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Original Research Article

Changes in some coagulation parameters among male cigarette smokers in Southern Nigeria

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Abstract

Background: Cigarette smoking is a major public health problem globally. In view of this complexity, cigarette smoke has multiple diverse effects on human health and the coagulation system. These effects have not been adequately explored in our population and among Africans with increasing high rate of smoking.
Aim: This study was conducted to determine and compare the association between the duration of cigarette smoking and coagulation parameters (prothrombin time and activated partial thromboplastin time) in male cigarette smokers living in Calabar.
Materials and Methods: This is a prospective comparative study that which compared the levels of PT and APTT in 106 male smokers and 83 non-smokers which were used as control participants. Cigarette smokers were further divided into two groups based on the number of cigarette sticks smoked per day, mild smokers, those who smoked 1-19 sticks per day and heavy smoker, those who smoked 20 sticks and above per day. Whole blood was dispensed into a trisodium citrate bottle; PT and APTT were quantified using kits from Giesse Diagnostics Italy. The methods were controlled and validated using Giesse control reagents from the manufacturer.
Results: The mean PT and APTT for the male smokers were; 11.7+ 0.9secs and 28.7 + 2.9secs respectively. These values were significantly lower than those of the non-smokers with PT and APTT of 13.03 + 0.9secs and 29.8 + 3.4secs (P<0.05). A significant negative correlation was observed between duration of smoking, PT and APTT in the male smokers (P<0.05). There was also a negative correlation between the no of sticks smoked per day and PT in male smokers (r = 0.212).
Conclusion: Findings from this study indicate that cigarette smokers are at a high risk of developing clotting problems compared to non-smokers if appropriate interventions are not considered.
Keywords: Prothrombin time, activated partial thromboplastin time, smoking, cigarette.

1. Introduction

Cigarette smoking is a major public health problem globally and in Nigeria, Cigarette smoke contains a complex mixture of about four hundred (4000) chemicals some of which are toxic and at least sixty (60) causes cancer [1].

In view of this complexity, cigarette smoke has multiple diverse effects on human health. The negative effects and high mortality associated with it has caused several works to be done in the health sector and beyond. The prevalence of cigarette smoking varies across the globe with the highest prevalence in developing countries. According to World Health Organization WHO (2008) out of the 1.22 billion smokers, one (I) billion of them live in developing countries.

WHO (2001) reports that 15% of men and 2% of women smoke cigarette in Nigeria. Studies on the effect of cigarette smoking on Prothrombin Time (PT) and Partial Thromboplastin Time with Kaolin (PTTK), revealed that the mean PT and PTTK of smokers were significantly reduced when compared with non-smokers [2]. Elevated plasma fibrinogen concentration, ESR and plasma viscosity in cigarette smokers was also reported [3]. Higher concentration of Serum nitrite and serum Nitrosamine concentration was found in cigarette smokers [4].

The coagulation system occurs as a series of complex steps terminating in the formation of fibrin clot, it is divided into two parts. These are the extrinsic pathway and intrinsic pathway [5].Numerous epidemiologic studies reveals that cigarette smokers have been found to have higher risk of heart attack, sudden death, coronary heart disease, haemorrhagic stroke, cancer, non-cancerous lung disease, thrombosis, ischaemia and complications in human reproduction. In line

with these findings, this study intends to provide information on their predisposition to thrombosis associated with decrease PT and APTT

2. Materials and Methods

2.1 Selection of subjects

A total number of 106 healthy adult male cigarette smokers resident in Calabar metropolis were enrolled for the study. The cigarette smokers that participated in the study are those who have smoked 100 cigarette sticks during their lifetime and who currently smoke everyday or some days. Only male between the ages range of 15 to 55 were enrolled. Eight three (83) apparently healthy adult males who are non-smokers (active and passive) were used as control subjects in this research.

A structured questionnaire was used to get data from each individual enrolled in the study, detailing his/her family history, age, sex, occupation, drinking habit, smoking habit and whether or not on medication that may affect test results.

2.2 Ethics statement

Ethical approval for the research was obtained from Cross River State Ministry of Health Research Ethic Committee Calabar, Nigeria. The subjects who participated in the study were educated on what the research was all about. Their consent was sought for and each participant signed a consent form prior to the study.

2.3 Sample collection

Four and a half milliliters (4.5mls) venous blood was collected under aseptic conditions and with minimal stasis from each subject using sterile syringe and needle from the ante- cubital vein. The blood sample was added into 0.5mls of 3.13% trisodium citrate for prothrombin time test (PT), Activated partial thromboplastin test (APTT).The samples were transported to the laboratory for analysis within one (1) hour of collection.

2.1 Quantitative determination of Prothrombin Time in the blood (method of Giesse)

Principle

PT is used as a screening tool and as a quantitative test for coagulation factors in the extrinsic and common pathways. The test will be prolonged in patients with Acquired or congenital disorders that reduce the activity of factor I (fibrinogen), II (prothrombin), V, VII and X. the PT is also widely used to monitor oral anticoagulant therapy. Oral anticoagulant reduces the activity of vitamin K-dependent clotting factors (II, VII, IX, X, protein C and protein X) and the PT is prolonged as a result. The kit measures the clotting of plasma after adding a source of tissue factor (thromboplastin and calcium. The recalcification of plasma in the presence of tissue factor generates activated factor Xa

(F.Xa). F.Xa, in turn, activates prothrombin to thrombin which converts fibrinogen to insoluble fibrin clots.

Reference Range: 11-15 seconds.

2.2 Quantitative Determination of activated partial thromboplastin test (APTT) using Giesse Diagonistics kits

Principle:

The kit is intended for use in performing the Activated Partial Thromboplastin Time (APTT) test, and for APTT based factor assays using ellagic acid activator. It is a test for the intrinsic coagulation factors; it's sensitive to deficiencies of all plasma clotting factors except factor VIII, IX, XI, XII and prekallikrein. The APTT is also commonly used to monitor heparin therapy since APTT prolongation is directly proportional to increasing amounts of heparin.The APTT test is performed by adding reagent containing a plasma activator and phospholipid to the test specimen .This mixture is incubated for 3 minutes at 37^0C for optimum activation. Calcium chloride is added and clot formation is timed.

Reference Range: - 24-35 seconds

2.3 Statistical analysis

Data was presented as mean ± SD. Data from 2 groups were compared using students 2 tailed t-test for paired samples. Data between groups were compared using a one way analysis of variance (ANOVA) Statistical Package for Social Science (SPSS) version 14 was used in all the statistical analysis.

3. Results

Prothrombin time (PT) and activated partial thromboplastin time (APTT) were determined in 106 male cigarette smoker and 83 male non-smokers.

Table 1 show the mean prothrombin time and activated partial thromboplastin time in male smokers and non-smokers which were used as control subjects. The result revealed that the mean values of PT and APTT were significantly lower in smokers compared to the control participants ($P < 0.05$).

Cigarette smokers were further divided into two groups based on the number of cigarette sticks smoked per day, mild smokers, those who smoked 1-19 sticks per day and heavy smoker, those who smoked 20 sticks and above per day. Prothrombin time and activated partial thromboplastin time were compared between the two groups. These comparisons are shown in table 2. Results from the table show that the mean values of PT was significantly lower in heavy smokers compared to the mild smokers ($P < 0.05$). No significant difference was observed in the mean values of APTT between the two groups ($P > 0.05$).

Table 1: Comparison of prothrombin time and activated partial thromboplastin time in smokers and control group

| Parameters	Smokers (n=106)	Control (n=83)	Calculated 't' value	Critical 't' value	P-value	Remarks
AGE (years)	30.39±8.68	29.90±9.11	1.35	1.96	<0.05	NS
PT(seconds)	11.68±0.96	13.04±0.90	9.89	1.96	>0.05	S
APTT (seconds)	28.74±2.87	29.81±3.40	2.34	1.96	>0.05	S

Mean ± SD

Table 2: Comparison of prothrombin time and activated partial thromboplastin time in smokers based on number of cigarette sticks smoked per day

| Parameters	Mild (1-19sticks) Per day (n=75)	Heavy(>20 sticks) Per day (n=31)	Calculated 't' value	Critical 't' value	P-value	Remarks
PT(seconds)	11.81±0.94	11.35±0.95	2.28	1.96	>0.05	S
APTT (seconds)	28.77±2.99	28.65±2.59	0.21	1.96	>0.05	NS

Mean ± SD

Correlation analysis was carried out for duration of exposure and prothrombin time in the smokers. Prothrombin time correlated positively with duration of exposure in the cigarette smokers (r = 0.249, P < 0.05) as revealed in Figure 1. Figure 2 shows a significant positive correlation (r = 0.234, P <0.05) between duration of exposure and activated partial thromboplastin time in the smokers
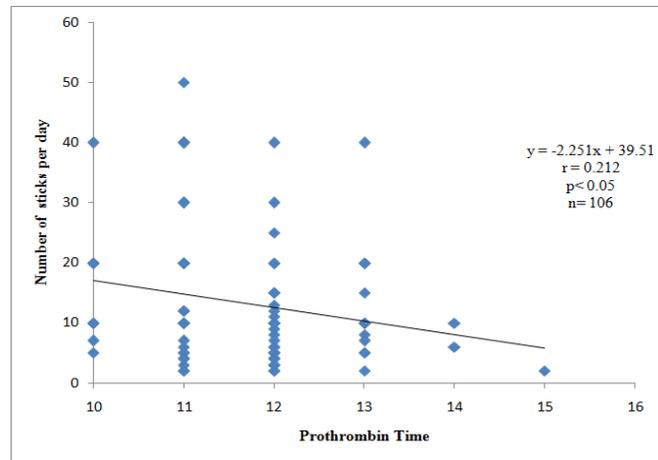
There was also a positive correlation between the numbers of sticks smoked per day and prothrombin time in the smokers as shown in figure 3 (r = 0.212, P < 0.05).
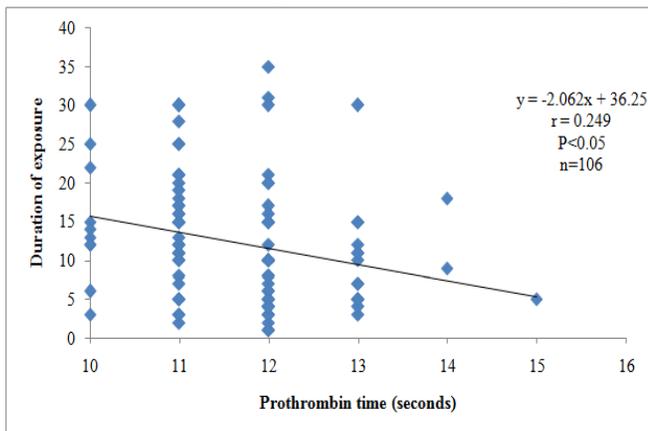
Figure 1: Correlation plot of duration of exposure against prothrombin time in the smokers group
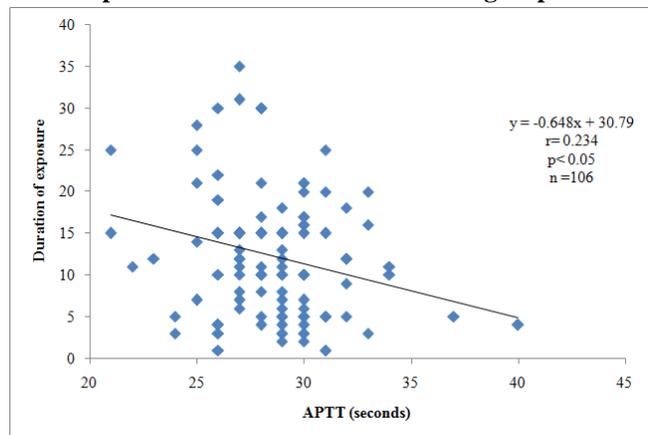
Figure 2: Correlation plot of duration of exposure against activated partial thromboplastin time in the smokers.

Figure 3: Correlation plot of no of sticks per day against prothrombin time in smokers.

4. Discussion

Smoking injures blood vessel walls by damaging endothelial cells, thus increasing permeability to lipids and other blood components. It is a major health problem that results in significant morbidity and mortality. This study was conducted to determine and compare the association between the duration of cigarette smoking and coagulation parameters (prothrombin time and activated partial thromboplastin time).

Prothrombin time (PT) and activated partial thromboplastin time with kaolin (PTTk) were investigated in 189 volunteers in Calabar, Cross-River state of Nigeria comprising 106 male cigarette smokers and 83 age and sex matched non-cigarette smokers.

The PT and APTT are the most commonly performed tests of hemostasis. The PT evaluates the extrinsic pathway of coagulation, whereas the APTT evaluates the intrinsic pathway of coagulation. In this study, the levels of prothrombin time and activated partial thromboplastin time were significantly lower (P <0.05) in cigarette smokers compared to the non-smokers control group. This indicates greater clotting activities in cigarettes smokers which can predispose them to thrombosis. During surgery, care should be taken since smokers are at the risk of thromboembolism due to increased thrombin generation. For decades,

epidemiological data have demonstrated the association of smoking with the incidence of coronary heart disease, myocardial infarction and stroke.

The findings of this study also revealed that heavy smokers who smoked greater than 20 sticks of cigarette per day had significantly lower prothrombin time compared to the mild smokers who smoked less than less than 20 sticks per day (P<0.05). Also, a negative significant association was observed between the number of sticks smoked per day and prothrombin time (P<0.05). This is in line with the study of Mohammed, 2010, who showed that heavy smokers had significantly lower clotting factor compared to the mild smokers. This marked difference in prothrombin time between these two groups of smokers could be as a result of the fact that increased smoking activities increases clotting activities in smokers thus resulting in the reduction of clotting factors such as prothrombin as seen in this study.

A significant negative relationship was also observed between prothrombin time and duration of smoking and activated partial thromboplastin time (APTT) and duration of smoking. This association further reveals the effect of smoking on clotting factor. The duration of smoking is calculated from the numbers of years an individual has been involved in smoking. The correlation shows that as the years of smoking increases, the clotting factors decreases.

It can be deduced from this study that age had no effect on the PT and APTT of cigarettes smokers. A striking feature in this research is that more than 50% (72 out of 106) of the smokers enrolled fell within the age range of 15 – 30 years. This has provided information that will aid cigarette control groups to focus and target this age range. Our finding also revealed that cigarette smoking habits start from that age range also.

5. Conclusion

From this study, it can be concluded that cigarette intake as well as duration of smoking reduces prothrombin time (PT) and activated partial thromboplastin time (APTT) values, thus may predispose cigarette smokers to rheologic abnormalities.

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