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Blood Pressure and Inflammation Parameter in the Healthy-Overweight Smoker in Yogyakarta

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Abstract

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BACKGROUND: The number of smokers in rural Indonesia is alarming. Overweight and smoking are the risk factor for hypertension, diabetes mellitus, and cancer. Cigarette smoke and overweight elevated oxidative stress and affected the blood pressure and inflammation response. However, the relationship between blood pressure and the response to inflammation in overweight-healthy smokers was unclear.

AIM: We have conducted a preliminary study to determine the difference in blood pressure and inflammatory parameters on overweight and non-overweight in healthy smokers.

METHODS: We have conducted a study with a cross-sectional design. Thirty-seven healthy smokers are the number of subjects who participated in our study; 20 were overweight, and the other 17 subjects were non-overweight. The smokers consumed 5–12 cigarettes/day regularly for at least 5 years. Furthermore, smokers were diagnosed in healthy condition by the doctor in the primary health care. Blood was drawn from the cubital vein by professionals. Hematology and inflammatory parameters were examined using a hematology analyzer and an ELISA method. We used the t-test to determine the mean difference in parameters between groups.

RESULTS: The study of 37 healthy volunteers who smoked showed that overweight status had higher blood pressure and IL-1 levels than the non-overweight. There was a difference in mean systolic and diastolic blood pressure and IL-1 levels between the overweight and non-overweight groups ($p < 0.05$). The overweight status was in accordance with the mean of BMI and body weight ($p < 0.05$). There were no differences in cholesterol, triglyceride levels and hemogram profiles, and other cytokines between the two groups ($p > 0.05$).

CONCLUSION: We concluded that the overweight group had higher blood pressure and IL-1 levels than the non-overweight group of healthy smokers.

Introduction

Smoking and obesity are the two main risk factors for cardiovascular disease [1]. Cigarette smoke (CS) causes considerable morbidity and mortality by inducing cancer, chronic lung and vascular diseases, and oral disease [2]. Despite the well-recognized risks associated with smoking, the habit remains unacceptably prevalent. Several toxins present in CS have immunomodulatory effects. The effects of CS on immunity are far-reaching and complex; both proinflammatory and suppressive effects may be induced [3]. The net effect of CS on immunity depends on many variables, including the dose and type of tobacco, the route and chronicity of exposure, and other factors at the time of immune cell stimulation, such as toll receptor ligands or other inflammatory mediators. CS impairs innate defenses against pathogens, modulates antigen presentation, and promotes autoimmunity [4].

At present, the prevalence of smokers in Indonesia is more than 33%, ranking the highest in

Southeast Asia. The increasing number of smokers has become a matter of concern that should be taken care of [5]. Especially, in the era of civilized development, people have started to focus on their health and think about avoiding diseases. Due to cigarette smoking, 4 million people are dying per year. This number of dying may duplicate or increase every year [6]. Numerous studies proved that cigarette smoking is the primary cause of abnormal and significant increases in hematological parameters, leading to the early atherosclerosis, cardiovascular diseases, and chronic obstructive pulmonary disease [7]. In addition, smoking addiction causes cancer, pancreatitis, periodontal disease, and gastrointestinal disorders [8]. The recognition of specific mechanisms by which CS affects host immunity is an essential step toward elucidating mechanisms of tobacco-induced disease, and it may identify novel therapeutic approaches for managing diseases that affect smokers.

It is estimated that by 2030 nearly two-thirds of the global population will be either overweight or obese [9]. Basic Health Research 2007 data show that

central obesity in adults (>15 years) according to BMI in Indonesia is 18.8% and increased to 31% in 2018. The prevalence of obesity by gender in Indonesia is 7.8% male and 25.5% female [10]. Obesity harms the health, health costs, and long-term productivity of a nation [11]. In terms of health, overweight or obesity results in various degenerative diseases, such as diabetes mellitus, coronary heart disease, stroke, and cancer. Obesity is one of the most important cardiovascular risk factors [12]. According to the NCD Risk Factor Collaboration, the number of worldwide obesity cases has tripled in the past 45 years, with over 1.9 billion adults (39% overweight and 13% obese). Presently, it is commonly known that obesity increases hypertension risk and impacts the response to antihypertensive drugs [13]. High blood pressure in healthy smokers is thought to increase the inflammatory response. We are concerned about the high prevalence of smokers in Indonesia, which is more than 32%, and the increasing number of new patients with hypertension, so we conducted a preliminary study to determine the differences in blood pressure and inflammatory parameters between overweight and non-overweight in healthy smokers. The data of this study will be the basis of the screening program and management of hypertension therapy in Indonesia.

Methods

Design, subject, and materials

We have conducted a cross-sectional study on healthy, active-smokers in Blawong Village. Our current study was carried out to scrutinize the relevant effects of cigarette smoking on inflammatory cytokines in a group of clinically overweight and normal-weight subjects.

Determination of the minimum sample size using the formula for the difference in the average BMI from www.openepi.com. We recruited subjects by purposive sampling. Volunteer recruitment criteria include male, healthy, active smokers aged more than 18–60 years, willing to be involved and follow the blood drawing procedure voluntarily. From the preliminary test results, it is known that if overweight has a BMI of $28.05 \pm 6.02 \text{ kg/m}^2$, while the normal-weight group with a BMI of $20.03 \pm 5.04 \text{ kg/m}^2$, it requires a minimum of 8 subjects for each group. Thirty-seven subjects participated in this study, 20 were overweight, and 17 were normal-weight in the 18–60 years. The volunteers were recruited from rural areas at Jetis 1 Public Health center, Bantul (J1PHC).

The smokers regularly consumed 30–60 cigarettes per week for at least 5 years. Moreover, consent was taken from each individual after we informed the research. The study protocol was confirmed by the Ethical Review Committee in Ahmad

Dahlan University. A questionnaire was completed for each volunteer, including name, age, number of cigarettes smoked/day, and duration of smoking. Participants with temporary diseases such as influenza, digestive system dysfunction, arthritis, and diabetes mellitus were excluded from the study.

Data collecting procedure

A professional laboratory staff has collected the samples; 3–5ml of venous blood was drawn from cubital venous; after that, the serum was isolated by centrifugation (nuve-NF200). Serum samples were investigated using ELISA Human Reader HS; the ELISA kit was also used to measure IL-1, IL2, IL4, IL-6, IL-10, and IL-13 levels. The inspection steps have been followed according to the kit's instructions, in which the producing company recommends. The blood samples obtained measured blood sugar levels, while triglycerides, cholesterol, urea, creatinine, SGOT, SGPT, and hemogram were also measured. Blood pressure, pulse, weight, and height were measured during blood collection and interview filling out the questionnaire.

Statistical analysis

Numeric data were described by (mean \pm SD). We use the independent t-test to compare two numeric variables if the data are parametric, but if the data are non-parametric; then, we test with McNemar. A level of significance of 0.05 was applied to the test (SPSS v.22 and Excel 2013) programs used to analyze current data.

Results

Subject characteristics

Terdapat 38 perokok aktif sehat sesuai kriteria seleksi bersedia menjadi sukarelawan dalam penelitian ini. One of the volunteers was excluded from the study for technical reasons. This study included 37 active smoker volunteers (Figure 1).

Thirty-seven subject divided into two groups based on overweight status, 20 overweight, and 17 in non-overweight. Table 1 shows the characteristics of 37 cases. From the interviews, it is known that the volunteers were consuming 5–12 cigarettes/day regularly for at least 5 years.

The results of the analysis of normality and distribution of data on BMI, BP, BW, blood chemistry, and inflammation parameters showed that the data were normal and homogeneous. Refer to Table 1, the overweight status in smokers in this study follows BMI and body weight. Overweight smokers have higher systolic (SBP)

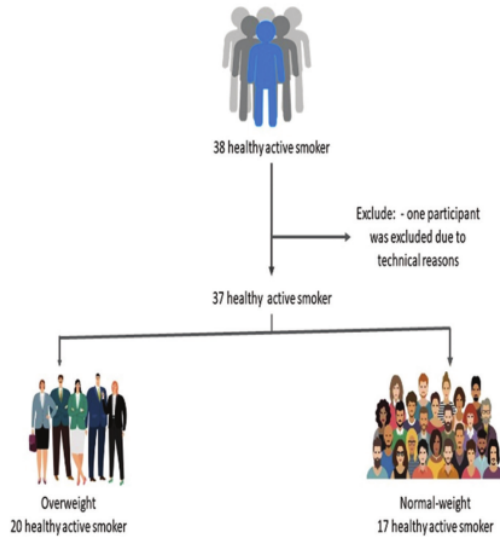


Figure 1: Flow chart of recruitment of subjects

Table 1: Anthropometric and clinical characters of healthy active smoker with overweight and normal-weight in J1PHC, Bantul regency, Yogyakarta

Parameters	Overweight (n = 20)	Normal-weight (n = 17)	p
Age	48.32 ± 13.23	45.47 ± 14.52	0.36
Systolic blood pressure	142.85 ± 20.50	127.94 ± 12.82	0.014*
Diastolic blood pressure	91.00 ± 12.35	80.29 ± 10.17	0.007**
Pulse	82.85 ± 10.36	79.29 ± 12.65	0.34
BMI	28.05 ± 3.95	20.26 ± 1.04	0.000**
Body weight	76.39 ± 8.65	56.92 ± 5.26	0.00**
Random blood sugar (RBS)	136.94 ± 57.97	149.67 ± 64.23	0.56
Triglyceride	157.82 ± 71.96	193.27 ± 111.51	0.45
Cholesterol	149.71 ± 27.95	160.13 ± 33.48	0.64
SGPT	21.02 ± 13.88	25.20 ± 21.16	0.47
SGOT	21.81 ± 6.09	23.21 ± 9.09	0.34
Ureum	21.54 ± 4.89	23.58 ± 3.96	0.32
Kreatinin	1.05 ± 0.19	1.07 ± 0.23	0.53
Food intake sampling			
Cholesterol intake	247.75 ± 141.17	247.75 ± 141.17	0.37
Protein intake	49.53 ± 20.06	46.22 ± 28.01	0.72
Lipid intake	40.22 ± 23.00	40.29 ± 34.72	0.85
Carbohydrate intake	100.53 ± 18.36	99.10 ± 17.49	0.91

and diastolic blood pressure (DBP) than non-overweight smokers, which are 142.85 ± 20.50 versus 127.94 ± 12.82 ($p < 0.05$) for SBP, and 91.00 ± 12.35 versus 80.29 ± 10.17 ($p < 0.00$) for DBP. Levels of triglycerides, cholesterol, urea, creatinine, SGPT, and SGOT were not associated with overweight status ($p > 0.05$).

Bivariate analysis of hemogram profile and cytokine to determine inflammatory parameter based on obesity status in a healthy smoker

Our results, in Table 2, showed no average difference in hemogram profile, IL2, IL-4, IL-6, IL-10, IL-13, and IFN- γ level in healthy smokers overweight compared with normal weight in rural areas of Yogyakarta ($p > 0.05$).

IL-1 level in the overweight healthy smoker group more than in the non-overweight healthy

Table 2: Mean difference (t-independent test) of hemogram, neutrophil-lymphocyte ratio, monocyte-lymphocyte ratio, and level of serum cytokine in overweight and non-overweight healthy smokers in J1PHC in Bantul regency, Yogyakarta

Parameter	Overweight (20)	Normal weight (n = 17)	p
WBC	8.48 ± 2.12	9.15 ± 1.79	0.33
RBC	4.95 ± 0.44	5.07 ± 0.48	0.45
HB	14.40 ± 1.48	14.90 ± 1.22	0.31
HCT	41.60 ± 3.51	42.28 ± 3.39	0.51
MCV	84.20 ± 4.81	83.48 ± 3.58	0.63
MCH	29.13 ± 2.27	29.43 ± 1.41	0.63
MCHC	34.57 ± 1.10	53.47 ± 75.10	0.65
PLT	241.00 ± 68.32	247.29 ± 47.99	0.76
Lymphocyte	34.453 ± 7.79	34.69 ± 7.85	0.93
MXD	8.73 ± 2.78	8.14 ± 3.03	0.57
Neutrophil	56.81 ± 6.08	53.97 ± 12.76	0.43
NLR	1.97 ± 0.96	1.59 ± 0.49	0.14
PLR	8.24 ± 5.82	7.00 ± 3.04	0.41
IL-4	14.19 ± 3.48	14.68 ± 3.62	0.71
IL-1	10.91 ± 12.00	4.24 ± 2.39	0.03*
IL-5	13.17 ± 4.13	12.07 ± 3.52	0.43
IL-13	73.18 ± 67.88	147.11 ± 137.40	0.07
IL-2	2.74 ± 2.45	2.61 ± 2.20	0.87
IFN- γ	20.60 ± 19.78	25.41 ± 22.70	0.53
IL-6	13.95 ± 5.40	12.37 ± 4.19	0.36

NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocytes ratio.

smoker group (10.91 ± 12.00 versus 4.24 ± 2.39 , $p < 0.05$). Overweight status was associated with changes in IL-1 levels and the ratio of monocyte IL-1, IL-2, IL4, IL-6, IL-10, and IL-13 was not affected by overweight status.

Discussion

Research data showed that overweight smokers had higher blood pressure than non-overweight smokers ($p < 0.05$). Clinically, overweight smokers have blood pressure in the hypertension group, while non-overweight smokers have normal blood pressure. Overweight status in smokers did not affect hemogram, kidney function, and liver function. Overweight conditions also do not affect temporary blood sugar, triglycerides, and cholesterol levels. IL-1 cytokine levels were higher in the overweight group than in the non-overweight group. Overweight status in smokers did not affect IL-2, IL-4, IL-6, IL-10, and IL-13.

Obesity is one of the most important cardiovascular risk factors [14]. It has been proven that overweight and obesity are associated with hypertension in the study group of patients with obesity and BMI of at least 30 kg/m^2 [15]. Overweight conditions in smokers certainly increase the inflammatory response and increase worsening conditions due to changes in the immune system's balance [16].

Cigarette smoke (CS) is a complex mixture of thousands of chemicals generated upon the burning or heating of tobacco leaves. CS contains thousands of chemicals with cytotoxic, mutagenic, carcinogenic, or antigenic properties [17]. Recent studies have approved that cigarette smoking hurts the human body [18], significantly affecting the immune system.

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Gaseous and particulate CS constituents first interface with the immune system at the mucosal surfaces lining the oral cavity, sinuses, and airways. CS constituents (particularly ROS) activate epithelial cell intracellular signaling cascades, leading to inflammatory gene activation [19]. The secretion of these inflammatory mediators promotes chronic immune cell recruitment and inflammation.

We recognize that this preliminary study has many weaknesses. The lack of the number of subjects and the design is the main weaknesses of this study, so it is necessary to research with a large sample size and a better design.

Conclusion

Based on the study results, we conclude that IL-1 levels and high blood pressure in healthy smokers are associated with overweight status. Although our data did not show an association between obesity status in healthy smokers with NLR, PLR, IL13, and other cytokines, the possibility of a relationship between these variables could not be eliminated.

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