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ORIGINAL ARTICLE

Acute effects of cigarette smoking in habitual smokers, a focus on endothelial function

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KEYWORDS

Cigarette smoking;
Aortic distensibility;
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Abstract *Background:* The chronic effect of cigarette (cig.) smoking is well established. The acute effect of smoking abolishes the concept, argued by heavy smokers, to decrease the number of smoked cigarettes instead of quitting.

Aim: To detect the acute effects of cigarette smoking and the duration of these effects.

Patients and methods: Thirty four smokers (age 21–35 years) were studied at 3 occasions; 9 h after the last cig. smoking, 5 min after one cig. smoking and 30 min after 3 cig. smoking within 30 min. They were subjected to measurement of both ventricular functions using standard and tissue Doppler imaging (TDI), aortic distensibility, stiffness and endothelial function assessment by endothelium-dependent flow-mediated dilatation (FMD) and maximum vasodilatation.

Results: After one cigarette smoking, we found a statistically significant effect on blood pressure, Heart Rate, FMD percent, Dilation Ratio, aortic distensibility ($P = 0.007$), and aortic stiffness index (ASI) ($P = 0.01$). Furthermore the LV diastolic function was significantly impaired after smoking. Despite disappearance of acute effect of 3 cig. smoking within 30 min on blood pressure, Heart Rate and aortic distensibility, a significant difference was still found as regards FMD percent and dilation ratio denoting the extension of the endothelial dysfunction for more than 30 min after the last cigarette.

Conclusion: Many acute changes occur following one cigarette smoking even in habitual smokers. Persistence of endothelial dysfunction parameters after smoking indicates the failure of circulation adaptation in response to such offense that might contribute to the precipitation of acute events in vulnerable patients.

1. Background

Smoking is one of the most important modifiable risk factors for coronary artery disease. Almost one in five adults is a current smoker in western societies and the numbers are higher in developing countries.[1]

Endothelial dysfunction, an early phenomenon in atherogenesis, has been described in brachial arteries of healthy chronic and passive smokers.[2] Long-term smoking gradually

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impairs the endothelial function in habitual and passive smokers, but it is still unclear whether smokers and nonsmokers have different acute responses regarding the endothelial dysfunction caused by cigarette smoking.[3]

2. Aim of the work

The aim of this work is to examine the acute effects of cigarette smoking on some circulatory parameters and the duration of these effects.

3. Patients and methods

This prospective, case-control study was carried out at the cardiology department, Al-Minia University Hospital, during the period from September 2009 to January 2010. Thirty four male healthy chronic smokers (Age < 35 years) were studied under 3 situations:

- Occasion 1: 9 h after last cigarette smoking.
- Occasion 2: 5 min after 1 cigarette smoking.
- Occasion 3: Half an hour after smoking 3 cigarettes within 30 min.

Subjects with any of the following criteria had been excluded from the Study:

1. Hypertension: either by history or by blood pressure measurement.
2. Other cardiovascular diseases (e.g., rheumatic, congenital, ischemic . . .etc.)
3. Diabetes: either by history or by estimation of fasting blood sugar (> 126 mg /dl).

All participants were subjected to:

- History and clinical examination for smoking index, exclusion of any cardiovascular diseases and diabetes and blood pressure measurement. Normal Bp was defined as < 140/90 mmHg.
- Laboratory assessment of fasting blood sugar and lipogram.
- Standard 12-lead ECG.
- Standard Echocardiography using General Electric vivid 3 ultrasound unit equipped with 2.5–3.5 MHz transducer. All measurements represent a mean of at least three consecutive cardiac cycles. Normal Diastolic function was defined as E/A ratio > 1. Ejection fraction (EF) was obtained by M-mode approach.
- Assessment of the Endothelial Function.

Endothelial function was assessed by measuring brachial artery flow–mediated vasodilation using a high-resolution 7.5 MHz ultrasound probe before and after one minute release from 5 min occlusion of the brachial artery[4](Fig. 1) and comparing it with total vasodilatation capacity of the blood vessel 5 min after sublingual administration of 5 mg isosorbide mono-nitrate.

4. Evaluation of aortic elastic properties

The aortic stiffness is measured using the following formulae[5]:

- Aortic diameter change (mm) = SD – DD.
- Aortic strain index = (SD − DD) × 100/DD.
- Aortic stiffness index = *ln*(SBP/DBP)/aortic strain.
- Aortic distensibility = (2 × strain)/(SBP—DBP).

Where SBP and DBP are the systolic and diastolic Bp respectively, SD is systolic aortic diameter and DD is diastolic aortic diameter measured with echocardiography 3–4 cm above the aortic valve from a transthoracic parasternal long-axis view and ln is the natural logarithm.

5. Statistical methods

Data were analyzed using Statistical Package for the Social Sciences (SPSS) v 10. Non-parametric variables were presented as numbers and % and compared using Chi-square test, while parametric data were expressed as mean ± standard deviation and compared using Student's paired *t*-test. Pearson's co-efficient (*r*) was used for correlation studies of any two variables. A probability level of $p < 0.05$ is considered significant in all tests.

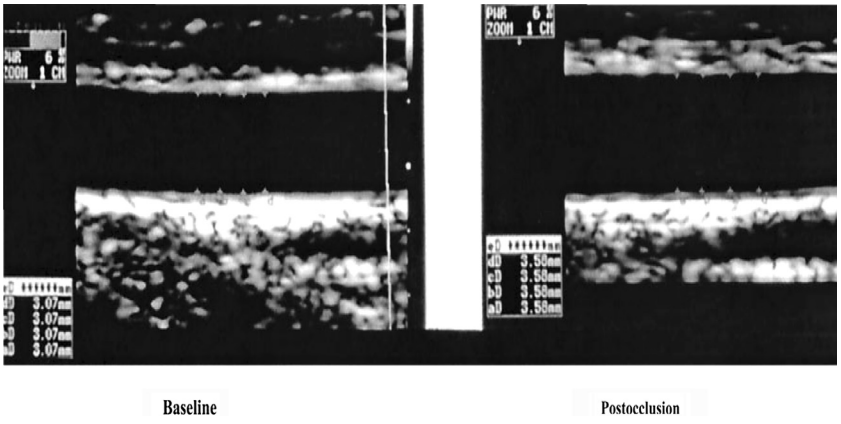

Figure 1 Ultrasound images of a brachial artery under baseline and after cuff-occlusion conditions.

Table 1 Demographic data of the participants (n = 34).

	Range	Mean ± SD
Age	35–21	27.6 ± 3.55
Cig/day	30–6	15.68 ± 6.16
Smoking duration (years)	16–2	8.61 ± 3.5
Smoking Index	360–20	138.53 ± 83.82
Fasting blood glucose (FBG)	110–77	95.79 ± 9.92
Cholesterol (total)	200–125	169.65 ± 17.61

Table 2 Comparison of hemodynamic parameters between occasions 1 and 2.

	Occasion 1	Occasion 2	P value
Systolic blood pressure	118.53 ± 9.25	128 ± 10.51	0.001
Diastolic blood Pressure	73.71 ± 6.15	79.53 ± 7.47	0.001
Heart rate	73.29 ± 8.68	79.03 ± 10.62	0.01
Pulse pressure	44.82 ± 8.92	48.29 ± 11.06	NS

Table 3 Comparison of aortic elasticity parameters between occasions 1 and 2.

	Occasion 1	Occasion 2	*P* value
AOS	3.23 ± 0.33	3.35 ± 0.31	0.048
AOD	3.06 ± 0.33	3.26 ± 0.31	0.020
Aortic strain	5.42 ± 2.92	3.2 ± 0.83	0.008
Aortic distensibility	2.48 ± 1.29	1.4 ± 0.4	0.001
ASI	10.09 ± 3.62	16.66 ± 4.99	0.001

AOS = Aortic diameter in systole, AOD = Aortic diameter in diastole.
ASI = Aortic stiffness index.

6. Results

The demographic data of the studied group are summarized in (Table 1).

Acute effects of one cigarette smoking are presented in Table 2 that shows a significant increase in blood pressure and heart rate but not the pulse pressure in occasion 2 compared to occasion 1

On the other hand, there was a statistically significant decrease in all aortic elasticity parameters in occasion 2 compared to occasion 1 (Table 3).

Table 4 Endothelial function parameters in groups 1 and 2.

	Occasion 1	Occasion 2	*P* value
Pre FMD	0.43 ± 0.055	0.42 ± 0.53	0.7
Post FMD	0.48 ± 0.6	0.45 ± 0.06	0.05
FMD %	11.8 ± 0.75	6.52 ± 0.86	0.001
Pre GTN	0.43 ± 0.05	0.43 ± 0.06	0.85
Post GTN	0.52 ± 0.07	0.51 ± 0.07	0.68
GTN %	20.21 ± 2.04	19.37 ± 2.18	0.1
Dilation Ratio	0.59 ± 0.07	0.34 ± 0.06	0.001

FMD = Flow mediated dilation GTN = Glyceryl Trinitrate induced dilation.

Table 5 Echocardiographic systolic and diastolic functions in Occasions 1 and 2.

	Occasion 1	Occasion 2	*P* value
EF	65.32 ± 4.57	65.91 ± 3.99	0.57
Mitral E/A ratio	1.38 ± 0.20	1.16 ± 0.17	<0.001
Tricuspid E/A ratio	1.35 ± 0.18	1.1 ± 0.16	<0.001

EF = Ejection fraction.

Table 6 Endothelial function parameters in occasions 1 and 3.

	Occasion 1	Occasion 2	*P* value
Pre FMD	0.43 ± 0.055	0.43 ± 0.056	0.9
Post FMD	0.48 ± 0.6	0.47 ± 0.06	0.54
FMD %	11.8 ± 0.75	9.3 ± 0.77	<0.001
Pre GTN	0.43 ± 0.05	0.43 ± 0.06	0.9
Post GTN	0.52 ± 0.07	0.52 ± 0.07	0.95
GTN %	20.21 ± 2.04	19.7 ± 2.15	0.33
Dilation Ratio	0.59 ± 0.07	0.48 ± 0.06	<0.001

FMD = Flow mediated dilation.
GTN = Glyceryl Trinitrate induced dilation.

Furthermore, the endothelial function parameters were significantly impaired in occasion 2 as compared to occasion 1 (Table 4).

Moreover, there was a significant deterioration in ventricular diastolic function in occasion 2 compared to occasion 1 while the ejection fraction remained unchanged in both occasions (Table 5).

7. Comparison between occasion 1 and 3

Comparing occasions 1 and 3 showed no significant differences regarding hemodynamic parameters, aortic elasticity parameters, systolic and diastolic functions denoting returning of all these parameters to the baseline in less than 30 min after smoking. Meanwhile, there was a statistically significant difference between both occasions as regards FMD percent and dilation ratio (Table 6, Figs. 2 and 3) denoting extending endothelial dysfunction for more than 30 min.

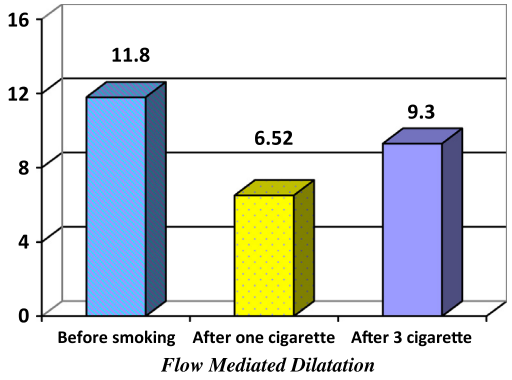

Figure 2 Comparison between means of FMD percent between study occasions.

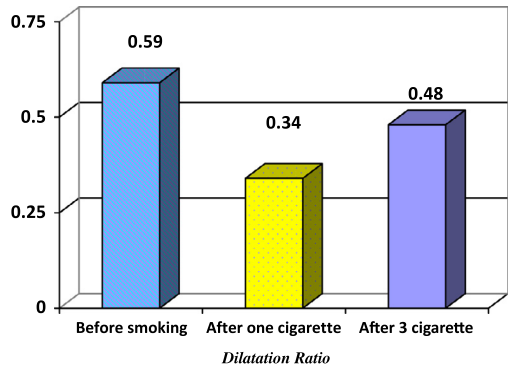

Figure 3 Comparison between means of dilation ratio between study occasions.

Table 7 Correlation of smoking index with variables below (in group 1).

Variables	Pearson's coefficient (r)	P value
Flow mediated dilatation %	0.15	0.4
Dilation ratio	0.19	0.29
Aortic distensibility	0.08	0.64
Aortic stiffness index	0.08	0.64
Ejection fraction	0.06	0.72

8. Comparison between occasions 2 and 3

There was a statistically significant increase in the hemodynamic parameters, a statistically significant decrease in the aortic elasticity and endothelial function parameters in occasion 2 compared to occasion 3.Also, there was a significant deterioration in diastolic function in occasion 2 compared to 3 while no significant difference in systolic function between both occasions.

As shown in Table 7 no significant correlation of smoking index was found with FMD%, dilation ratio, aortic distensibility, ASI. or EF. in all groups.

9. Discussion

Numerous prospective investigations have demonstrated a substantial decrease in CHD mortality for former smokers compared with that of the continuing smokers.[6] Furthermore, the patient who has recently developed a clinical illness is very motivated to quit smoking. Several studies have shown that intervention in this "teachable moment" can be very effective as the provision of smoking cessation advice is associated with a 50% long-term (>1 year) smoking cessation rate in patients who have been hospitalized with a coronary event, and even modest telephone-based counseling can increase this percentage to 70% in a particularly cost-effective manner.[7]

Our results revealed that smoking only one cigarette immediately induced acute hemodynamic changes in the form of increased heart rate, systolic blood pressure, and diastolic blood pressure. These acute changes disappeared within an hour despite continuing smoking (3 cigarettes Smoking in one hour). These results are similar to those of Kim et al., 2005 who found that heart rate as well as systolic and diastolic blood pressure increased immediately after smoking, and returned to baseline values at 5–15 min after smoking.[8] These hemodynamic changes may be attributed to nicotine that temporarily decreases nitrate, nitrite, and serum antioxidant concentrations in the plasma and is associated with accelerated heart rate and higher blood pressure.[9]

Cigarette smoking yielded an acute deterioration in left ventricular (LV) diastolic function as well as right ventricular diastolic function after smoking one cigarette as assessed by conventional transmitral and transtricuspid flow velocities by Doppler imaging with no changes in systolic function. These changes disappeared significantly within one hour after smoking (even after 3 cigarette smoking). The evidence of changes in LV diastolic function after cigarette smoking is also in accordance with the current available data as Kim et al., 2005 revealed a significant acute deterioration in left ventricular (LV) diastolic function after smoking one cigarette for 30 min in healthy volunteers, whereas for 75 min after smoking in patients with diabetes and no significant changes in systolic LV function.[8] The acute deterioration in RV diastolic function as well as LV diastolic function is similar to the results of a study of Giacomin et al., 2008 that evaluated the acute effects of caffeine and cigarette smoking on ventricular function in healthy subjects.[10] Similarly, Ilgenli, et al., 2007 studied acute effects of smoking on right ventricular function by evaluating twenty healthy young males by echocardiography before and after smoking one cigarette. Both right and left ventricle diastolic functions were impaired significantly with no change at systolic functions. Pulmonary artery pressure increased significantly concomitant with the impairment of right ventricular diastolic function. All the changes seen after smoking a cigarette almost returned to baseline levels after 30 min.[11]

The present study demonstrates that smoking clearly influences the elastic properties of the aorta and results in acute deterioration of ascending aortic elastic properties (Aortic strain, aortic distensibility and aortic stiffness index) in young subjects included in this work and returned to baseline values within an hour after smoking. (Even with 3 cig. Smoking). Our results are similar to the results of a study of Sassalos et al., 2006 who studied the acute and chronic effects of cigarette smoking on the elastic properties of the ascending aorta in healthy male subjects. They revealed that cigarette smoking acutely results in a deterioration of ascending aortic elastic properties in healthy male subjects.[12] It is well known that smoking results in sympathetic activation.[13] Furthermore, active smoking induces systemic inflammation.[14] So, mechanisms through which smoking may decrease aortic elastic properties may include sympathetic activation[15]and inflammation.[16]

Christodoulos et al., 1997 reported that the deterioration of aortic elastic properties was the net result of the combination of the passive distention of the aorta due to an increase in blood pressure and the active stiffening of the vessel due to elevated muscular tone.[17] However, the mechanism of the impairment of the elastic properties of the aorta might also be related to the impaired endothelial function of the aortic wall itself as shown in our study.

The current study revealed that flow-mediated dilatation which is an endothelial dependent dilatation was significantly impaired within 5 min after only one cigarette smoking. In contrast to other parameters, this deleterious effect on endothelial function was maintained for at least 1 h without

development of tolerance. These results are in accordance with the current available data as Karatzi et al., 2007 compared acute endothelial dysfunction caused by smoking one cigarette between smokers and nonsmokers and found that cigarette smoking caused a significant decrease in flow-mediated dilatation (FMD) in both smokers and non-smokers. Endothelial dysfunction after cigarette smoking remained significant for one hour in smokers and non-smokers.[18]

Also, our results are similar to those of Lekakis et al., 1998 that evaluated the effect of acute cigarette smoking on endothelium-dependent brachial artery dilatation in healthy individuals and showed that flow-mediated dilatation of systemic arteries is impaired after short-term smoking. This reduction in vasodilator capacity might lower the threshold for ischemia when the metabolic demand increases in patients with peripheral vascular disease.

The persistence of smoking induced endothelial dysfunction more than one hour leads to a conclusion that habitual smokers (e.g., 1 cigarette every hour) suffer endothelial dysfunction for a long period during the day, even without permanent endothelial damage. It is likely that after multiple smoking exposures, some lasting damage on endothelial function may occur despite the absence of correlation between smoking index and different parameters (FMD, Dilation Ratio, Aortic Distensibility, ASI and EF). Furthermore, this persisting deleterious effect on endothelium could contribute to acute cardiovascular events and accelerated atherogenesis.[19]

10. Conclusion

Many acute changes occur following smoking only one cigarette even in habitual smokers. Persistence of endothelial dysfunction parameters for more than 30 min after smoking indicates the failure of circulation adaptation in response to such offense and habitual smoking (e.g., 1 cigarette every hour) could be associated with endothelial dysfunction for a long period during the day that might contribute to the precipitation of acute events in vulnerable patients.

11. Limitations

Our study population consisted only of young male subjects, so our results may not be applicable to other population groups. Healthy participants were selected by a normal history and normal findings at the resting ECG and echocardiography. No stress test was performed. It is unclear whether any of the participants had silent myocardial ischemia. However none of the participants showed any sign of wall motion abnormality after smoking.

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