Research Article

Evaluation of the impact of cigarette smoking on platelet parameters

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Abstract

Background: Smoking has been established as a chief causative factor for cardiovascular diseases, inflammatory disorders, and oxidative stress stimulation. It is known that the total peripheral blood leukocyte count increases by cigarette smoking; however, its influence on platelet parameters is largely unknown. Early detection of thromboembolic diseases can be achieved by the potentially useful platelet indices. Enhanced activity is shown by platelets with increased volume when compared with platelets with smaller volume. Hence, mean platelet volume (MPV) can act as a indicator for platelet activity. **Aims and Objective:** To study the impact of cigarette smoking on platelet parameters. **Materials and Methods:** This cross-sectional study included 50 healthy young male cigarette smokers and 50 healthy male nonsmokers in the age range of 18–50 years at SRM Medical College, Tamil Nadu, India, after approval by the institutional ethical committee. Subjects with acute illness and diabetes mellitus and those on antiplatelet drugs were excluded. History regarding current smoking status, number of cigarettes smoked per day, pack-years of smoking, and years since quitting was noted. Complete blood count including platelet indices such as platelet count, MPV, platelet distribution width (PDW), platelet large cell ratio (P-LCR), and plateletcrit (PCT) were determined. On the basis of their smoking characteristics, smokers were grouped as mild, moderate, and heavy. **Result:** Compared with nonsmokers, smokers showed significantly high values of MPV, and PDW ($P < 0.05$). MPV, PDW, and P-LCR were found to be positively associated with intensity of smoking, pack-year, and duration of smoking. **Conclusion:** The smokers showed higher MPV, PDW, and P-LCR, which might forecast possible high risk for developing thromboembolic disease in smokers.

KEY WORDS: Smokers; Platelet Count; Mean Platelet Volume

Introduction

The only legal drug that kills many of its consumers when used accurately as proposed by the manufacturers is tobacco, and an estimation by WHO shows that about six million deaths worldwide each year, with most of them as premature deaths, occur owing to tobacco use (smoking and smokeless).[1] Despite of the fact that tobacco smoking is positively associated with many diseases, increasing prevalence of smoking among young people is still a problem of severe concern for health professionals. A cigarette smoke contains over 4000 chemicals,[2] and a cigarette smoker is exposed to a number of harmful substances including nicotine, free radicals, carbon monoxide, and other gaseous products.[3] It is widely known that smokers have higher risk for cardiovascular diseases, hypertension, inflammation, stroke, clotting disorder, and respiratory disease.[4–8] In addition, cigarette smoking enhances the pathogenesis in various types of cancers such as lung, pancreas, breast, liver, and kidney.[5,9] Similarly, it also

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enhances pH in stomach that result in peptic ulcers and gastric diseases.[6,10] During the last decade, it was suggested that cigarette smoking affects the blood characteristics and leads to death.[4]

Platelets are formed from bone marrow megakaryocytes. They are nonnucleated and possess little viable mitochondria, glycogen, many types of morphologically variant granules (dense core granules and lysosomes), and a complex membranous system. The granules contain adhesion molecules, which help in platelet–platelet interactions and platelet interactions with other blood cells, mitogenic factors, plasma proteins, some coagulation factors, and fibronectin. Platelets are important for hemostasis, wound healing, and inflammation.[11]

The increased platelet activity and thrombus formation and thromboembolic diseases are among the major cause of mortality in developed countries. Successful management of these diseases relies on early detection of progressive activation of coagulation. Recently, many reliable markers which play a role in the activation of coagulation, such as prothrombin fragment $1 + 2$ and thrombin–antithrombin complex, and involved in the platelet activation, such as β-thromboglobulin or soluble platelet P-selectin have been investigated.[12] Nonetheless, the laboratory assessment of these indices is strenuous and costly. Moreover, routine laboratory tests cannot contain the aforementioned indices.[13,14]

Mean platelet volume (MPV) and the platelet distribution width (PDW) are the indicators of platelet activation. The size of the platelet is correlated with the activity and the function of the platelet. Larger platelets are more active than the smaller ones. PDW is a marker of differences in the platelet size, which can be an indicator of active platelet release. These platelet parameters are estimated routinely by automated blood counters.

As the point that platelet activation results in morphologic variations of platelets is known, a sequence of platelet parameters measured by hematology analyzers have been applied by several researchers. The MPV is perhaps the most widely studied platelet activation parameter.[15–17] Mean platelet component and platelet component distribution width are the new indices that are assessed recently as potential platelet activation markers.[18] Nevertheless, these indices are not assessed by all the hematology analyzers.

There are a very few studies relating the effect of smoking on platelets. In addition, many of the studies have not compared the data with those of the nonsmoking control groups.[19,20] Kario et al.[21] found elevated MPV in smoking patients, which reduced after the patients stopped smoking. However, Butkiewicz et al.[22] studied the impact of smoking on platelet activation and few other morphological indices including MPV and found no effect on MPV by smoking. Thus, studies on this have reported conflicting results. Hence, this work was undertaken to study the effect of cigarette smoking on platelet parameters. We postulated the hypothesis that smoking contributes to heightened platelet reactivity and, hence, will result in an increase in the platelet volume indices.

Materials and Methods

This cross-sectional study was conducted at SRM Medical College and Hospital, Tamil Nadu, India, between 50 smokers as study group and 50 age-matched nonsmokers as control group. All were apparently healthy male subjects between the age group of 18–50 years. The study group (smokers) showed the history of smoking of one or more cigarette per day, regularly for at least the last one year. Institutional Ethical Committee permission and approval obtained .Written informed consent was obtained from all the subjects.

The socioeconomic status, age, height, weight, and daily activity were comparable between the study and the control groups. Subjects with history of coagulation disorders, diabetes, hyperlipidemia, hypertension, peripheral vascular disease, chronic renal disease, hypertension, and any infectious or debilitating illness and those who are on any medication such as aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs)were excluded from this study. All subjects were free from other habits such as tobacco chewing and alcohol intake. The subjects who were passive smokers and ex-smokers and those who underwent radiotherapy were also excluded. Since smoking is extremely rare among women in this area owing to cultural reasons, women were not included.

A detailed history regarding current smoking status, number of cigarettes smoked per day, years of smoking, and years since quitting was obtained by using a pretested questionnaire. Nonsmokers were the respondents who affirmed that they have not smoked yet.The pack-year is a unit for measuring the amount a person has smoked over a long period of time and was calculated by using the following formula: pack-years = (number of cigarettes smoked per day $\times$ number of years smoked)/20. In our study, the smokers were classified into mild, moderate, and heavy based on the number of pack-years as 10–14, 15–19, and 20 years and above, respectively.[23]

The subjects underwent the following tests: blood pressure examination to rule out hypertension, complete blood count and platelet parameters such as platelet count (PLT), plateletcrit (PCT), MPV, PDW, and platelet-large cell ratio (P-LCR) were estimated using Sysmex II Autoanalyser. MPV was calculated by the following formula: MPV (fL) = [(plateletcrit (%)/platelet count ($\times 10^9$/l)] $\times$ 10^5. PCT was the ratio of the platelet volume to the whole blood volume. PDW and P-LCR were analyzed from a histogram of platelet size distribution. The distribution width at the level of 20% (the peak of the histogram is 100%) was defined as PDW, and the percentage of platelets with a size of more than 12 fL was defined as P-LCR.[24]

All the results of laboratory investigations were loaded in computerized SPSS 12.0 programer, and statistical significance were analyzed by unpaired Student's "*t*" test and ANOVA. Results were expressed as mean ± standard deviation (SD). The *P* value of < 0.05 has been considered as significant.

Table 1: Comparison of anthropometric data between smokers and nonsmokers.

Parameters	Group I, smokers (n = 50) (mean ± SD)	Group II, control subjects (n = 50) (mean ± SD)	*P*
Age (years)	35.8 ± 8.9	39.4 ± 11.7	0.09
Height (cm)	158 ± 11	161 ± 8.8	0.226
Weight (kg)	65 ± 10.9	64.7 ± 11.6	0.926
BMI (kg/m^2)	26.06 ± 4.03	24.81 ± 4.24	0.244

Results

Table 1 compares the anthropometric parameters between smokers and nonsmokers, which shows that there is no significant difference between the two groups. Table 2 compares the platelet parameters between smokers and nonsmokers and shows a statistically significant increase in MPV and PDW in the smokers. Table 3 compares the platelet parameters between mild, moderate, and heavy smokers, which shows that the parameters MPV, PDW, and P-LCR were significantly increased in heavy smokers.The abnormalities of platelet parameters were more significant when the smoking intensity increases.

Table 2: Comparison of platelet parameters between smokers and nonsmokers.

Platelet parameters	Group I, smokers (n = 50) (mean ± SD)	Group II, control subjects (n = 50) (mean ± SD)	*P*	*t*
PLT	305.23 ± 69.15	284.92 ± 73.81	0.22	1.238
PDW	11.86 ± 1.75	11.04 ± 1.28	0.02*	2.333
MPV	10.24 ± 0.69	9.915 ± 0.59	0.03*	2.167
P-LCR	25.47 ± 5.39	24.64 ± 4.95	0.48	0.697
PCT	0.305 ± 0.06	0.287 ± 0.06	0.24	1.188

*$P < 0.05$, statistically significant.

Discussion

Tobacco smoking has been associated to be a reason for various major morphological and biochemical complications in individuals. In this study, we compared the platelet parameters between smokers and nonsmokers. Table 1 shows that both the groups were comparable. The experimental results showed differences in platelet parameters such as MPV and PDW, which were significantly high ($P < 0.05$) in smokers when compared with nonsmokers [Table 2].

MPV and PDW increased during platelet activation. To achieve a larger surface area, platelets modify their shapes during activation. Their shape changes from discoid to spherical. Pseudopodia are formed as well. On the basis of impedance technology, the hematology analyzers estimate the platelet volume by the distortion of electrical field, which depends on the platelet vertical diameter.

In acute thrombotic events, platelet activation can be assessed by an increase in MPV, a well-known marker. It is alleged that carbon monoxide (CO) establishes a vital role in the cigarette smoke-induced cardiovascular diseases. The researchers found significant correlations between MPV and COHb levels (r = 0.55, P = 0.0001) and between MPV and lactate levels (r = 0.65, P = 0.0001) after smoking and have shown that 1-h exposure to passive smoking enhances the platelet activation, which may be the mechanism that leads to an enhanced risk of thrombotic events in healthy people. It is probable that continued exposure to passive smoking might pose even higher impacts. Passive smoking exposure should be avoided by healthy people in order to prevent from increasing risk of thrombotic events.[25]

Varol et al.[26] have shown that chronic smoking causes platelet activation and smoking cessation improves platelet function. However, Arslan et al.[27] investigated the effects of smoking on MPV in young healthy male population (smokers, 56; nonsmokers, 46), and they found no significant difference in MPV between the smoking and nonsmoking healthy male participants.

The increase of MPV among the smokers in this study may be attributed to platelet activation and the increase of PDW to platelet anisocytosis, which results from pseudopodia

Table 3: Comparison of platelet parameters between smokers.

Parameters	Mild smokers (pack-years, 10–14)		Moderate smokers (pack years, 15–19)		Heavy smokers (pack-years, 20 years and above)		*F*	*P*
	Mean	SD	Mean	SD	Mean	SD		
PLT	329.8	85.8	300.42	37.58	277	63.403	1.994	0.151
PDW	10.97	0.63	11.83	1.1	13.13	2.56	6.146	0.005*
MPV	9.62	0.42	10.45	0.32	10.84	0.59	25.03	0.000*
P-LCR	22.09	3.15	26.5	4.42	28.73	6.75	6.512	0.004*
PCT	0.318	0.084	0.305	0.035	0.287	0.053	0.733	0.487

*$P < 0.05$, statistically significant.

formation. Ihara et al.[28] and Khandekar et al.[29] found the same observation in patients with ischemic heart disease.

The MPV, PDW, and P-LCR were significantly increased as the intensity of smoking increases, as shown in Table 3. This increase of MPV and PDW and P-LCR comparatively suggests that young platelets are released into circulation, which are comparatively more reactive.[30] For decades, epidemiological data have demonstrated the association of smoking with the incidence of coronary heart disease, myocardial infarction, and stroke. In majority of the acute clinical scenarios, there is incidence of thrombotic occlusion of the vessel, a process that is habitually related to platelets. Therefore, the definition of the relation between platelets and smoking seems important.[31] Hung et al.[32] demonstrated smoking-stimulated platelet aggregate formation in habitual smokers. Another effect of smoking found by different groups is an increase in the serum fibrinogen levels.

In addition, platelets shape and volume might differ, even in healthy persons. Thus, sequential assessment of MPV and PDW might be beneficial but unrealistic for the identification of progressive platelet activation. Instead, concurrent enhancement of MPV and PDW might suggest platelet activation, as shown by Vagdatli et al.[33] Platelet activation by cigarette smoking is related to thrombosis formation, which may lead to initiation of myocardial infarction. A paucity of studies that estimate all of the platelet parameters, including MPV, PDW, and PCT, exists in the literature. Some limitations of our study include the relatively small sample size and lack of investigation of women owing to their denial of smoking.

Conclusion

In our study, cigarette smoking in healthy men was accompanied by significant effects on platelet indices, such as increase in the mean MPV and PDW values in comparison with nonsmokers, which were also pronounced in heavy smokers along with increase in P-LCR. We propose that these platelet parameters should be routinely reported with other hematological parameters in complete blood count reports. In light of the adverse effects on platelet function, cessation of smoking should be encouraged. Future research should be carried out with larger sample sizes including female subjects to explain these morphological changes in platelets following smoking.

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