THE EFFECTS OF SHORT-TERM SMOKING CESSATION ON METABOLIC SYNDROME PARAMETERS

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ABSTRACT

Objective: Smoking cigarettes and metabolic syndrome (MetS) are among preventable health problems. On the other hand, smoking cessation may also lead to gaining weight and MetS. Here, we aimed to investigate the effects of short-term smoking cessation on MetS parameters.

Materials and methods: The study was performed in 150 subjects willing to cease cigarette smoking. Varenicline or bupropion was started to the subjects ceasing smoking as a supportive treatment, and current diet exercises were continued. MetS incidence was evaluated before and at week 12 with the National Cholesterol Education Program, Adult Treatment Panel (NCEP ATP III).

Results: Of 150 subjects, 74 continued smoking cessation at week 12. Compared to the baseline values, it was seen that body weight (p<0.001), waist circumference (WC) (p<0.001), body mass index (BMI) (p<0.001) and high density lipoprotein (HDL)-cholesterol (p<0.001) levels increased at the 12th week. However, blood pressure (BP), blood glucose and triglyceride (TG) levels remained unchanged. Presence of MetS was found 8.1% at the baseline and 17.6% at the end of the study (p=0.118). Of all subjects, while present in 43.2% at initial, WC criteria for MetS, then, increased to 54.1% at week 12 (p=0.039). Although present in 68.9% of subjects at the baseline, HDL-cholesterol criteria decreased to 50.0% at week 12 (p=0.001).

Conclusions: Although an increase was observed in WC, body weight and BMI, we observed no changes in MetS frequency within 12-week period. Administration of appropriate calorie-restricting diet and exercise may prevent weight gain and MetS to develop after smoking cessation.

Keywords: Cigarette, metabolic syndrome, smoking cessation.

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Introduction

Tobacco consumption remains to be the most important cause of mortality and morbidity worldwide⁽¹⁾. According to data from the World Health Organization, there are over 1 billion tobacco users worldwide, and 4.9 million people die each year due to conditions related to tobacco usage⁽²⁾.

The co-existence of obesity and smoking has important consequences for health. In the study performed by Framingham, the life expectancy of obese smokers was 13 times lower than that of normal-weight non-smokers⁽³⁾. The same study also reported that nearly 33 to 50% of obese smokers died between the ages of 40 and 70 years although only 10% of normal-weight non-smokers died at the same ages.

Smoking and metabolic syndrome (MetS) are global, preventable and serious health problems. The fear of gaining weight constitutes the most important barrier for quitting smoking. MetS, the most common endocrinopathy, is defined as the cooccurrence of metabolic risk factors in the development of both type 2 diabetes mellitus (DM) and coronary artery disease (CAD). MetS is also associated with increased cardiovascular morbidity and mortality⁽⁴⁾. In a cross-sectional study, it was shown that MetS was seen at higher rates in smokers, compared to non-smokers⁽⁵⁾.

Smoking is known to increase visceral adiposity, but not overall obesity⁽⁶⁾. In literature, however, controversial results were reported about weight changes occuring after smoking cessation. Previous epidemiological studies showed that smoking cessation is associated with an increased prevalence of MetS and/or its components^(7, 8). On the other hand, some studies showed that continuation to smoking is associated with insulin resistance (IR) and MetS^(9, 10). In the present study, we aimed at evaluating the effects of short-term smoking cessation on MetS and related parameters.

Material and methods

This prospective study was conducted in 150 individuals between the ages of 18-65, willing to cease cigarette smoking and admitted to the outpatient clinics of family medicine department of Konya Training and Research Hospital, University of Health Sciences between March and July 2016. The study protocol was approved by the ethics committee of Selcuk University. All individuals were informed about the study design, and written consent was obtained from those accepting to take part. The subjects with any known active infections, malabsorbtion, anorexia, inflammatory diseases, such as Crohn's, ulcerative colitis, rheumatoid arthritis, systemic lupus erythematosus, benign or malignant hematologic disorders, any solid tissue cancers, and those exposed to liposuction, any surgical intervention within the past six months, with pregnancy and breast feeding, on illegal drugs, consuming alcoholic drinks and continuing cigarette smoking after the enrollment into the study were excluded from the study.

Age, gender, height, weight, waist circumference (WC), blood pressure (BP), exercise status, initial smoking age, number of cigarettes smoked per day, duration of smoking, and number and length of attempts to quit smoking were recorded on study charts. The 6-item Fagestrom's Nicotine Addiction Test (FNAT), scored between 0-10, was performed in all the subjects⁽¹¹⁾. In FNAT, those receiving scores between 0-4 are described as mild nicotine addictives, those with scores between 5-6 as moderate addictives, and those with scores between 7-10 as severe nicotine addictives. The validity and reliability of Turkish version of the test was conducted by Uysal et $al^{(12)}$. in 2004, and the reliability was found at moderate level as α =0.56.

Height (m) and weight (kg) were measured with underwear clothing. WC was measured as the minimum size between iliac crest and lateral costal margin. Body mass index (BMI) was calculated as weight (kg)/height square (m²). Carbon monoxide (CO) in expiration breath was measured with a carboxymeter device (Smokerlyzer, Bedfont Scientific Ltd. Washington DC, USA). The test was performed by the same researcher, while the subjects were in sitting position and took deep breath for 15 sec and expired slowly. The test results were presented as parts per million (ppm). Blood samples of 5 cc were iv drawn from all subjects to measure triglyceride (TG) and high density lipoprotein (HDL)-cholesterol after 12-h fasting in the morning, and the samples were chilled, centrifuged and stored at -800C until TG and HDL analyses were performed.

All participants were supported and encouraged to cease smoking and treated with bupropion (Zyban®, Glaxo-Smith Klein, GB) as 150 mg twice per day or varenicline (Champix, Pfizer, USA) as 0.5 mg once per day for 3 days, titrated to 0.5 mg twice per day for days 4 to 7 and then to 1 mg twice per day until the end of the study. Except for routine daily exercises, the study population was recommended no additional dieting and exercises during the study, and the participants kept on their normal diet and exercise habitus.

All the subjects were invited at week 12 after the first visit as to the attempts for smoking. The smoking cessation of the subjects was based on CO in the expiratory air. Anthropometric measurements and laboratory tests were repeated 12 weeks after deciding to smoking cessation.

The diagnosis of MetS was performed under the criteria of the National Cholesterol Education Program, Adult Treatment Panel (NCEP ATP III)⁽¹³⁾ in accordance with the presence of three of the following five criteria: 1) fasting blood glucose levels≥100 mg/dL or drug use for DM, 2) HDL-cholesterol levels<40 mg/dL in men, <50 mg/dL in women, 3) TG levels≥150 mg/dL or receiving lipidlowering treatment, 4) WC≥102 cm for men, ≥88 cm for women, and 5) BP≥130/85 mmHg or taking antihypertensive drug treatment. The levels of HDL-cholesterol [(NR), 40-90 mg/dL] were measured with immune reaction (antigen-antibody complex) using an Olympus AU 5800 device (Beckman Coulter Inc, CA, USA), and TG levels [(NR), 0-200 mg/dL] were measured using a routine enzymatic method with an auto analyzer, Olympus AU 5800 device (Beckman Coulter Inc, CA, USA).

Statistical analysis

The data normality was analyzed with the Shapiro-Wilk test. The descriptive statistics for variables with normal distribution of continuous data [mean±standard deviation (SD)] and with no normally distributed variables [median (min-max)] were indicated. The numerical variables were compared with the Wilcoxon signed rank test, and categorical variables were compared with the Wilcoxon signed rank test, and categorical variables were compared with the McNemar test in intragroup comparisons. All statistical analyses were performed by SPSS 21.0 statistical programme (SPSS Inc Chicago, IL, USA). A p value≤0.05 was accepted significant. Statistically significant values are indicated in bold in Tables.

Results

Sevety-four (49.3%) out of 150 participants achieved to cease smoking. The mean age was 41.5 ± 10 years, and 28 patients (37.2%) were female. The demographic, anthropometric, biochemical and metabolic characteristics of participants are summarized in Tables 1 and 2. In terms of professional distributions, the most frequent professional groups were workers (27%), retirees (17.6%) and doctors (16.2%). When educational status was evaluated, 40.5% of patients were found to have primary school graduates.

When participants' history of smoking was investigated, it was determined that average initial age of starting to smoke was 16.8 ± 3.9 years, patients had been smoking cigarettes for average 23.8 ± 9.8 years, and the average number of cigarettes smoked per day was 23.1 ± 8.4 . In our study, the average exposure of patients to cigarettes, average amount of CO in expiration air and average score of Fagerstrom nicotine dependence scale were calculated to be 24.1 ± 11.7 packet/year, 5.8 ± 3.6 ppm and 6 ± 2.7 , respectively. The participants were found to attempt to cease smoking 1.4 ± 1 times. In terms of' exposure to second-hand smoking, while 36.5% of all participants were found to live with other smokers at home, 56.8% were found to live with other smokers at work. The amount of patients consuming alcoholic drinks was 2%. As a modality of smoking cessation, 87.8% of patients were determined to be treated with bupropion, while 12.2% received varenicline. Patients' characteristics related to smoking cessation are presented in Table 2.

	Mean±SD	
Age (years)	41.5±10.0	
	n (%)	
Sex		
Female	28 (37.8)	
Male	46 (62.2)	
Occupation		
Workers	20 (27)	
Retired	13 (17.6)	
Doctors	12 (16.2)	
Artisans	6 (8.1)	
Others	23 (31.1)	
Educational status		
Literate	1 (1.4)	
Primary schools	30 (40.5)	
Secondary schools	15 (20.3)	
High schools	16 (21.6)	
Higher education	12 (16.2)	

 Table 1: Demographic characteristics of study population.

The amount of CO in the expiratory air was 5.8 ± 3.6 ppm at the beginning and 1.48 ± 1.10 ppm at the end of 12 weeks. There was a statistically significant difference between them (p = 0.000).

Compared to the baseline values, it was seen that body weight (p<0.001), WC (p<0.001), BMI (p<0.001) and HDL-cholesterol (p<0.001) levels increased at week 12, although systolic and diastolic BP, blood glucose and TG levels remained unchanged during the study (Table 3).

The presence of MetS was found to be 8.1% at the baseline and 17.6% at the end of the study (p=0.118). While WC, one of the parameters of MetS, was positive in 32 patients (43. 2%) at the baseline, the parameter was found positive in 40 patients (54.1%) at the end of the study (p=0.039). Even though TG parameter was found positive in 31 patients (41.9%) at the baseline, it was found positive in 32 subjects (43.2%) at the end of the study (p=1.000).

	Mean±SD	
Onset of smoking (years)	16.8±3.9	
Cigarettes per day	23.1±8.4	
Years of smoking	23.8±9.8	
Pack per year	24.1±11.7	
CO (ppm)	5.8±3.6	
Fagerstrom addiction points	6±2.7	
Number of attempts for smoking cessation	1.4±1	
	n (%)	
Other smokers at home		
Absent	47 (63.5)	
Present	27 (36.5)	
Other smokers in workplace		
Absent	32 (43.2)	
Present	42 (56.8)	
Alcohol consumption		
Absent	64 (97)	
Present	2 (3)	
Drugs used for smoking cessation		
Bupropion	65 (87.8)	
Varenicline	9 (12.2)	

 Table 2: Characteristics of smokers.

	Baseline	Week 12	р
	Mean±SD	Mean±SD	
Height (cm)	167.8±8.3	-	<0.001
Body weight (kg)	78.1±18.1	80.8±17.4	<0.001
Waist circumference (cm)	95.3±13.5	97.2±12.9	0.243
Systolic blood pressure (mmHg)	111.7±14.9	109.9±14.2	0.222
Diastolic blood pressure (mmHg)	71.4±9.9	72.3±10.4	0.065
Plasma glucose (mg/dl)	90.2±8.3	92.2±9.7	0.586
Triglyceride (mg/dl)	167.5±121.9	174.6±115.9	<0.001
HDL- cholesterol (mg/dl)	39.9±8.7	43.5±9.3	<0.001
Body mass index (kg/m²)	27.6±5.5	28.6±5.3	
	n (%)	n (%)	0.118
Metabolic syndrome			
Absent	68 (91.9)	61 (82.4)	
Present	6 (8.1)	13 (17.6)	

Table 3: Changes in metabolic syndrome parametersbefore and after smoking cessation.HDL-Cholesterol: High density lipoprotein-cholesterol

		Baseline %)	Week 12 n(%)	р	
Waist circumference≥102 cm for men, ≥88 cm for women	No	42 (56.8)	34 (45.9)	0.039	
	Yes	32 (43.2)	40 (54.1)		
Triglyceride levels≥150 mg/dL or receiving lipid lowering treatment	No	43 (58.1)	42 (56.8)	1	
	Yes	31 (41.9)	32 (43.2)		
HDL-cholesterol<40 mg/dL in men, <50 mg/dL in women, or receiving lipid lowering treatment,	No	23 (31.1)	37 (50.0)	0.001	
	Yes	51 (68.9)	37 (50.0)	0.001	
Blood pressure≥130/85mmHg or drugs used for hypertension	No	64 (86.5)	64 (86.5)	1	
	Yes	10 (13.5)	10 (13.5)	1	
FBG levels≥100 mg/dL or drugs used for DM	No	66 (89.2)	58 (78.4)	0.077	
	Yes	8 (10.8)	16 (21.6)		
Presence of MetS according to criteria of NCEP-ATP III	No	68 (91.9)	61 (82.4)	0 118	
	Yes	6 (8.1)	13 (17.6)	0.110	

Table 4:	Presence	of metal	bolic	syndrome	components
according	to NCEP	-ATP III	criter	ia.	

HDL-Cholesterol: High density lipoprotein-cholesterol, FBG: Fasting blood glucose, DM: Diabetes mellitu, NCEP-ATP III: National Cholesterol Education Program-Adult Treatment Panel III

However, the positivity of HDL-cholesterol parameter was present in 51 subjects (68.9%) at the initial of the study, although positivity was determined in 37 patients (50.0%) at the end of the study (p=0.001). BP was also positive in 10 patients (13.5%) at both the baseline and end of the study (p=1.000). While initially positive in eight patients (10.8%), fasting blood glucose parameter was found positive in 16 patients (21.6%) (p=0.077) (Table 4).

Discussion

In this study, we determined that there was a significant increase in the levels of body weight, WC, BMI ve HDL-cholesterol in such a short period as 12 weeks after smoking cessation, compared with initial levels, and that however meaningess it was, MetS frequency increased from 8.1% to 17.6%. In addition, while the number of the cases with WC criteria of MetS was detected to increase during 12 weeks, the number of the subjects with HDL-cholesterol criteria was found to decrease.

Cigarette and other tobacco products constitute an important health challence for human beings, and the maladies, including respiratory tract and cardiovascular system diseases, are among the most important preventable reasons of many others disorders, such as atherosclerosis or cancers. Although the struggle against smoking cigarettes is still actively continued, expected and targeted goal has yet to be reached. Although powerful factors leading to addiction to cigarettes and other tobacco products seem to be the biggest obstacle ahead of this success, the most important barrier causing individuals to cease smoking is the fear and anxiety of weight gain after smoking cessation. It is a generally known weight gain and MetS are seen at a higher rate in those ceasing smoking than nonsmokers⁽¹⁴⁻¹⁶⁾. Weight gaining after smoking cessation increases the risk of restarting to smoke/relapse especially in individuals with normal weight and overweight on a diet continously⁽¹⁷⁾, and also among men⁽¹⁸⁾.

In the study where 5407 men undiagnosed with MetS were followed for 2.9 years, Byung et al.⁽¹⁹⁾ found MetS frequency among non-smokers as 8%, new smokers as 7.1%, ex-smokers as 17.1% and sustained smokers as 13.9%, respectively, and reported that on logistic regression analysis, the risk of developing MetS was higher among ex-smokers than sustained-smokers when weight changes were excluded, but no difference was observed when weight changes were included [OR 1.45 (95% CI 1.06-1.98)]. In the same study, while weight changes were 0.31+2.81 kg in non-smokers, weight increases were reported as 1.56+3.12 kg in ex-smokers and 0.73+2.82 kg in sustained-smokers.

After smoking cessation, average increases of 2.8-4.4 kg in men and 3.8-5 kg in women take place during 10-year period^(20, 21). On the other hand, in the Hitachi Health Study⁽²²⁾ where visceral fat tissue was calculated through abdominal computerized tomography (CT), although current/sustainedsmokers were determined to have similar visceral adipose tissue volume to that of never-smokers, it was detected that visceral fat tissue volume of exsmokers was higher than that of never-smokers, and volume of visceral fat tissue decreased as smoking cessation time prolonged, especially after the 15th year. In the same study, volume of subcutaneous fat tissue was reported to be higher in never-smokers and >5-year ex-smokers, compared to currentsmokers. Smoking cigarettes is known to cause weight loss by increasing metabolic rate and decreasing appetite, although it is still not fully understood how smoking cessation leads to weight gain^(21, 23). While a 3% increase was observed in energy expenditure in 30 min after smoking one cigarette,⁽²⁴⁾ resting metabolic rate was reported to decrease 16% in 30 min after smoking in women smokers⁽²⁵⁾. Heggen et al.⁽⁸⁾ reported that no change was witnessed in patients' body weight for 12 weeks after smoking cessation in combination with calorie-restricting diet, and MetS frequency declined from 44.9% to 37.9%. Although smokers have less weight compared to non-smokers, abdominal obesity that is the most important component of MetS is woefully seen among smokers^(26, 27). Abdominal adipocytes are known to be more active, more atherogenic than general subcutaneous adipocytes⁽²⁸⁾. In former smokers, waist/hip ratio (WHR) was reported to be disproportionate to duration of smoking cessation⁽²⁶⁾.

In our study, a significant increase was detected in both WC and body wieght of patients at week 12 after smoking cessation, compared to baseline scores. In our study, no calorie-restricting diet was recommended to our subjects in order to evaluate only the effects of smoking. However, if a calorierestricting diet or exercises were recommended to our subjects, we considered that weight gain would not be so higher. A study supporting our thinking has recently been performed by Heggen et al.⁽⁸⁾ and in the 12-week study where 108 cases ceasing smoking were assessed, it was reported that when daily calorie intake was reduced to 500 kCal, no change was seen in insulin resistance, homeoestatic model of assessment (HOMA) and body weight, a significant decrease was found in TG and diastolic BP levels in both genders, a significant decrease was also present in systolic BP among men, and a significant increase was observed in women's HDL-cholesterol levels. The absence of another group for whom both medical nutrition therapy and exercise were recommended was one of the limitations in our study.

Impaired glucose intolerance or DM is important components of MetS. In the Physicians' Health Study, the risk of developing DM was reported to be >70% among men smoking more than 20 cigarettes per day⁽²⁹⁾. Similar findings were also reported in women⁽³⁰⁾. On the other hand, the risk of developing DM decreases among ex-smokers and returns to normal over years^(29, 30). In a meta-analysis of 14 observational studies including 98.978 cases, Kar et al.⁽³¹⁾ reported that smoking cessation led to no increase in HbA1c levels and decreased vascular complications in the long term due to its positive contributions to serum lipid profile.

Although weight gain and a temporary increase in HbA1c levels were reported in other studies, a definite decrease was reported in mortality in the long run⁽³²⁾. Though increased weight gain was asserted as a risk in the development of DM, Sung et al.⁽³³⁾ reported that the risk of developing DM within two years after smoking cessation increased independently of weigth gain. When compared to the baseline scores in our study, no change was observed in glucose levels at week 12 after smoking cessation. However, when assessed according to blood glucose criteria of NCEP ATP III, these criteria were obtained in eight patients (10.8%) at the baseline and then in 16 (21.6%) at the end of the study, but no statistically significant difference was determined (p=0.077) (Table 4). Since we recommended no diet or exercises to prevent weight gain, we speculated that an increase in weight and WC could contribute to impaired glucose tolerance after ceasing smoking, so such individuals should be closely followed-up and encouraged to join a calorie-restricting and exercise program.

Dyslipidemia is frequently accompanied by MetS, and smoking often aggrevates dyslipidemia. In several studies, positive and important improvements were reported to be seen in lipid profile following smoking cessation^(34, 35). A 15% increase was reported to be observed in HDL-cholesterol levels 48 h after ceasing smoking^(31, 36). Heggen et al.⁽⁸⁾ reported that a significant decrease was observed in TG levels in combination with calorie-restricting diet in both genders during 12 weeks after smoking cessation, and in only women, a significant increase occured in terms of HDL-cholesterol levels. In our study, while a significant increase (nearly 3.5 mg/dL) was seen in HDL-cholesterol levels at the baseline, no significant change was observed in TG levels. As to HDL-cholesterol criteria of MetS, while the criteria was obtained in 52 patients (68.9%) prior to smoking cessation, the number of patients with the criteria reduced to 37 (50%) during 12 weeks after smoking cessation. Again, considering TG criteria of MetS, while it was detected in 31 patients (41.9%) the baseline, the criteria was obtained in 32 subjects (43.2%) at the end of the study. If a calorie-restricting diet and exercise had been recommended to the study subjects, and weight gain had been prevented in these individuals, it is predictable that an improvement would have been observed in more patients in terms of HDL-cholesterol and TG levels, diagnostic criteria of MetS.

Even though BP is increased higher among smokers than non-smokers⁽³⁷⁾, there are studies with

controversial findings reporting that smoking cessation has effects on BP^(38, 39). In a 4-year observational study, Lee et al.⁽³⁸⁾ reported that the risk of hypertension increased independent of weight in those ceasing smoking. Heggen et al.⁽⁸⁾ reported that a significant decrease was observed in diastolic BP in combination with calorie-restricting diet in both genders during 12 weeks after smoking cessation, and in only men, a significant decrease was detected in systolic BP levels. In our study, no significant change was seen in systolic and diastolic BP levels after smoking cessation, and no difference was also found in the number of patients with BP criteria of MetS.

While 65 patients were treated with bupropion, nine cases were administered with varenicline, and because of limited number of cases, no comparison was performed. Although they have delaying effects on weight gain, medications used for smoking cessation are known not to prevent weight gain⁽⁴⁰⁾. In addition, due to the decreasing effect of both agents on glucose stimulated insulin secretion⁽⁴¹⁾, the safety and importance of these agents may bring back to the agenda in smoking cessation therapy in the future.

In conclusion, we determined in our study that an increase was present in the levels of body weight, BMI, WC and HDL-chlosterol after smoking cessation, the number of cases meeting WC criteria of MetS increased, the number of cases meeting HDL-cholesterol criteria decreased, and as a whole, no change was seen in MetS frequency at week 12 after smoking cessation. However, in light of previous implications in literature, it may be suggested that if a calorie-restricting diet and exercise are not recommended to patients, an increase may develop in the long-term MetS frequency. So, patients admitted to smoking cessation theraphy should be certainly encouraged to join a calorierestricting diet and exercise program, and such patients should strive not to gain weight.

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