Evaluation Of Impact Of Cigarette Smoking On Platelet Parameters And Coagulation Profile In Young Healthy Male Subjects

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Abstract: Aim: This study aims to assess the impact of smoking on platelet parameters and coagulation profile in young healthy smokers. Material And Methods: A total of 100 apparently healthy males, aged between 20–50 years were taken. 60 smokers who have smoked regularly for a minimum of 1year and 40 age and sex matched non-smokers/controls were included in the study. The smokers were further classified into light and heavy smokers according to 'Pack Years'. 2ml EDTA and 2ml citrated blood samples were withdrawn to perform CBC and coagulation profile respectively. The levels of these parameters were recorded and statistically analysed. Result: The study shows that frequency and duration of smoking is directly proportional to the adverse effects on the body. We found that there was significant increase in WBC count in chronic smokers (>8000 10^6/L) consistent with other published reports. There was significant reduction in platelet count found in chronic smokers more than light smokers. We also observed that increased duration and frequency of cigarette smoking was associated with significant shorter PT (10.94 s) and APTT (27.29 s) in heavy smokers. Conclusion: Hence we conclude that cigarette smoking should be strictly discouraged. Awareness about deleterious effects produced by smoking should be done as harmful effects of smoking are reversible if stopped at an early phase. [Jain A Natl J Integr Res Med, 2019; 10(5):53-57]

Key Words: Platelet count , Male Smokers , Prothrombin time , Partial Thromboplastin Time

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Introduction Smoking is a major health hazard having several co-morbidities associated with it. More than 4,000 different toxic and carcinogenic chemicals have been found in the cigarette smoke [1]. These chemicals like nicotine, tar, carbon monoxide etc., have numerous deleterious effects on the various systems of the body. It is particularly associated with the pathogenesis of pulmonary and cardiovascular diseases such as COPD, lung cancer, atherosclerosis and coronary artery disease and hypertension. While many people are aware of the negative effect of cigarette smoking on the lungs, less consideration is given to its effect on haemostasis.

Smoking seems to interfere with hemostasis through multiple pathways. This includes effects on the function of the endothelial cells, platelets and coagulation factors through mechanisms such as altered NO structure, decreased NO availability, increased oxidative stress or generation of procoagulant microvesicles[2,3].

Reports on effect of smoking on coagulation profile have been controversial. Earlier studies have observed an increase[4], decrease [5] or no change [6] in platelet aggregability and coagulation parameters following smoking. Cigarette related alteration of the function of endothelial cells and coagulation factors appears to also play a central role[7,8] . Even though, previous studies have reported various coagulation defects in chronic smokers, the relationship between duration of smoking and degree of coagulation impairment in the coagulation pathways remains unclear.

A study on chronic cigarette smokers showed that long-term smokers are more at risk of bleeding or coagulation disorders than non-smokers [9]. Long-term smoking has been shown to affect PT and APTT, with significantly lower values in those subjects[10] .Similarly smoking also affects platelet count and platelet volume parameters[9]. However, the consequences of smoking intensity on the degree of harm on coagulation pathways still remains unclear[10].

Thus the relationship between long term smoking and coagulation and platelet parameters needs to be studied further which may provide advance insight for treating these patients during hemostatic emergencies.

Material & Methods : The study was a prospective cross sectional study conducted on a total of 100 apparently healthy males, aged between 20–50 years. 60 smokers and 40 age and sex matched non-smokers/controls were included on the basis of their detailed history. A written informed consent was taken from all the subjects prior to the study.

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 year = (No. of cigarettes smoked per day x No. of years smoked) / 20.

The smokers were further categorized into two groups according to 'Pack years' (1 pack year is 20 cigarettes per day for 1 year). Group1 comprised of 30 light smokers with <15 pack years history of smoking and group 2 consisted of 30 heavy smokers with a duration of >15 pack years . Both light and heavy smokers must have a minimum smoking duration of 1year continuously The control group included healthy subjects who have never smoked and are not having any other addiction related to tobacco (like tobacco chewing, gutakha, pan masala, rajnigandha etc.)

Exclusion criteria: Subjects on anticoagulant therapy, having diseases such as anemia, hypertension, diabetes mellitus, liver cirrhosis, hemophilia, malignancy, vascular and cardiac disorders and its complications were excluded from the study. Passive smokers, Female smokers and Tobacco chewing individuals were not considered in this study.

Blood sampling and Laboratory procedures: Blood samples were collected from the antecubital vein without the use of a tourniquet. EDTA as an anticoagulant was used for complete blood counts including platelet count and platelet indices (MPV, PDW, PCT). These hematological parameters were measured using the automated blood cell counter (Nihon Kohden 6420 P). Sodium citrate (3.8%) , in a ratio of 1: 9 was used for performing Coagulation tests via The Stago Coagulometer (Start4).

Prothrombin Time (PT): to assess the extrinsic pathway of coagulation.

Activated partial thromboplastin time (APTT): to assess the extrinsic pathway of coagulation.

Statistical analysis: Statistical analysis was carried out using SPSS version 22.The mean and standard deviation was calculated for each group. Using 1 Way ANOVA, a comparison of means was determined between the 3 groups. The relation between heavy smokers and non-smokers, light and heavy smokers was evaluated by unpaired t-test. P value <0.001 was considered highly significant statistically and P value < 0.05 was considered significant. Institutional Ethics Committee clearance for the research protocol was obtained prior to the commencement of the study.

Results : A total of 100 male subjects were included in the present study. The study subjects were categorized on the basis of "pack years" into 3 groups as shown in (Table 1).

A comparison of the platelet and certain hematological parameters across the three study groups showed a significant difference ($p < 0.05$) in total WBC count and platelet count. However we did not find any significant difference in terms of Hb%, MPV, PDW and Plateletcrit as depicted in (Table 2).

Table 1 : Demonstrates characterization of study subjects according to smoking habit.

Subjects	Age (yrs)	Duration of smoking (yrs)	Frequency of smoking (no. of cigarettes per day)	Pack years
Control (n=40)	29.7±5.6	0	0	0
Light smokers (n=30)	30.1±5.4	6.93±5.83	8.43±5.20	3.9±5.03
Heavy smokers (n=30)	37.1±5.5	19.13±5.01	31.4±5.96	30.66±11.23

*All values in 3 groups are expressed as mean ± 2SD.

Table 2 : Comparison of platelet and haematological parameters across 3 study groups by 1way ANOVA

Parameters	Control(n=40)	Light smokers (n=30)	Heavy smokers (n=30)	P-value
Hb (g/dl)	14.57 ± 1.48	14.57±1.42	14.5±1.60	0.975
WBC count (10^6/L)	7007.5 ± 1678.88	7385±2251.25	8370± 1847.48	**0.014**
TPC (lakh/cumm)	2.73±0.60	2.62±0.47	2.34±0.67	**0.022**
Pct (%)	0.17±0.05	0.17±0.05	0.16±0.058	0.814
MPV (fl)	6.49 ± 2.69	6.73±2.88	6.69±2.60	0.92
PDW (%)	16.06± 2.91	16.67±2.35	16.71±1.041	0.414

*All values in 3 groups are expressed as mean ± 2SD.

P<0.05 was considered statistically significant. P<0.001 considered highly significant.
Hb: Haemoglobin ,WBC: White blood cell, TPC: Total platelet count, Pct-Plateletcrit , MPV: Mean platelet volume. PDW: Platelet distribution width.

Similarly, a comparison of the coagulation parameters across the three study groups showed a significantly shorter PT and APTT in smokers when compared to the control subjects as depicted in (Table 3).

Table 3 : Comparison of coagulation profile across 3 groups by 1-way ANNOVA.

Parameters	Control (n=40)	Light smokers (n=30)	Heavy smokers (n=30)	P value
PT (s)	12.21± 1.52	11.25±1.82	10.94±1.62	**0.005**
APTT (s)	34.28 ± 3.41	32.28± 3.44	27.29± 2.75	**0**

*Data expressed as mean±2SD. P<0.05 was considered statistically significant. P<0.001 is highly significant. PT:Prothrombin time, APTT: Activated partial thromboplastin time.

To assess the effect of duration and frequency of smoking on the various platelet parameters and coagulation profile, a comparison of these parameters was done between the control vs light smokers and light vs heavy smokers group.

The results revealed a significantly higher WBC count and lower PT and APTT values when controls were compared to heavy smokers thus establishing the deleterious impact of chronic heavy smoking on these variables (Table 4 & 5).

Table 4 : Comparison of hematological, platelet and coagulation profiles in controls and heavy smokers using unpaired t-test

Parameters	Mean Difference	Std. Error Difference	P value
Hb (g/dl)	0.072	0.37	0.84
WBC (10^6/L)	-1362.5	423.33	**0.002**
TPC (lakh/cmm)	0.97	0.68	0.16
Pct (%)	0.008	0.014	0.56
MPV (fL)	-0.20	0.64	0.75
PDW (%)	-0.65	0.55	0.24
PT (s)	1.26	0.37	**0.001**
APTT (s)	6.9	0.76	**0.000**

*P<0.05 was considered statistically significant. P<0.001 considered highly significan

Table 5 : Comparison of hematological, platelet and coagulation profiles in between light and heavy smokers using unpaired t-test.

Parameters	Mean Difference	Std. Error Difference	P value
Hb (g/dl)	0.07	0.39	0.84
WBC (10^6/L)	-985	531	0.069
TPC (lakh/cmm)	0.28	0.15	0.067
Pct (%)	0.008	0.014	0.59
MPV (fL)	0.04	0.7	0.95
PDW (%)	-0.04	0.47	0.93
PT (s)	0.31	0.44	0.48
APTT (s)	4.99	0.8	**0.000**

*P<0.05 was considered statistically significant. P<0.001 considered highly significant.

Discussion : Tobacco smoking has been correlated to cause several major morphological and biochemical changes in individuals. Although strong epidemiological evidence links cigarette smoking to cardiovascular disease, cancer and chronic obstructive pulmonary disease (COPD), the exact mechanisms of these links remain poorly understood. Some of the adverse effects of smoking include: initiation of endothelial injury[11], acceleration of coronary progression and new lesion formation [12] and overall alterations in lipid and hemostatic systems.[13]

WBC count is perhaps the most useful, inexpensive and simple biomarker for assessing endothelial damage. The high WBC count in chronic smokers in this study is consistent with other published reports [14,15]. While leukocytosis may simply be a marker of smoking-induced tissue damage, the high count can promote cardiovascular diseases through multiple

pathologic mechanisms that mediate inflammation, plug the microvasculature, induce hypercoagulability and promote infarct expansion[16,17]. The high WBC count in our male smoking subjects may also suggest that they might be at greater risk for developing atherosclerosis and cardiovascular diseases than non-smokers.

Platelets are the unnucleated fragments of bone marrow megakaryocytes that are involved in hemostasis, wound healing and inflammation. Changes in the platelet count, platelet morphology and coagulation parameters enhance the risk of thrombosis. The study revealed a significant decrease in the total platelet count of the smokers which in turn may predispose smokers to increased risk of hemostatic dysfunction. This decrease in platelet count could
be due to nicotine-induced decreased thrombopoietic activity in chronic smokers. However the study did not reveal any significant changes in plateletcrit (PCT), mean platelet volume (MPV) or platelet distribution width (PDW) between smokers and non-smokers. Studies undertaken by Butkiewicz et al. and Arslan et al. also found no significant difference in MPV between the smoking and non-smoking healthy male participant. [18,19]

We observed that increased duration and frequency of cigarette smoking was associated with a significant reduction in the PT and APTT. Doll and Peto[20], in a study on the effect of duration on inflammatory indices in male chronic smokers aged 40-79 years, reported duration as the most important predictor tool rather than intensity of smoking. As duration smoked increases, the smoking effect increases. Hioki et al., 2001 and Hunter et al., 2001 too indicated that prolonged cigarette in-take causes an increased amount of fibrinogen in plasma which could lead to hastened bleeding arrest, thrombosis or DIC.[21,22]

In the present study , PT and APTT of heavy smokers was significantly lower compared to light smokers. This is consistent with a report by Nascetti and colleagues who argued that the decrease in PT, INR and APTTK values associated with cigarette smoking is proportional to the number of cigarette smoked per day[23]. Hence, smoking induces hypercoagulability and hyperthrombotic state, possibly by increased platelet aggregation and adhesiveness as a result of its nicotine content.

Thus, not only long term smokers but smokers in general are at risk, hence there is a need for increased awareness of the harmful effects of cigarette smoking on health and organization of rehabilitation programs.

Conclusion: To deduce, Smoking is an imminent health hazard. At least half of all lifelong smokers die earlier than non-smokers. The findings from the present study suggest that with increase in duration and frequency of smoking, the WBC count, total platelet count and coagulation parameters (PT, APTT) are adversely affected. Thus, new and effective strategies are urgently needed to curb and discourage adolescent smoking as its toxic effects are reversible if discontinued at an early age. Extensive rehabilitation measures should be promoted and smokers should be provided with nicotinic substitutes for primordial prevention of major non-communicable diseases like CAD, malignancies, thromboembolic events and its complications**.**

References:

1. 1. David M. Burns, Nicotine Addiction, Harrison's Principles of Internal Medicine: Vol.II, 2008, 17th Edition; Page no. 2736-2739, McGraw Hill, USA.
2. 2. Mohammed H Saiem Al-Dahr. Impact of Smoking on Platelet, Coagulation and Lipid Profile in Young Male Subjects. World Applied Sciences Journal 11 (1): 118-123, 2010
3. 3. Triplett DA. Coagulation and bleeding disorders: Review and update. Clin Chem 2000;46 8(B):1260-9.
4. 4. Morita H, Ikeda H, Haramaki N, Eguchi H, Imaizumi T. Only two‐week smoking cessation improves platelet aggregability and intraplatelet redox imbalance of long‐term smokers. J Am Coll Cardiol 2005;45:589‐94.
5. 5. Dotevall A, Rångemark C, Eriksson E, Kutti J, Wadenvik H, Wennmalm A. Cigarette smoking increases thromboxane A2 formation without affecting platelet survival in young healthy females. Thromb Haemost 1992;68:583‐8.
6. 6. Suwansaksri J, Wiwanitkit V, Soogarun S. Effect of smoking on platelet count and platelet parameters: An observation. Clin Appl Thromb Hemost 2004;10:287‐8.

7. 7. Barua, R.S. and Ambrose, J.A. 2013. Mechanisms of coronary thrombosis in cigarette smoke exposure, Arterioscler Thromb Vasc Biol, 33(7), 1460-1467.
8. 8. Csordas, A. and Bernhard, D. 2013. The biology behind the atherothrombotic effects of cigarette smoke, Nat Rev.
9. 9. Akpotuzor JO, Agwunobi LE, Inyama MA. Prothrombin Time (Pt) and Partial Thromboplastin Time with Kaolin (Pttk) of cigarette smokers in Calabar, Cross-river State, Nigeria. Adv Med Dent Sci. 2001;3:17–20.
10. 10. Hassan A. Almarshad, Fathelrahman M. Hassan. Alterations in blood viscosity among young male cigarette smokers of Al-Jouf region in Saudi Arabia. Clini appl thromb hemost December 10, 2014.
11. 11. Pittilo RM: Cigarette smoking, endothelial injury and cardiovascular disease. Int J Exp Pathol 2000; 81:219–230.
12. 12. Waters D, Lesperance J, Gladstone P, Boccuzzi ST, Cook T, Hudgin R, Krip G, Higginson L. Effects of cigarette smoking on the angiographic evaluation of coronary atherosclerosis: a Canadian Coronary Atherosclerosis Intervention Trial (CCAIT) substudy. Circulation 1996; 94:614–621.
13. 13. Tsiara S, Elisaf M, Mikhailidis DP. Influence of smoking on predictors of vascular disease. Angiology 2003; 54:507–530.
14. 14. Freedman DS, Flanders WD, Barboriak JJ, Malarcher AM, Gates L. Cigarette smoking and leukocyte sub population in men. Ann Epidemol 1996; 6(4):299-306.
15. 15. Kawada T: Smoking-induced leukocytosis can persist after cessation of smoking. Arch Med Res 2004; 35:246–250.
16. 16. . Abel GA, Hays JT, Decker PA, Croghan GA, Kuter DJ, et al. Effects of biochemically confirmed smoking cessation on white blood cell count. Mayo Clin Proc 2005; 80(8):1022-1028.
17. 17. Blann AD, Lip GY. The endothelium in atherothrombotic disease: assessment of function, mechanisms and clinical implications. Blood Coagul Fibrinolysis. 1998; 9:297–306.
18. 18. Butkiewicz AM, Kemona-Chetnik I, Dymicka-Piekarska V, Matowicka-Karna J, Kemona H, Radziwon P. Does smoking affect thrombocytopoiesis and platelet activation in women and men? Adv Med Sci 2006; 51:123-126.
19. 19. Arslan E, Yakar T, Yavasoglu I. The effect of smoking on mean platelet volume and lipid profile in young male subjects. Anadolu Kardiyol Derg 2008; 8(6):422-425.
20. 20. Doll R, Peto R. Cigarette smoking and bronchial carcinoma: Dose and time relationships among regular smokers and lifelong non-smokers. J Epidemiol Community Health. 1978;32:303–13.
21. 21. Hioki, H., Aoki, N., Kawano, K., Homori, M., Hasumura, Y., Yasumura, T., Maki, A., Yoshino, H., Yanagisawa, A. and Ishikawa, K. 2001. Acute effects of cigarette smoking on platelet-dependent thrombin generation, Eur Heart J, 22, 56–61.
22. 22. Hunter, K.A., Garlick, P.J., Broom, I., Anderson, S.E. and McNurlan, M. 2001. Effects of smoking and abstention from smoking on fibrinogen synthesis in humans, Clin Sci , 100, 459–465.
23. 23. Nascetti, S., Elosua, R., Pena, A., Covas, M.I., Senti, M., Marrugat, J. and REGICOR Investigators. 2001. Variables associated with fibrinogen in a population-based study: interaction between smoking and age on fibrinogen concentration, Eur J Epidemiol. , 17(10), 953-958.

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