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RESEARCH ARTICLE

Platelet aggregability, prehypertension, and heart rate in male smokers: An unwelcome circumstance for prothrombotic activity

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ABSTRACT

Background: Smoking makes the blood stickier and the blood cells clump together due to which there is reduced blood flow which further leads to blockages in the heart. Cigarette smoking globally known risk factor for public health and being responsible for many illnesses such as hypertension, lung cancer, coronary heart disease, and stroke. It has a negative impact on endothelial function which leads to thrombotic episodes by enhancing platelet aggregation and also important for developing hypertension. There are various mechanisms by which it affects the cardiovascular system. Nicotine, main ingredient, is said to increase cardiac output by increasing both heart rate (HR) and myocardial contractility. **Aims and Objectives**: Considering above known facts, the objectives were assessed in the form of platelet aggregability by method given by O'Brien and early prediction of hypertension in smokers and non-smokers by measuring blood pressure (BP) and resting HR. **Materials and Methods**: Platelet aggregability was measured by method given by O'Brien and BP was recorded using sphygmomanometer taking the average while radial pulse was taken for HR. **Results**: Our result shows that platelet aggregability and systolic BP with diastolic BP to be highly significantly $P < 0.0000$ in smokers along with statistically significant $P < 0.05$ resting HR. **Conclusion**: The study thus highlights the endothelial damage with increased sympathetic activity which leads to increased platelet activation and aggregation in smokers, prehypertension also worsens platelet activation, appropriate prevention measures needs to be implemented to reduce the risk of cardiovascular disease.

KEY WORDS: Platelet Aggregability; Prehypertension; Thrombotic; Smoking; Sympathetic

INTRODUCTION

Smoking is one of the habit humans have been indulging in various forms since prehistoric era. If we see the history of smoking, dates back as early as 5000–3000 BC when this agricultural product started to be cultivating in Southern America; consumption later evolved either by accidental burning the plant substance or exploring it by other means such as practices like shamanistic rituals. Many ancient civilizations such as the Babylonians, Indians, and Chinese, burnt incense as a part of religious rituals and rites as did the Israelites and the later catholic and orthodox Christian churches. Probably smoking in the Americas had its origins in the incense-burning ceremonies of shamans but was later adopted for pleasure and as a social tool. Smoking consumption is generally 5 times seen higher among males than women, however, this gender gap declines with younger age and trend.[1] Cigarette smoking, a major risk factor adversely affecting public health, the World Health Organization (WHO) has estimated that there are about 100 million smokers in the world with one-third of global population between 15 years age and over. Majority found

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in developing countries like India.[2] Smoking is not only associated with lung cancer but is also strongly linked to cardiovascular diseases (CVDs), tuberculosis, chronic respiratory diseases, and stroke. The risk of developing CVD (coronary heart disease [CHD]) increases with duration and intensity of exposure to cigarette smoke. Overall, smokers have a 70% greater mortality rate from CHD than non-smokers.[3] Prothrombotic effects of smoking are well documented such as increased circulating levels of fibrinogen, endothelial dysfunction, platelet activation, and platelet aggregation. Therefore, the adverse prognostic effects of smoking may not only increase risk of developing atherosclerosis but also risk of occlusive thrombosis and myocardial infarction.[4] Smoking even one cigarette has shown that thromboxane B2 and platelet aggregation *in vitro*, significantly increases platelet aggregation.[5] The walls of the arteries are very much prone to the damage caused by cigarette smoking which may lead to the pathologic changes in the arterial walls like atherosclerosis. This atherosclerosis causes the narrowing of the lumen and increases the pressure of the blood flow inside the arteries, thus leading to hypertension. About 1.1 million deaths per year in the globe suffer elevated blood pressure (BP), a leading modifiable risk factor for the premature death and CVD. This is a health challenging to the WHO.[6,7] Smoking and hypertension are two well-known independent risk factors affecting both heart and blood vessels. In most instances, cases of hypertension usually can be missed or get undiagnosed or late diagnosed because they do not show any signs and symptoms in its initial stage. The major component, i.e., nicotine in cigarette causes sympathetic activation by releasing catecholamines which also leads to an immediate effect on blood vessel rheology and thus having an impact on one's heart rate (HR) too. A person's HR shoots up by 30%. Resting HR is considered to be a good parameter of overall health. Resting heart rate is considered to be a good parameter of overall health. According to the individual's BP level and severity of hypertension, it is classified into three main categories (normal BP, prehypertension, and hypertension).[8,9] If diagnosis is done prematurely, i.e., at an early stage, prevention from CVD is possible by further reducing burden of morbidity and mortality. Despite various evidences about platelet activation and aggregation in hypertension but data on prehypertensive individuals are very limited. The association of cigarette smoking with the development of hypertension is still not clear and a matter of concern. Furthermore, only few studies are done on this subject. Hence, therefore, the aim and objectives of our present study was to identify the early prothrombotic activity the form of platelet aggregability, BP, and HR in male smokers, and thereby prevent from further damage.

MATERIALS AND METHODS

The study was a cross-sectional type of study and was conducted in 100 young males from the staff members of medical college and hospital in the age group of 40–50 years. The study was conducted between August 2012 and December 2012 after approval of the institutional ethical committee. It included males of 40 to 50 years of age with history of smoking minimum 5 cigarettes/day for more than 3 years & having normal body mass index (BMI) and was compared with males who never smoked. Occupational history and any significant history or family history were also noted. Information about the number of cigarettes smoked per day. Each subject selected in the study was included in one of the following groups.

Non-smokers: People who have never smoked. Smokers: People who smoked five or more cigarettes per day. Written consent was taken from all the subjects after explaining the nature of the study to them. Fasting blood samples were collected from both the groups from antecubital vein under all aseptic precautions. To avoid the effect of diurnal variations on platelet aggregability, the time of collection of blood was kept constant between 9 am and 11 am. Platelet aggregability was measured by method described by O'Brien as it is practicable and reliable.[10] BP was measured with a standard mercury sphygmomanometer on the right arm in sitting position after 1 min of interval. Phase I and V Korotkoff sounds were used to determine systolic BP (SBP) and diastolic BP (DBP) measurements. The average of three measurements was used. Participants were required to refrain from smoking or consuming caffeine. Normal BP was defined as SBP <120 and DBP <80 mmHg without antihypertensive medication use. Prehypertension was defined by SBP of 120–139 mmHg with DBP <90 mmHg or DBP of 80–89 mmHg with SBP <140 mmHg without antihypertensive medication use. Hypertension was defined as SBP ≥140 or DBP ≥90 mmHg on antihypertensive medication.[11] Resting HR or pulse rate is an easy counting measurable parameter, with high prognostic value, measured by finding the radial pulse for complete 1 min.

Exclusion criteria for the subjects were subjects undergoing regular exercise, subjects on medications such as statins, glitazones, fibrates, niacin, clopidogrel, aspirin, iron/vitamins supplements, and antihypertensives, and subjects having a history of any major disease such as ischemic heart disease, hypertension, kidney or liver disease, diabetes mellitus, dyslipidemia, malignancy, venous thrombosis, systemic or pulmonary embolism, congenital hemorrhagic disease, and thrombocytopenia. Data were expressed as mean ± standard deviation. Statistical analysis was done using Student's unpaired *t*-test in Microsoft office excel and $P < 0.0000$ was considered as highly statistically significant while <0.05 as statistically significant. Results were taken and statistically matched with the control group.

RESULTS

The results obtained from the observations are summarized in Tables 1-3. It included males of 40–50 years of age with history of smoking minimum 5 cigarettes/day for more than 3 years & having normal body mass index (BMI). Our study population was anthropometrically matched.

Table 1: Participants anthropometric characteristic distribution

Parameters	mean±SD	
	Non-smokers	Smokers
Age (years)	46.5±3.55	44.9±3.43
Height (cms)	167.83±8.26	166.45±7.82
Weight (Kgs)	68.71±8.26	67.21±8.95

Data expressed as mean±SD. SD: Standard deviation

Table 2: Comparison of platelet aggregability in non-smokers and smokers

Parameter	*n*=50		*P* value
	Non-smokers	Smokers	
Platelet aggregability mean±SD	0.424±0.109	0.746±0.052	**0.0000

Data expressed as mean±SD, *P*<0.00001=HS: Highly significant. SD: Standard deviation

Table 3: Comparison of BP and pulse rate in non-smokers and smokers

Parameters	mean±SD		*P* value
	Non-smokers	Smokers	
SBP (mmHg)	118±11.31	139±12.72	**0.0000
DBP (mmHg)	69±1.414	85±7.07	**0.0000
Pulse rate (bpm)	75±7.071	83±1.41	*<0.05

Data expressed as mean±SD, *P*<0.00001=HS: Highly significant, *P*<0.05=Significant (S). BP: Blood pressure, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SD: Standard deviation

Table 2 summarizes comparison of platelet aggregability in males in non-smokers and smokers group. There is statistically highly significant increase in platelet aggregability in males of smokers group.

Table 3 shows both systolic and diastolic blood pressure higher in the smokers when compared to non-smokers. High resting heart rate was also noted in smokers. This clearly states that there is direct relationship with blood pressure, resting heart rate & smoking severity. Both SBP and DBP was observed to be higher in the smokers when compared to non-smokers. High resting HR was noted in smokers. This clearly states that there is direct relationship with BP, resting HR, and smoking severity.

DISCUSSION

The results in our study showed that the study population was anthropometrically matched as seen in Table 1 with mean age as 46.5 ± 3.55. So far, the effect of cigarette smoke on blood coagulation and on different body systems and its pathophysiological effect has been an interest of investigation. In Table 2, platelet aggregability when compared in males of smokers and non-smokers individuals, $P < 0.00001$ found to be highly statistically significant. Bliden *et al*. noted findings similar to ours. They too found that there was increase in platelet aggregation in smokers.[12] Bordia has also shown that platelet aggregation was markedly increased after smoking and when treated with garlic oil showed inhibition of platelet aggregation.[13] Some have demonstrated increased platelet aggregability immediately after smoking while others have found no such change. Suwansaksri *et al*. observed no alteration in platelet aggregation in smokers.[14] Lassila and Laustiola demonstrated that platelet aggregation responses to adenosine diphosphate (ADP) were similar in non-smokers and smokers.[15] Similar findings were also supported by Higman *et al*., platelet aggregation was reduced in smokers than non-smokers *in vitro* studies.[16] Cigarette smoke contains over 4000 or more known harmful substances enlisting nicotine, tar, ammonia, carbon monoxide, free radicals, and other gaseous products to name a few which exerts a negative impact on the platelet function and augment platelet aggregability. Normally in circulation, platelets are in quiescent state but after endothelial injury due to cigarette smoke they get activated. Platelet aggregation can be stimulated *in vitro* by a number of agonists that affect platelet receptors including ADP, epinephrine, collagen, and morphologically platelets undergo conformational change and adheres to each other by surface integrins glycoprotein IIb/IIIa forming larger aggregates. Activated platelets are known to facilitate the coagulation cascade and final common pathway of fibrin formation of fibrin.[17] In the present study, the BP, both systolic and diastolic in smokers were found to be highly statistically significant ($P < 0.00001$) than non-smokers, respectively. While some studies conducted on BP found that acute BP increase from tobacco smoking.[18] and that decreases 1-week after smoking cessation.[19] Rabinowitz *et al*. noted in their work that there was an acute rise in BP in smokers which was mediated through elevation in circulating catecholamines.[20] However, Okubo *et al*. had found in Japanese subjects that the BP of smokers was lower than that of non- and ex-smokers.[21] Conversely, there was no difference in the SBP when compared to smoker and non-smoker younger men aged 16–44 years and the DBP in both the age groups who smoke and who do not were at the identical level.[22] There has been various hypothesis proposed to explain the relation between smoking and BP. While comparing the resting pulse rate or HR in smokers [Table 3], statistically significant ($P < 0.05$) results were observed. High resting HR was noted in subjects with a history of smoking.[23] Minami *et al*. found that the HR on average 7 bpm was faster in smokers than in non-smokers.[19] Overall, HR responses to cigarette smoking may have a link between smoking and CVD. However, these effects seem to be age-dependent, exposure intensity, relatively little is known about how smoking affects HR in young adults.[24] Thus, there may be a direct relationship with resting HR and smoking severity. The HR is under the regulation of autonomic nervous system, i.e., the sympathetic nervous system and parasympathetic, sympathetic gets activated due to nicotine found in cigarette smoke. It is known to be a sympathomimetic substance that promotes the release of catecholamines which increases platelet aggregation, increased

HR and SBP directly.[25] We characterized our individuals into early prothrombotic tendency with prehypertension as having an increased risk for transitioning to hypertension. Whereas, a known fact about smoking with high or low nicotine content it makes the heart to work much harder by increasing HR, SBP and DBP. There has been various hypothesis proposed and tried to explain the relation between smoking and platelets, BP and heart activity, but still the relation is uncertain. Strength of this study is that although our sample is representative of general population aged 40–50 years of men. Here, we unravelled an indirect observations which can help to assess the role of smoking related to prothrombotic activity, such as platelet aggregation, also prehypertension alone making it predisposal to hypertension, working condition of heart in both smokers and non-smokers. On the other hand, this study has limitations. This is a cross-sectional study and the data are not sufficient enough to allow the final conclusions. Therefore, cohort studies are needed in future to further understand the chronic effect of smoking. Furthermore, sample size was relatively small, and more studies need to examine the association between smoking, platelet aggregation, BP, and HR in larger sample with younger age groups. In addition, BMI, age, alcohol consumption, and ethnicity might be more useful. Likewise, confounding factors due to lifestyle cannot be excluded.

CONCLUSION

Increased platelet aggregability in smokers could be due to endothelial injury and increased sympathetic activity. SBP, DBP, and HR are higher in smokers as compared to non-smokers. It appears that for a given scenario, a close relationship may exist between these factors. Majority of the adverse health effects of smoking can be reversible if found early and there is opportunity to prevent the transition to hypertension and prevent prothrombotic effect on cardiovascular system. Lifestyle modification and non-pharmacological interventions among adults with prehypertension can be implemented. Hence, there is an urgent need to sensitize smokers in the society about its ill-effects on health and prevents the morbidity and mortality.

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