Cent. Eur. J. Med. • 3(2) • 2008 • 167-172
DOI: 10.2478/s11536-008-0019-9

VERSITA

Central European Journal of **Medicine**

Homocysteinemia, hypertension, and family history of diabetes in a smoking male population in Saudi Arabia

Research Article

Nasser M. Al-Daghri*, Omar S. Al-Attas

King Saud University College of Science, Biochemistry Department, P.O Box 2455, Riyadh 11451, Kingdom of Saudi Arabia

Received 4 November 2007; Accepted 10 February 2008

Abstract: Arabs have a lower incidence of atherosclerosis than other ethnicities, but few studies have examined homocysteine (HCYS) as a risk factor for cardiovascular disease in this population. Here, we investigated the association between serum HYCS levels and risk factors for cardiovascular disease (smoking, hypertension, and family history of diabetes) in Saudi males. A total of 50 smokers and 72 nonsmokers completed a general health questionnaire. In addition, their lipid profiles were measured using routine methods and HCYS levels by high-performance liquid chromatograph with electrochemical detection. Regression analysis showed negative associations between HCYS and glucose ($r = -0.22$; $P < 0.05$) as well as family history of diabetes ($r = -0.21$; $P < 0.05$). HCYS levels were similar between hypertensive and nonhypertensive smokers, but they were significantly elevated in hypertensive nonsmokers ($P = 0.027$) and lower in smokers with family history of diabetes ($P = 0.01$). Levels of HCYS among nonsmokers inversely correlated with history of diabetes and elevated glucose. Nonsmokers' HCYS levels were significantly elevated in the presence of hypertension and correlated with diastolic blood pressure. Thus, HCYS may be a predictor of hypertension among nonsmokers. Until further trials are conducted, we recommend vitamin B6/folic acid supplementation for the Saudi hypertensive population as an adjuvant therapy.

Keywords: *Smoking • Homocysteine • Lipids, Blood pressure • Family history of diabetes • Saudi Arabia*

1. Introduction

Homocysteine (HCYS) is a sulfur-containing amino acid and is an intermediary product of methionine metabolism. Demethylation of methionine produces HCYS, which can either be remethylated to methionine by a process dependent on folic acid and vitamin B12, or it can be converted to cystathionine in a reaction dependent on vitamin B6. HCYS, like other thiols, readily auto-oxidizes to the disulfide HCYS or to other mixed disulfides, which together account for the major fraction of plasma HCYS. Several studies have identified elevated plasma HCYS as a risk factor for cardiovascular disease (CVD) [1-2]. In particular, hyperhomocysteinemia appears to stimulate oxidative stress and inhibit nitric oxide formation, which could explain the atherogenic effects described in type 2 diabetics [3]. Furthermore, the HCYS level is affected by age, and multiple studies suggest a relationship between HCYS levels and establish risk factors for CVD in elderly subjects [4-5].

In addition, previous studies suggest that HCYS levels are elevated in both smokers and those at risk for hypertension, but the combined effects of smoking and hypertension on the HCYS level remains unclear [6-8]. It is well established that cigarette smoking is the most important risk factor of coronary heart disease (CHD) in countries where the incidence of CHD is high [9-11]. The overall prevalence of smoking in Saudi Arabia has been reported to be as high as 21.1% for males, whereas it is only 0.9% for females. Most smokers (78%) are between 21 and 50 years of age. Within this smoking population prevalence appears higher among married people, uneducated people, and those in certain occupations, namely, manual workers, businessmen, army officers, and office workers [12]. Cigarette smoking is an important public health problem in Saudi Arabia, with the risk of CVD in smokers being two to three times that of

* *E-mail: aldaghri2000@hotmail.com*

nonsmokers, and it does not appear that noninhalation or the use of filtered cigarettes offers any protection. In addition, passive smokers are also at risk of developing CHD [13]. Cigarette smoking modifies haemostatic parameters via thrombosis, resulting in a higher rate of cardiovascular events [14] with studies indicating associations between HCYS levels and CVD risk [15].

In the kingdom of Saudi Arabia, the urban population has a higher prevalence of CHD than the rural population (6.2% vs. 4%, respectively) [16]. Additional analysis of diet has shown that smokers have lower levels of the B-vitamins folate, vitamin B6, and vitamin B12 [17-18], all of which affect HCYS levels by acting as cofactors (vitamins B6 and B12) or as a cosubstrate (folate) for enzymes controlling HCYS metabolism [19-21]. Despite these observations, there is no available data on HCYS levels among the Saudi smoking population, and its likely associations with factors linked to the development of CHD.

Here, we carried out a cross-sectional study to investigate whether HCYS levels in smokers are an important biomarker for determining the associated risk of hypertension in the Saudi population. Furthermore, we investigated the influence of factors that can alter HYCS levels in smokers and nonsmokers such as a history of diabetes and other metabolic parameters.

2. Material and Methods

2.1. Subjects

The subject population was drawn from adult, ambulant, non-diabetic Saudi males aged 30-80 years old, attending the blood bank of Riyadh Medical Complex and King Khalid University Hospital in Riyadh, Saudi Arabia. Ethical approval was obtained from the ethics committee of the College of Medicine, King Saud University in Riyadh, Kingdom of Saudi Arabia. Volunteers were asked to give verbal and informed consent prior to inclusion. Subjects were classified as smokers or nonsmokers. For purposes of this cross-sectional study, a smoker is defined as someone who has been actively involved in cigarette smoking for at least one year prior to the study. A nonsmoker was someone who may have previously smoked and with minimum exposure to a smoking environment (e.g., working and living in a nonsmoking environment). All subjects underwent a full physical examination and completed a general questionnaire. Data on socio-demographic characteristics, personal and family medical history including diabetes, and CHD (first-degree relatives who have had diabetes and/or CHD); and health-relevant behaviors including smoking, exercise, and diet were obtained by a standardized interview at the time of presentation. Patients with known illnesses other than hypertension including diabetes or a fasting blood sugar > 7.0 mmol/L and/or creatinine levels > 2000 mg/day were excluded from the study.

2.2. Data Collection

Anthropometric measurements such as height were measured to the nearest 0.5 cm using a standardized stadiometer; weight to the nearest 0.1 kg using a standardized weighing scale; waist and hips to the nearest 0.5 cm using a nonstretchable measuring tape. Blood pressure was measured twice after 30 min rest with a 15-min interval. The mean of the two readings was recorded. The presence of hypertension was defined as a blood pressure ≥ 140/90 mmHg after several readings and/or on hypertensive medications.

Blood samples were collected after a 12-h fast for the determination of total cholesterol, high-density lipoprotein, triglycerides, and HCYS concentrations. Plasma samples were stored at –70°C prior to analysis. Serum glucose, total cholesterol, triglycerides, and 24-h creatinine clearance were measured using standard enzymatic methods and a fully automated analyzer (Kone Instruments, Helsinki, Finland). High-density lipoprotein-cholesterol levels were determined by phosphotungstic acid/magnesium chloride precipitation (Kone Instruments). The low-density lipoprotein level was calculated using the Friedewald equation [22].

HCYS was measured by high-pressure liquid chromatography (HPLC) with electrochemical coulometric detection [23]. Briefly, samples were reduced with dithiothreitol to liberate HCYS, protein was precipitated with sulphosalicylic acid, and the supernatant was analyzed by HPLC.

2.3. Statistical analysis

Data were analyzed using SPSS for Windows, version 10 (SPSS, Chicago, IL, USA). Variables that exhibited a positive skew were log-transformed to normalize the distribution. For these variables, the geometric means are given along with the estimates of the percentage difference in geometric means between never smokers and current smokers. An independent *t*-test was used to compare the levels of the two groups and, if not normally distributed, by a Mann-Whitney *U*-test. The Pearson correlation coefficient was calculated to determine the association between selected parameters and other variables, and stepwise regression analysis was performed to identify significant factors affecting variables of interest.