ejpmr, 2017,4(3), 263-266.

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

FIBRINOGEN AS THE BIOMARKER OF SUBCLINICAL ATHEROGENESIS IN ADULT MALE SMOKERS.

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Article Received on 24/12/2016 **Article Revised on 14/01/2016** **Article Accepted on 04/02/2017**

ABSTRACT

Smoking of cigarettes is one of the major health hazards of the world population as it is contributing to the cardiovascular diseases and to the increasing proportion of the sudden deaths. Fibrinogen is one of the independent & significant marker of cardiovascular mortality. The aim of the study is to identify the earlier marker of atherogenesis in healthy adult male smokers for the better risk prediction and screening purpose. 60 adult healthy men of age group 19-49 years were enrolled. 30 smokers & 30 non- smoker. Smokers were compared with the non-smokers by doing the blood tests which included blood glucose, lipid profile and Fibrinogen**.** Smokers had significantly higher levels of total serum cholesterol [245.03±72.82 vs160.07±21.39 p<0.000], LDL levels [149.17±48.87vs.98.67±14.93p<0.000] and triglyceride levels [152.43±52.40vs. 94.83±17.75p<0.000]. HDL levels were low in smokers. Fibrinogen levels were higher in smokers [644.20±231.38vs300.20±49.91p<0.000] respectively. There is a positive correlation between the duration of smoking Fibrinogen levels [r=0.917p<0.000]. This case control study shows significantly higher Fibrinogen levels in smokers in proportion to the duration & amount of cigarettes smoked pre day, as compared to the non-smokers. Thus hsCRP & Fibrinogen can be used as the bio markers of sub-clinical atherogenesis screening in healthy adult male smokers.

KEYWORDS: Fibrinogen, Atherosclerosis, Smokers.

INTRODUCTION

Cigarette smoking is a serious health problem and the most avoidable cause of sudden deaths worldwide. WHO has named tobacco as one of the greatest public health threats of the twenty first century. Tobacco smoking is an escalating public health problem especially in the developing country like India. The prevalence of smoking in India varies from about 15% to over 50% among men with physical and/or psychological dependence.[1] Nicotine causes increase in triglycerides, cholesterol, LDL & VLDL levels and decrease in HDL levels, Augestin later on[2], also studied that long term consumption of oral nicotine increased LDL cholesterol and decreased HDL cholesterol. Nicotine increases the circulatory pool of atherogenic LDL via accelerated transfer of lipids from HDL and impaired clearance of LDL from plasma compartment. Therefore it increases the deposition of LDL cholesterol in the arterial wall. Honjack[3] Endothelial dysfunction and inflammation are strongly associated with coronary artery disease (CAD). Inflammation plays a crucial role in the formation of atheromatous plaque, as well as its progress.[4] The secretion of pro – inflammatory cytokines from the vascular endothelium as well as from macrophages induces the production of inflammatory molecules that are measured in the circulation, such as High sensitive C-reactive protein (hsCRP) and fibrinogen.[5] Fibrinogen infiltration of the vessel wall increases blood viscosity, platelet aggregation and thrombus formation. Plasma fibrinogen is also a prominent acute-phase reactant. It augments the degranulation of platelets in response to adenosine-di-phosphate (ADP), when taken up by the granules.[6] Fibrinogen and products of its decomposition mediate the transportation of adhesion molecules in the surface of endothelium and their further migration to the intima.[7] Fibrin participates in the close linkage of low density lipoprotein (LDL) and lipid accumulation, leading to the creation of the lipid nucleus of atherosclerotic lipid nucleus of atherosclerotic lesions.[8] Fibrinogen participates in the formation of atherosclerotic plaque during the first stages of CAD, suggesting that it is a causative factor rather than a result.[9]

MATERIALS AND METHODS

The study was conducted in Narayana Medical college hospital. Participants included males of 19-49 years in generally good health. Smoker status was defined as the self reported smoking of atleast 5 years and no use of any other nicotine containing products and alcohol intake. Diabetes mellitus, Hypertension, Tuberculosis, Malnutrition Cancer, chronic disease and Females were all excluded. Written informed consent was obtained from each subject before entering the study. At visit 1,

details of the subjects were documented and advised about the fasting condition. At visit 2, the next day morning after 8hours of fasting, blood samples were collected, centrifuged and stored at -20cc. Blood glucose measured by Glucose oxidase method [GOD-POD]. Cholesterol by cholesterol oxidase method and triglycerides by direct enzymatic method. The fibrinogen levels (Normal range:200-400 mg/dl) were measured by using ACL 7000 auto analyser. Statistical analysis of the values done using spss 16 version and obtained mean, SD and p values. Pearson correlation coefficient was obtained between the variables.

RESULTS

Our study revealed significantly higher levels of cholesterol, LDL, VLDL, and triglycerides in the smokers population & low levels of HDL levels. The levels of fibrinogen were significantly high. The mean serum total cholesterol in non-smokers was cholesterol 160.07±21.39mg/dl while it was significantly higher in smokers, i.e245.03±72.82 mg/dl. There is a significant rise in total cholesterol in smokers with p value <0.000. This finding is similar to the study done by Wendy Y Craig, Glenn E Palomaki, James E Haddow, they concluded that serum cholesterol concentrations were higher in smokers, leading to a significant overall increase of 3.0% (p<0.001).[10] The mean serum triglycerides levels in smokers and non-smokers were [152.43±52.40vs94.83±17.75] respectively. There is a significant raise in triglycerides in smokers with p value <0.000.The mean LDL-C and VLDL-C values in non-smokers were 98.67±14.93mg/dl and19.23±4.91mg/dl respectively. But these values were significantly higher in smokers (LDL-C =149.17±48.87mg/dl, VLDL-C =29.70±10.61 mg/dl. The mean HDL-C in non-smokers was 64.27±20.96mg/dl and was 42.17±6.35mg/dl in smokers respectively [p value <0.00]. This finding is similar to that of Rosenson[11] who reported that there is fall in HDL-C level by 3-5 mg/dl in smokers. A recent meta -analysis has demonstrated accordingly that HDL cholesterol is about 6% lower in smokers. Similar findings have been reported by.[12] This finding is similar to the study done by Wendy Y Craig, Glenn E Palomaki, James E Haddow, they concluded that smoking was associated with significantly higher cholesterol, triglyceride, very low density lipoprotein cholesterol and low density lipoprotein cholesterol concentrations and significantly lower high density lipoprotein cholesterol (all p <0001). The mean plasma fibrinogen levels in non-smokers was [300.20±49.91mg/dl] while it was significantly higher in smokers [644.20±231.28mg/dl]. There is a significant rise in plasma fibrinogen level in smokers with p value <0.000. This study is similar to the Framingham study, in this study results showed that plasma fibrinogen values were significantly higher in smokers than in non-smokers. Results show that lipid profile levels and fibrinogen levels are directly proportional to the increase in the duration of smoking. Cases with smoking history of 5-10, 11-20 & 21-30 years had mean total cholesterol levels of 180.17±25.64 mg/dl, 275.64±52.20 mg/dl & 332.50±68.53mg/dl respectively.

Mean TGL levels of 5-10, 11-20 & 21-30 years of smoking were 123.83±34.07 mg/dl, 163.93±52.42mg/dl & 183.00±69.28mg/dl respectively. Mean HDL levels of5-10, 11-20 & 21-30 years of smoking were 44.02±1.7mg/dl, 41±2.45mg/dl, 38±1.31mg/dl respectively. Mean LDL levels of 5-10, 11-20&21-30 years of smoking were 106.08±15.10mg/dl,168.71±35.21mg/dl & 210.00±52.32mg/dl respectively. Mean VLDL levels of 5-10, 11-20 & 21-30 years of smoking were 23.50±6.55mg/dl,34.36±10.46mg/dl &32.00±13.92mg/dl respectively. Mean Fibrinogen levels of 5-10, 11-20 & 21-30 years of smoking were 400.83±65.53mg/dl,783.07±126.97mg/dl & 888.25±159.99g/dl respectively.

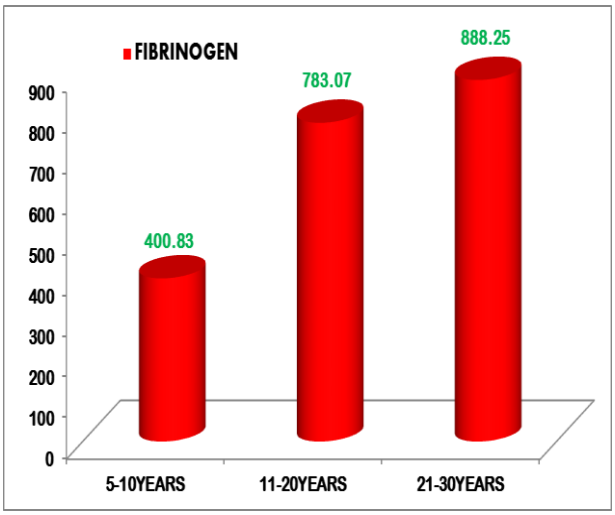

FIGURE: 1 SHOWS THE COMPARISION BETWEEN FIBRINOGEN& SMOKING DURATION.

Results show that fibrinogen levels increase proportionally with the increased quantity of smoking .Cigarettes smoked per day has positive correlation with Fibrinogen [r=0.814, p<0.000]. The results were similar to the Framingham study Where there was a dose-dependent increase with smoking in both sexes; ex-smokers had values as low as those of non-smokers.

TABLE: 1 SHOWING COMPARISION OF BLOOD GLUCOSE, LIPID PROFILE, FIBRINOGEN IN SMOKERS AND NON SMOKERS.

Parameters [mg/dl]	Smokers	Non smokers	P value
Blood glucose	96.00±9.54	89.53±9.76	0.120
Cholesterol	245.03±72.82	160.07±21.39	0.000

Triglycerides	152.43±52.40	94.83±17.75	0.000
LDL	149.17±48.87	98.67±14.93	0.000
VLDL	29.70±10.61	19.23±4.91	0.000
HDL	42.17±6.35	64.27±20.96	0.000
Fibrinogen	644.20±231.38	300.20±49.91	0.000

DISCUSSION

In our cross sectional study, we found that the levels of lipid profile & Fibrinogen were higher among smokers. The increase in Fibrinogen was proportionate with the smoking duration and cigarettes per day. In smokers the levels of total cholesterol, LDL cholesterol, Non-HDL cholesterol were significantly elevated when compared with the controls.[13] The fibrinogen levels were also found to correlate with a higher risk of ischaemic stroke, which was independent of the blood glucose levels.[14] Cigarette smoking is strongly associated with increased plasma fibrinogen levels and the adverse cardiovascular effects of smoking may partly be mediated through an increase in plasma fibrinogen levels. Indeed, each cigarette smoked per day increases mean plasma fibrinogen by 0.35 g/l.[15] A role in subclinical atherosclerosis has been also attributed to this acute phase protein, as higher levels of fibrinogen during young adulthood were positively associated with prevalence of coronary artery calcification and increased carotid intima-medial thickness in middle age, while the magnitude of the association decreased with aging.[16] Fibrinogen was levels were strong predictors of subclinical atherosclerosis (associated with an extension of carotid atherosclerosis) in hypertensive postmenopausal women.[17] Supporting data had previously shown that fibrinogen is involved in the subclinical phase of extra coronary and coronary atherosclerosis and may add to the atherogenic effect of hyperlipidemia.[18]

This study suggests that smoking potentially increases LDL-C and Fibrinogen levels in healthy adult males. The synergetic increase of fibrinogen level in smokers is dose dependent and is also directly related with duration of smoking. Our study not only suggests that smoking is the individual risk factor for atherogenesis and it further indicates that smoking more than 5years increases the atherogenic risk in otherwise healthy males. Moreover our study suggests that Fibrinogen can be used as the sensitive and specific biomarkers to predict the atherogenic risk in sub–clinical stage among healthy adult male smokers.

CONCLUSION

Our present study reveals that the elevation of plasma fibrinogen and dyslipidemia are important cardiovascular risk factors in otherwise healthy smokers. Our study concludes smoking may increase the inflammation and dyslipidemia which contributes to atherosclerosis in smokers and suggests fibrinogen as a bio-marker of atherogenic risk prediction among healthy male smokers.

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