C-REACTIVE PROTEIN AND FIBRINOGEN LEVELS IN SMOKERS WITH CORONARY ARTERY DISEASE

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Introduction

Cigarette smoking is a major modifiable risk factor for the development of cardiovascular diseases. Smoking is associated with alteration in lipid profile, coronary vasomotor reactivity, platelet aggregation, and prothombotic states. These are the main factors related to atherosclerosis. Cigarette smoking is also associated with increase in several inflammatory markers such as C-reactive protein (C-RP), interleukin -6 and tumor necrosis factors-α. These inflammatory responses are essential factors for initiation and the development of atherosclerosis. Since smoking has a fairly high prevalence in Sri Lanka, we assessed the CRP and fibrinogen concentrations of male patients awaiting Coronary Artery Bypass Graft surgery both smokers and non-smokers to study their association with disease severity score.

Materials and Methods

The study is a cross sectional descriptive study carried out at the Cardio-thoracic Unit of Sri Jayewardenepura General Hospital. The ethical approval was obtained from University of Sri Jayewardenepura (Approval No.635/12) and Sri Jayewardenepura General Hospital. There were 64 (age 56.9 ± 10) male patients in the study group. C-RP was determined using immuno-turbidometry assay and fibrinogen was determined by thrombin time. An interviewer administered questionnaire was used to collect data on smoking. Coronary Artery Disease (CAD) severity was evaluated by Gensini score (Gensini 1975). The Gensini score was computed by assigning a severity score according to the degree of luminal narrowing and geographical importance of each coronary stenosis as seen in the coronary angiogram. The assigned severity score according to the degree of luminal narrowing was multiplied by a factor considering the geographical importance of coronary artery (Table 1). The sum of all coronary arteries was expressed as the Genisini score. Mann-Whitney U test was used to analyse the result (SPSS version 16).

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Results and Discussion

The results of the study are presented in Table 2. Among the total study population more than 2/3 was smokers. Smokers had significantly high C-RP (U=320, p< 0.05) and fibrinogen (U=285, p< 0.05) level compared to non-smokers. The concentrations of both parameters of 20 -25 % of smokers were closer to the upper limit of the normal or higher. Previous studies have reported that increase in CRP and fibrinogen in smokers compared to non-smokers (Bazzano et al. 2003).

Table 1. Assigned score according to luminal narrowing and multiplying factor according to location of lesion

Degree of luminal narrowing %	Assigned severity score (a)	Geographical location of lesion	Multiplying factor (b)
30 – 50	1	Left main coronary artery (LMCA)	05
51 – 70	2	Proximal Left anterior descending (LAD) or proximal circumflex (LCX)	2.5
71 – 90	4	Mid LAD	1.5
91 – 99	8	Distal LAD, 1st diagonal, mid LCX,distal LCX, obtuse marginal, proximal right coronary artery (RCA), mid RCA, distal RCA, posterior descending artery (PDA)	1.0
100	16	2nd diagonal, posterolateral ventricular branch (PLV)	0.5

Note: Gensini score = a × b

Previous prospective cohort studies revealed elevated CRP and fibrinogen associated positively with ischemic heart disease (Danesh et al. 1997). According to Tracy et al. (1997) Smoking is associated with dose-dependent and time-dependent increase in C-RP concentration in both men and women. However, there was no significant difference in C-RP and fibrinogen, irrespective of the number of cigarettes (> 5 per day or < 5 per day) smoked or the duration (> 10 years or < 10 years) in the present study. Also CRP and fibrinogen of smokers who have stopped smoking (>10 yrs) and who currently smoke were also not significantly different. This also emphasizes that duration and quantity had not affected C-RP and fibrinogen in this study group.

Although the association of cigarette smoking and development of cardiovascular diseases have been reported, the dose dependent correlation between risk of cardio vascular events and number of cigarettes smoked or the pack-years exposure were not confirmed (Price et al. 1999). We also noted that the individuals who had stopped smoking before 10 years also had comparatively lower values for the Gensini score than those who had stopped smoking < 10 years ago.

Table 2. Result of the CRP, fibrinogen and Gensini score of individuals

Smoking status	Frequenc y (%)	CRP concentration (mg L^{-1}, median-Inter quartile range)		Fibrinogen concentration (mgdL^{-1}, median-Inter quartile range)		Gensini score (mean ± SD)	
Smokers	67	5.2 (8.0)	P=0.0 2	302 (53)	P=0.0 2	48 (23)	P=0.9
Non smokers	33	2.8 (3.2)		273 (65)		52 (27)	

From the individuals of smoking (n = 41), according to number of cigarette smoke per day

| >5 per day | 60 | 5.2 (8.0) | P=0.9 | 302 (60) | P=0.5 | 54 (24) | P=0.1 |
| <5 per day | 40 | 4.9 (9.6) | | 290 (84) | | 41 (22) | |

From the individuals of smoking (n = 41), according to number of years smoke

| >10 years | 79 | 5.2 (7.7) | P=0.9 | 309 (46) | P=0.1 | 50 (23) | P=0.5 |
| <10 years | 21 | 5.4 (9.4) | | 290 (72) | | 41 (26) | |

Individuals of smoked previously (n = 34), according to number of years cessation of smoking

| >10 years | 40 | 4.5 (6.7) | P=0.0 5 | 296 (131) | P=0. 9 | 35 (44) | P=0.07 |
| <10 years | 60 | 5.6 (20.4) | | 300 (30) | | 55 (42) | |

Note: *The normal range for CRP and fibrinogen is < 6mg L^{-1} and 150 – 400 mg dL^{-1}, respectively.

Conclusions and Recommendations

Smokers had significantly increased CRP and fibrinogen concentrations compared to non-smokers. There was no significant difference in CRP and fibrinogen, irrespective of the number of cigarettes (> 5 per day or < 5 per day)

smoked or the duration (> 10 years or < 10 years).Even though not significant those who had smoked for more than 10 years had higher Gensini score compared to those who smoked for <10 year. This indicate that the severity of the CAD is less in the individuals who stopped smoking before 10 years compared to individuals stopped smoking < 10 years ago. Even though this is not significant it indicates the severity of CAD is reduced if the period of smoking is less.

Acknowledgment

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