ACUTE EFFECT OF CIGARETTE SMOKING ON VENTRICULAR REPOLARIZATION PARAMATERS

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Background: *Acute cigarette smoking has been reported to increase heart rate and blood pressure as a consequence of sympathetic stimulation. In this study we sought to determine if single dose cigarette smoking influences ventricular repolarization paramaters in habitual smokers.*

Method and Results: *The study population consisted of twenty-four long-term heavy smokers. A 12-lead surface ECG recorded at a paper speed of 50 ms/s was obtained from all participants before and average 15 min. after cigarette smoking. Maximum QT (QTmax), minimum QT (QTmin) intervals, QT dispersion (QTd) and corrected QT dispersion (QTcd) were calculated on each ECG record. QT and RR intervals in V2 leads (QTV2 and RRV2) were also measured before and after smoking. Hart rate and RRV2 significantly increased after smoking a cigarette (67±7 vs. 72±8 beat/min, 984±169ms vs. 875±150ms, respectively p<0.05). However, the other parameters including QTmax, QTmin, QTd, QTcd and QTV2 did not alter compared to baseline values.*

Concusion: *Single dose cigarette smoking does not seem to be associated with ventricular heterogeneity both in habitual smokers although it leads to sympathetic hyperactivity.*

Key words: *Cigarette smoking, ventricular repolarization, and arrhythmia.*

Cigarette smoking is one of the strongest contributors to the risk of cardiovascular diseases, including coronary heart disease, stroke, sudden death, peripheral artery disease, and aortic aneurysm.1-2 Acute cardiac events, such as ventricular fibrillation and sudden death, are increased by cigarette smoking, particularly in the presence of preexisting coronary disease.3 Moreover, smoking as few as one to four cigarettes per day has been found to be associated with a doubling of risk for coronary artery disease.4 It has also been shown that short-term cigarette smoking causes an increase in blood pressure and heart rate and sympathetic outflow.5 More

recently, it has also been shown that acute cigarette smoking alters carotid artery flow and impairs vascular endothelial function.6,7 Sympathetic nerve hyperactivity caused by smoking has been reported to be one of the reasons for sudden death.8,9 However, the mechanisms through which cigarette smoking exerts its deleterious effects are understood only incompletely.

Prolonged QT interval and increased QT dispersion (QTd) have been shown to be related to the occurrence of ventricular arrhythmias and sudden death.10,11 It has also been shown that changes in autonomic nervous system may influence QT interval duration and QTd.12-16 Accordingly, the influence of cigarette smoking on the autonomic nervous system has been well documented. Besides, although the previous studies have extensively studied the effect of cigarette smoking on QT interval duration and QTd, conflicting results have been reported.17-23 Moreover, the short-term effect of cigarette smoking has not been adequately clarified. We wanted to test the hypothesis that acute sympathetic and hemodynamic responses to cigarette smoking could affect QT interval duration and dispersion. Therefore, the objective of this study first, was to assess whether single dose cigarette smoking influences ventricular repolarization paramaters in habitual smokers.

METHOD

Twenty-four healthy long-term heavy smokers (18 males and 6 females, mean 31±5 age, with smoking habit of ? 1 pack/day) were included to the study. A complete physical and echocardiographic examination was performed before the study. All study subjects were free from the other risk factors for coronary artery disease and no subject was receiving any medication at the moment of study. All subjects were asked to refrain from smoking, food intake and caffeine containing beverage at least 8 hours before attending the study. The subjects were taken to the test room and rested in supine position at least 15 minutes on a comfortable bed to stabilize heart rate and the 12-lead ECG records at a paper speed of 50-mm/s and 2mv/cm standardization were obtained from all participants. After completion of baseline records, all participants were asked to smoke a cigarette (1.1 mg nicotine, 15 mg tar) and inhalation of smoke was encouraged. Then, second ECG records were obtained average 15 minutes after smoking. The QT interval was measured from the beginning of the QRS complex to the end of the T wave. QT maximum (QTmax) and minimum QT (QTmin) was measured in all leads of the 12-lead ECG recorded at a speed of 50 mm/s for 2 consecutive cycles. QTd was defined as the maximum minus minimum QT intervals, and corrected QT dispersion (QTcd) was measured according to Bazett's formula to adjust heart rate.24 If the T wave could not be reliably determined or if it had very low amplitude QT measurements were not obtained, and these leads were excluded from the analysis. For QT interval measurement we selected the QT interval in V2 leads (QTV2), since right precordial leads were reported to be the most reliable leads.25 RR intervals in V2 leads (RRV2) were also measured before and after smoking.

STATISTICAL ANALYSIS

All data were presented as mean value ± SD. ECG parameters before and after cigarette smoking were tested by Wilcoxon signed-rank test. Intra and inter-observer variability for ECG measures was tested by Pearson's correlation coefficient and it yielded minimal variability ($r=0.97$ $p<0.0001$ and $r=0.95$ $p<0.0001$, respectively). Relation between the number of years

of habitual smoking and the number of cigarettes smoked per day, and ECG parameters were assessed by Pearson's correlation coefficient. A p value <0.05 was considered as statistically significant.

RESULTS

On physical examination no clinically significant disorder were detected in any of the study subjects. Echocardiographic examination revealed no significant cardiac disorder. All study subjects had sinus rhythm. The number of the leads in which QT interval duration could be measured ranged from 8 to 12 leads. Either QTV2 or QTd and QTcd remained unchanged after smoking one cigarette while heart rate and RRV2 significantly increased (Table-1). In addition, there was no significant correlation between the number of years of habitual smoking, the number of cigarettes smoked per day, and QTcd, or QT interval in smoker group.

Table 1. Comparison of QT interval duration and dispersion before and after smoking a cigarette.

Variable	before smoking	after smoking	p values
QTmax, ms	390±18	400±25	NS
QTmin, ms	355±14	364±23	NS
QTd, ms	35±11	36.5±16.6	NS
QTcd, ms	34.9±12.5	39.7±17	NS
QTV2, ms	370±16	378±13	NS
RRV2, ms	984±169	875±150	0.001
Heart rate, beat/min.	67±7	72±8	0.014

NS: Statistically not significant

DISCUSSION

In the present study, we have noted that 1) Single dose cigarette smoking does not alter ventricular repolarization in habitual smokers although heart rate increases. 2) There is no association among the QT interval duration and QTd and the number of years of habitual smoking and the number of cigarettes smoked per day in smokers.

Cigarette smoking is a well-known risk factor for cardiovascular disease and consists of many chemicals, including nicotine, tar with its many carcinogens, and gaseous compounds including carbon monoxide. Nicotine, the main constituent of the cigarette, has well known acute and chronic cardiovascular effects, mainly through sympathetic activation.26 Indeed, it has been shown that nicotine in cigarette smoke blocks multiple types of potassium ion currents involved in the repolarization process and increases the propensity toward arrhythmias.4,27 On the other hand, acute effect of cigarette smoking has been well documented. Stephanotis et al.28 have observed a prompt increase in heart rate and blood pressure during the first 5 minutes after smoking. It has also been shown that circulating and locally released catecholamines rise to maximal at the end of 10-minute smoking period and return to baseline levels 30 minutes after the start of smoking.9,28 In this context, giving the sympathetic and hemodynamic responses to acute cigarette smoking we have speculated that single dose cigarette smoking may influence QT interval duration and QTd.

Increased QTd and prolonged QT interval duration have been associated with increased vulnerability to regional variation in ventricular repolarization, which may increase the risk of sudden death caused by malignant arrhythmias.10,11 Experimental and clinical evidences suggest that the autonomic nervous system modulates the duration of ventricular repolarization by conditioning ventricular repolarization to alterations in the heart rate and that failure of

such adaptation mechanism might trigger ventricular arrhythmias. The prolonged QT interval is regarded as a marker of imbalanced distribution of sympathetic nervous system activity on the heart, indicating that the autonomic neural tone is an important determinant of QT interval duration and QTd.12-14 Previous studies have shown that QTd is abnormally increased in patients with primary autonomic failure.14,15 Increased QTd has been found to be correlated with increased sympathetic activity and decreased parasympathetic activity in healthy volunteers.16 In this study we failed to observe the changes in QT interval and QTd after one cigarette smoking compare to baseline. However, in accordance with the previous reports we observed an increase in heart rate after one cigarette smoking.

The influence of cigarette smoking on the heterogeneity of ventricular repolarization has been extensively evaluated previously; however, published reports provide conflicting data and frequently focused on the chronic rather than acute effects of cigarette smoking on ventricular repolarization.17-23 Moreover, to our knowledge, the influence of single dose smoking on ventricular heterogeneity has not been adequately studied in otherwise healthy subjects. A previous study has evaluated ventricular heterogeneity during smoking in a combined cohort of middle-aged healthy subjects and patients with coronary artery disease.17 Although prolongation of the corrected QT interval during smoking was observed, the confounding effects of other factors that influence ventricular heterogeneity and differed between the 2 subgroups of that study were not taken into consideration. On the contrary, another study showed no association between smoking and the overall incidence of hyperventilation-induced repolarization abnormalities in a healthy cohort.18 Fauchier et al.19 examined a sample of 2.894 healthy subjects and found a positive relation between the heart rate-corrected QT duration and tobacco use, among men who smoked, the number of cigarette smoked per day was positively related to the corrected QT duration after adjustment for age. In contrast, in a population consisting of 2,358 mean and 3,454 women, deBruyne et al.22 found no correlation between smoking status and QTcd. In agreement with this study, we also found no dependent-relation among the smoking status and QT interval duration and QTd in smokers. Romero Mestre et al.20 found no significant differences in the duration of the QT interval between smokers and nonsmokers. Moreover, Karjalinen et al.21 found that smoking was associated with the shortening of the corrected QT interval duration. More recently, Dilaveris et al.23 found that only corrected QT interval marginally prolonged in smokers, however, that QTd did not differ between smokers and nonsmokers. The authors concluded that although ventricular heterogeneity was altered in young cigarette smokers, the difference resulted from the heart difference between two groups. Indeed, higher heart rates have already been reported in smokers.5,8,28 Therefore, in our study we particularly constituted the study groups with identical heart rates to minimize the possible errors that may result from the formula used, since Bazzet's equation has been criticized because of its inaccuracy, especially at high and low heart rates.29,30

STUDY LIMITATIONS

Our study has some limitations. First, we included only a small number of subjects and therefore our results should be confirmed by prospective large-scale studies. Second, one another limitation of this study may be the measurement errors and poor reproducibility of QTd

method although our intra and inter-observer variability yielded minimal variability. Regardless of the technique used, QTd is difficult to measure. The end of repolarization, assessed as the end of T wave, is a gradual process and therefore hard to define. The definition of the end of the T wave is further complicated by low amplitude T waves. However, this simple and cheap method has been shown to be a strong and independent predictor of ventricular heterogeneity and cardiac mortality.10,11,21,22 Thirty, we studied on extremely young population and no participants had the cardiovascular or systemic disease and these might have effected our results, because it is well known that the risk of acute cardiac events associated with cigarette smoking increases particularly in the presence of coronary artery disease.3 Therefore, our results should be inter
preted with caution.

CONCLUSION

In conclusion, our results may indicate that although single dose cigarette smoking induces sympathetic activity, it does not influence QT interval duration and QTd in habitual smokers. However, whether or not single dose smoking influences ventricular repolarization; particularly in the presence of preexisting cardiovascular disease remain to be determined.

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