SUPPLEMENT

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Autonomic Cardiac Activity in Patients with Smoking and Alcohol Addiction by Heart Rate Variability Analysis

Abstract

Purpose: Smoking and alcohol addictions are common and worldwide. In the present study, we aimed to investigate the effects of these addictions on cardiac rhythm using heart rate variability (HRV) analysis.

Methods: Addicts (n=42 men: 22 cigarette; 20 cigarette and alcohol) and age-matched controls (n=34 men) were included in the study. All patients fulfill the criteria for dependence according to DSM-IV-TR. Electrocardiography (ECG) recordings were obtained for a total of 30 minutes. Fagerstrom Nicotine Addiction Test (FNAT) and CAGE questionnaire (Cut down, Annoy, Guilt, Eye opener) was applied to all patients.

Results: Almost all HRV parameters were significantly decreased in cigarette and cigarette and alcohol addicts compared with controls ($p<0.05$). The mean heart rate (bpm) increased in both addict groups compared with control group, and this increase was particularly significant in cigarette and alcohol addicts.

Conclusions: The cardiac autonomic balance shifted in favor of sympathetic activity by suppressing the parasympathetic activity in addicts; therefore, the present study shows that smoking and/or alcohol addiction leads to sympathetic activation and parasympathetic inhibition. Reduced vagal activity also predisposes to cardiac arrhythmias. This suggests an increased risk of cardiovascular mortality in subjects with smoking and alcohol addiction.

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The autonomic nervous system in heart control, it can be determined by a standard method called heart rate variability (HRV), which is often related to the diagnosis and prognosis of cardiac disease. Several patterns observed in HRV dynamics are related to myocardial infarction, cardiac arrhythmias and atrial fibrillation. Additionally there are some risk factors that affect HRV directly or indirectly, such as smoking and alcohol consumption.

It is well known that smoking is a leading cause of cardiovascular disease; cigarette smoking is a preventable main risk factor for acute ischemic cardiac events such as myocardial infarction and sudden death [1]. Usually, a dose-dependent relationship exists among the number of cigarettes smoked per day and cardiovascular mortality and morbidity [2]. Coronary heart disease is the first (54%) and the cerebrovascular disease the second (25%) most frequent cause in smoking-related cardiovascular death [3]. In particular, smoking may cause cardiovascular events like acute myocardial infarction, ventricular fibrillation and sudden death especially in patients with coronary artery disease [4]. It has been reported that smoking has been implicated 50% of the early myocardial infarction [5]. Endothelial dysfunction, coronary vasoconstriction, platelet aggregation and increased sympathetic activity are trigger mechanisms for these adverse cardiovascular events [6]. It is also known that smoking causes autonomic changes, such as increasing sympathetic activity. Nicotine, one of the major harmful compounds of cigarette, leads to increased levels of catecholamine by sympathetic stimulation, thereby accelerating heart rate [7].

Lee and Chang found that smoking activates sympathetic cardiac control in female university students [8]. Cagirci *et al.* found that smoking more than 20 cigarettes per day lead to negative effects in the autonomous system [9]. Furthermore, the effect of smoking on autonomic activity disappeared immediately after cessation.

With respect to alcohol dependency, the frequency of alcohol consumption was closely related with cardiovascular disorders. Alcohol addicts often considered the group of heavy alcohol consumption; however, heavy alcohol consumption is caused increased risk of many cardiovascular diseases such as hemorrhagic stroke, cardiomyopathy, systemic hypertension and supraventricular arrhythmias. Furthermore, mild to moderate alcohol consumption is associated with atherothrombotic conditions including coronary artery disease, ischemic stroke and heart failure [10].

Acetaldehyde has been found to cause cardiovascular symptoms in alcoholics. Catecholamine secreted from sympathetic nerve endings or the adrenal medulla caused an

increase in heart rate that was secreted by acetaldehyde [11]. It was previously suggested that alcohol was a coronary vasodilator, but the existing data now suggests that alcohol has no direct major effect on coronary blood flow [12]. Furthermore, it was reported that after the uptake of significant amounts of alcohol, ectopic ventricular activity increases [13]. Additionally, alcohol consumption predisposes a subject to atrial arrhythmias, such as atrial fibrillation, which is the most common cardiac arrhythmia especially in heavy drinkers [10].

HRV has emerged as a simple, noninvasive method to evaluate the sympathovagal balance that is affected by smoking and alcohol consumption. HRV shows temporal changes in sinus rhythm, which is controlled by the autonomic nervous system and is also affected by a number of factors such as exercise, physical and mental stress and emotional impact. It has been used in a variety of clinical situations including myocardial infarction, sudden death, diabetic neuropathy and congestive heart failure [14, 15].

Smoking and alcohol addictions are common and increasing worldwide. In the present study we aimed to investigate the effects of these addictions on cardiac rhythm, which is an important determinant of the autonomic nervous system by using HRV [16].

Materials and Methods

The patient group included 42 men who ranged in age from 20 to 40 years. Twenty two patients who smoked (mean age 30.41 ± 4.99), 20 patients who had both cigarette and alcohol addiction (mean age 30.65 ± 4.89) and 34 age-matched controls (mean age 27.88 ± 6.64) were included in the study. Female volunteers were excluded from the study to eliminate the possible effects of gender on heart rhythm. The patients with cigarette and alcohol addictions who applied to the Alcohol and Drug Addiction Treatment and Training Center, Ankara, Turkey for diagnosis and treatment, but who had not received addiction treatment before, were included the study. The control group was selected by random sampling from general healthy population who had never smoked or used alcohol before. There was no difference between ages of patients and controls. Diagnoses were made on the basis of information provided from clinical interviews and Structured Clinical Interview for DSM-IV-TR. In addition, exclusion criteria were health problems that affect the autonomic nervous system like diabetes mellitus, hypertension, obesity and cardiac disease. The study was conducted in accordance with the requirements of the Ethical Committee of the Faculty

of Medicine of the University of Fatih. The Institutional review board approved the study.

All patients fulfill the criteria for dependence according to DSM-IV-TR. Also, FNAT [17] was applied to all patients in whom total points were 10 and CAGE questionnaire was applied to cigarette and alcohol addicts in which total points were 4 [18].

Recording ECG

All subjects were rested for 10 minutes initially without recording electrocardiogram (ECG) for stabilizing autonomic parameters. Continuous ECG recordings were obtained over a total of 30 minutes. Measurements were carried out between 10:00 to 14:00 hours, where possible, to avoid intra-day autonomic instability. The noise was reduced to a minimum and the ambience was prepared to support participants' own optimal heartbeat.

Three self-adhesive ECG electrodes were administered for assessing Lead II according to the standard Einthoven Triangle in the right wrist; right and left legs. ECG was recorded using PowerLab 26T (ADInstruments, Australia), a measuring device used for multimodal monitoring of biosignals. The digital signals were then transferred to a laptop and analyzed using the LabChart[®] software (MLS310/7 HRV Module). A full continuous ECG could be viewed and saved for later analysis, and software-based filters were used for exclusion of movement artifacts and ectopic beats prior to HRV analyses.

Statistical Analyses

Statistical analysis was performed using SPSS for Windows (version 16.0) statistical program (SPSS, Inc., Chicago, IL). Measured values are given as a mean and standard deviation (SD). For statistical evaluation, the Kruskal Wallis and Mann-Whitney U tests for significance of the difference between nonparametric data and one-way ANOVA in parametric data was used. Results 95% confidence interval, significance at $p < 0.05$ were evaluated.

Results

The FNAT score was 8.07 ± 1.13 in patients with smoking addictions, indicating that the smoking severity index was very high in this group. In the cigarette and alcohol addicts group, the mean FNAT score was 5.15 ± 1.50 and mean CAGE score was 3.65 ± 0.67 , indicating that the smoking addiction was moderate but the alcohol addiction was high and clinically significant.

HRV is a physiological event of variation in the beat to beat intervals of heart rhythm. The term, cycle length variability, can be used for HRV analysis. The HRV analysis results were examined in two categories: as time-domain and frequency-domain. Elevated HRV parameters refer to a better cardiac health, but reduced parameters show negativity in cardiac rhythm [16, 19].

In the present study, all subjects were in sinus rhythm according to their ECG examinations. The standard deviation of the NN intervals (SDNN) (ms), the standard deviation of the averages of NN intervals in all 5-minute segments of the entire recording (SDANN) (ms), the square root of the mean of the sum of the squares of differences between adjacent NN intervals RMSSD) (ms) and the percentage of difference between adjacent NN intervals that are greater than 50 ms (pNN50) (%), total power (ms^2), power in the very-low frequency range (0.003–0.04 Hz) (VLF) (ms^2), power in low-frequency range (0.04–0.15 Hz) (LF) (ms^2) and power in high-frequency range (0.15–0.4 Hz) (HF) (ms^2) values were measured.

HRV parameters mentioned above were markedly decreased in cigarette and alcohol addicts group compared with the control group ($p < 0.05$). SDNN, SDANN, RMSSD, pNN50, total power, VLF and HF levels were decreased in the cigarette addicts group compared with the control group significantly ($p < 0.05$). The mean heart rate (bpm) increased in both groups compared with the control group, and these increases were particularly significant in the cigarette and alcohol addicts group (Table 1).

Discussion

Cigarette smoking is one of the most important preventable risk factors for cardiovascular disease (including sudden death, coronary artery disease and stroke) [4]. Cessation of smoking rapidly decreases these risks caused by smoking [3]. It is known that smoking can even lead to sudden death, with pathophysiological effects on the autonomic nervous system [20].

HRV measurement is an analysis that based on successive R waves relationship on the ECG recording and provides important information about the cardiac autonomic activity. Increased HRV reflects the endurance against abnormal changes of the heart. Inversely, decreased HRV means that suppression in vagal tone and elevation in sympathetic tone; and it almost always indicates a poor prognosis. Decreased HRV means an increased risk of ventricular fibrillation and sudden death; however, it has been shown that decreased HRV

TABLE 1. Comparison of each groups according to the results of mean heart rate variability parameters

	Cigarette Addicts (n=22)	Cigarette and Alcohol Addicts (n=20)	Controls (n=34)	F	p
Mean heart rate (bpm)	71.79 ± 8.03	77.04 ± 13.45 ^a	67.87 ± 8.45 ^a	5.42	0.015
SDNN (ms)	50.81 ± 21.20 ^b	44.16 ± 16.28 ^a	65.14 ± 22.32 ^{a,b}	7.33	0.001
SDANN (ms)	32.81 ± 20.48 ^b	32.07 ± 19.90 ^a	47.36 ± 25.77 ^{a,b}	3.98	0.013
RMSSD (ms)	32.80 ± 20.47 ^b	32.06 ± 19.90 ^a	47.34 ± 25.75 ^{a,b}	3.98	0.013
pNN50 (%)	12.79 ± 16.53 ^b	12.03 ± 16.53 ^a	21.55 ± 17.46 ^{a,b}	2.93	0.014
Total power (ms ²)	2747.29 ± 2637.13 ^b	2122.91 ± 1640.39 ^a	4155.33 ± 3032.82 ^{a,b}	4.28	0.005
VLF (ms ²)	1244.65 ± 1326.54 ^b	891.48 ± 689.46 ^a	1772.49 ± 1224.84 ^{a,b}	3.97	0.004
LF (ms ²)	857.99 ± 621.40	630.39 ± 563.74 ^a	1224.00 ± 906.37 ^a	4.22	0.006
HF (ms ²)	567.96 ± 755.55 ^b	484.09 ± 509.12 ^a	1025.45 ± 1286.42 ^{a,b}	2.41	0.014
LF/HF	2.57 ± 1.59	2.09 ± 1.60	1.91 ± 1.21	1.45	0.247

a: p < 0.05; comparison of control group with smoking and alcohol-dependent group

b: p < 0.05; comparison of control group with smoking dependent-group

was associated with increased mortality in healthy adults; and was an independent risk factor for sudden death [21].

In the present study, mean heart rate increased in cigarette addicts and more than cigarette addicts in cigarette and alcohol addicts compared to controls significantly. These results suggest that a further increase in the average heart rate occurs in alcohol consumption in addition to cigarette smoking. Thus, the increased heart rate from baseline is important in cardiac mortality.

With respect to HRV parameters, SDNN reflects the parasympathetic component of autonomic function. Decreased SDNN indicates suppressed vagal activity and increased sympathetic activity of the sinus node [19]. RMSSD and pNN50 parameters nearly always indicate the vagal activity and show the changes in autonomic tone.; they are independent, resulting from the diurnal changes and other factors in heart rate. RMSSD is more stable according to the pNN50 and used more frequently in clinical practice [15, 22]. Physiological interactions of VLF, a frequency domain indicator, are poorly understood; however, LF reflects the both sympathetic and parasympathetic activity together was reported. Also, HF is a key determinant of heart rate changes related to parasympathetic activity [22, 23].

All HRV parameters decreased in cigarette addicts and reduced considerably in cigarette and alcohol addicts. According to our findings, smoking addiction decreased HRV and smoking and alcohol addiction decreased HRV markedly.

At this point, the reduced HRV values that are even lower in alcohol-consuming group is a critical situation.

In light of the changes in HRV parameters, it can be said that smoking increased the sympathetic activity of the heart and alcohol consumption accelerated this condition even more. In patients who were addicted to smoking and/or alcohol, the cardiac autonomic balance shifted in favor of sympathetic activity by suppressing the parasympathetic activity. Therefore, the present study showed that smoking and/or alcohol addiction led to sympathetic activation and parasympathetic inhibition. Reduced vagal activity also predisposes to cardiac arrhythmias; this means an increased risk of cardiovascular mortality, including sudden cardiac death.

There is a widespread opinion in literature that some alcoholic beverages, when consumed daily at a certain level, may be beneficial in terms of heart health [10, 11, 24]. But, when alcohol is consumed together with smoking, the adverse effects of smoking on the heart are further exacerbated as shown in the present study.

A number of study in young adults show that there is a positive relationship between alcohol consumption and cigarette smoking [25, 26]. McKee *et al.* reported that 74% of all smoking periods together with the influence of alcohol among college students [27]. Furthermore, cigarette smoking may not always accompanied by alcohol consumption but alcohol consumption is often accompanied by cigarette

smoking. Cigarette smoking appears to be the first step of alcohol consumption.

From another aspect, alcohol consumption, considering its effect of creating dependency, is not so innocent. Alcohol increases dopamine secretion as nicotine. Secretion of dopamine and norepinephrine provides pleasure [28]. A positive relationship between dopamine and heart rate were determined. Even in small doses, alcohol intake strengthens the pleasurable effects of nicotine. For this reason, simultaneous usage of alcohol and cigarette may increase pleasurable effects of each other. People who smoking while drinking alcohol tend to smoke more. There were no alcohol addicts who were not also smokers among the patients who applied to our hospital during the two-month research process.

It is scientifically known that consumption of alcohol several times is an invitation to dependency. Additionally, it is commonly believed that alcohol has beneficial effects on cardiac health. This may be true in a sense, but it must have been said considering the rate of benefits and harms. Easily addictive effects of alcohol are ignored most of the time by some researchers. Consequently, contrary to common belief, alcohol consumption is not innocent sufficiently according to our study.

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