects of age, sex and smoking on erythrocytes and leukocytes. Am J Clin Pathol, 63:35-44.
13. Ernest E, Matria A, Schmolz CH, Magyarosy I. (1987). Dose effect relationship between smoking and blood reheology . Br J Heamatol, 65: 485-487.
14. Sparrow D, Glynn RJ, Cohen M, Wiss ST. (1984). The relationship of the peripheral leukocyte count and cigarette smoking to pulmonary function among adult men. Chest, 86:383-386.
15. Kawada T. (2004). Smoking –induced leukocytosis can persist after cessation of smoking. Archives of Med Research, 35(3):246-250.
16. Doll R, Peto R, Wheatley K, Gray R, Sutherland I. (1994). Mortality in relation to smoking: 40 years observation on male British doctors. Br Med J, 309:901-911.
17. MacNee W. (2000). Oxidants/antioxidants and COPD. Chest, 117:303S-317S.
18. Waterhouse DF, Cahill RA. (2008). Prediction of calculated future cardiovascular disease by monocyte count in an asymptomatic population. Vascular Health and Management, 4(1):177-187.
19. Buhler FR, Vesanan K, Watters JT, Boilli P. (1988). Impact of smoking on heart attacks, strokes, blood pressure control, drug dose and quality of life aspects in the international perspective. Primary Prevention Study in Hypertension. Am H J, 115:282-287.
20. Benowitz NL and Gourlay SG. (1977). Cardiovascular toxicity of nicotine: implications for nicotine replacement therapy. J Am Coll Cardiol,29:1422-1431.
21. Yeung MC and Buncio A. (1984). Leukocyte count, smoking and lung function, Am J Med, 76:31-37.
22. Sunyer J, Munoz A, Peng Y, Margolick J, Chmiel JS, Oishi J, Kingsley L, Samet JM. (1996). Longitudnal relation between smoking and white blood cells. Am J Epidemiol, 144(8):734- 741.
23. Tell GS, Grimm RH, Vellar OD, Theodorsan L. (1985). The relationship of white blood cell count, platelet count and heamatocrit to cigarette smoking in adolescents: The Oslo Youth Study. Circulation, 72:971-974.
24. Morrison D, Rahman I and Lannan SI. (1999). Epithelial permeability , inflammation and oxidant stress in the air spaces of smokers. Am J Respir Crit Care Med, 159:473-479.
25. Kannel WB, D'Agostino RB and Belanger AJ. (1987). Fibrinogen, cigarette smoking and risk of cardiovascular disease: insights from the Framingham Study. Am H J, 113:1006-1010.
26. Haim M, Boyci V *et al*. (2004).Predictive value of elevated white blood cell count in patients with preexisting coronary heart disease. Arch Intern Med, 164:433-439.
27. Lowe GDO, Rumley A *et al*. (2004). Interleukin-6, fibrin D-dimer, and coagulation factors VII and XIIa in prediction of coronary heart disease. Arterioscl throm vas, 24:1529.
28. Tamhane UU, Aneja S and Montgomery D. (2008). Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. Am J Cardiol,102(6):653-57.
29. Baetta R, Corsini A. (2010). Role of polymorphonuclear neutrophils in atherosclerosis: Current state and future perspectives. Atherosclerosis, 210(1):1-13.
30. Demirkol S, Balta S, Unlu M, Arslan Z, Cakar M, Kucuk U, Celik T, Arslan E, Turker T, Lyisoy A, Yokusoglu M. Neutrophils/Lymphocytes Ratio in Patients With Cardiac Syndrome X and Its Association With Carotid Intima-Media Thickness. Clin Appl Thromb Hemost. 2012 Nov 26. [Epub ahead of print].
31. Wu T, Chien K *et al* .(2013).Total white blood cell count or neutrophil count predict ischemic stroke events among adult Taiwanese: report from a community-based cohort study. BMC Neurology 13:7. http://www.biomedcentral.com/1471-2377/13/7.