ELEVATED HOMOCYSTEINE AND HYPERTENSION IN XINJIANG PROVINCE, CHINA

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Background: Few data are available comparing homocysteine (Hcy) levels in patients with hypertension in different ethnic groups.

Objectives: This study sought to determine whether there are associations of blood pressure and Hcy levels in patients with hypertension from Xinjiang Province, China.

Methods: We examined the serum total Hcy levels in a total of 451 Chinese of various ethnic groups (Han $n=234$ [51.9%], Uygur $n=102$ [22.6%], Kazak $n=61$ [13.5%], Hui $n=54$ [12.0%]) aged 18–78 years. Two groups of subjects were studied: 1) non-hypertensive, $n=101$; (2) hypertensive, $n=350$. We investigated the serum Hcy levels relationship with hypertension.

Results: Hcy levels of Kazak in no hypertension and hypertension patients were highest (11.9±9.8 vs 19.0±11.8 umol/L, respectively, unadjusted $P=.004$, adjusted $P=.016$). This pattern of higher Hcy values in hypertension patients was consistent across all ethnic groups even after adjustment (all $P<0.05$). The hypertension risks in the elevated Hcy (>13.9 umol/L) was 3.5 (95% CI, 2.2–5.4) times the normal Hcy (≤13.9 umol/L) ($P<0.001$). Even after adjustment for potential confounders, this difference remained 3.1 times higher (95% CI, 1.9–4.8) ($P<.001$). Bivariate correlation analysis revealed a statistically significant relationship of Hcy with systolic or diastolic blood pressure across all ethnic groups.

Conclusion: This study confirms the existence of a significant association between hypertension and Hcy in Chinese population groups. (*Ethn Dis*. 2010;20:7–10)

Key Words: Hypertension, Cardiovascular Disease, Homocysteine, China

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INTRODUCTION

Elevated homocysteine (Hcy) has been suggested to be an independent risk factor for cardiovascular disease, and a series of prospective epidemiologic studies have shown that higher levels of Hcy are associated with incident cardiac and vascular events in cardiovascular disease patients.[1,2] Clinical investigations demonstrate an association of Hcy with cardiovascular endpoints including stroke, myocardial infarction, and peripheral vascular diseases.[3–5] Many studies have focused on the direct relations of Hcy to blood pressure (BP) or hypertension.[6] Important questions remain regarding whether the relationship is similar across multiple ethnic groups.

China is undergoing rapid westernization of lifestyle, as evidenced by the rapid increase in the prevalence of obesity.[7] Other risk factors for cardiovascular disease are also quickly increasing.[8] In Xinjiang Province, China, for example, the Kazaks have a diet rich in animal fats and low in fiber, fruits and vegetables. Few data are available comparing Hcy levels in different ethnic Chinese groups; therefore, in this cross-sectional design we explored associations of BP and Hcy levels among 451 Chinese patients and sought to determine ethnic differences in the distribution of Hcy levels.

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METHODS

We conducted a survey based on clinical diagnosis and laboratory findings for 451 Chinese patients of various ethnic groups: Han, $n=234$ (51.9%); Uygur, $n=102$ (22.6%), Kazak, $n=61$ (13.5%), Hui, $n=54$ (12.0%). Participants were patients aged 18–78 years and admitted to Urumqi Third People Hospital, Xinjiang Province, China. All participants were first interviewed by completing a health history to provide information on age, sex, ethnicity, history of hypertension, diabetes, alcohol use and smoking. Except hypertension medication, none of the patients were taking any other medicine. Hypertension was determined if: 1) systolic BP (SBP) ≥140 mm Hg and/or diastolic BP (DBP) ≥90 mm Hg, or; 2) a patient had a self-reported history of hypertension and current use of antihypertensive medications. Patients were assigned into one of three classes according to blood pressure level and severity of other concomitant diseases. According to their clinical diagnosis, some hypertensive patients had concomitant coronary heart disease (CHD). Coronary heart disease was indicated by: chest pain; dyspnea; pericardial discomfort or clinical findings of left ventricular dilatation, defined as left ventricle end diastole dimension over 50 mm, and ST-T changes in electrocardiogram or as documented by coronary angiography to have more than 50% reduction in at least one main coronary artery.[9] Hypertensive or hy-

pertensive with concomitant CHD patients were selected as the hypertensive group. Free of CHD was defined as no typical chest pain on exertion, no myocardial infarction by history or electrocardiogram, negative exercise test, and less than 50% luminal narrowing of the coronary arteries. Free of CHD and non-hypertensive patients were selected as the controls to this study.[9] The local ethical committee approved this study.

All subjects underwent clinical assessment and age, sex, height, weight, SBP, and DBP were recorded. Anthropometric measurements (height and weight) were recorded by standardized protocols. Body mass index (BMI) was calculated (weight in kilogram/height in meter^2). Blood pressure was measured, by mercury sphygmomanometer with appropriate cuff size, on the patient's arm, with the participant in a sitting position after a 5-minute bed rest. Serum Hcy level was determined by high-performance liquid chromatography (HPLC) (RF-535-type apparatus, Japan) according to routine methods.

Table 1. Baseline clinical characteristics of patients by different BP groups

Variables	Non-hypertensive (*n*=101, 22.4%)	Hypertensive (*n*=350, 77.6%)	*P*
Age (mean±SD,years)	54.9±16.9	61.8±13.7	.001*
Sex (%)			.335†
Men	24.2	75.8	
Women	20.5	79.5	
Ethnicity (%)			.034†
Han	25.2	74.8	
Uygur	26.5	73.5	
Kazak	16.4	83.6	
Hui	9.3	90.7	
BMI (mean±SD, kg/m^2)	23.7±2.4	24.4±2.9	.020*
SBP (mean±SD, mm Hg)	107.0±16.5	151.2±25.4	<.001*
DBP (mean±SD, mm Hg)	65.5±10.9	90.0±14.6	<.001*
Diabetes (%)			<.001†
Yes	11.2	88.8	
No	71.4	28.6	
Alcohol use(%)			.017†
Never	76.0	24.0	
Former	19.4	80.6	
Current	21.9	78.1	
Smoking(%)			.022†
Never	75.8	24.2	
Former	16.3	83.7	
Current	27.1	72.9	

BMI=body mass index. SBP=systolic blood pressure; DBP=diastolic blood pressure.
* *t* tests; † chi-square.

STATISTICAL ANALYSIS

Data were entered in SPSS Windows software, version 16.0. Differences in baseline characteristics by hypertension status were determined by Chi-Square and Student's *t* tests. To approximate normal distribution, serum Hcy concentrations were logarithmically transformed (used in all calculations) and then back transformed (used in the presentation of the results). To evaluate the risk of hypertension, we used multinomial logistic regression to estimate the unadjusted odds ratio (OR) plus 95% confidence interval (CI). Similar logistic regression models were also used to determine the probability of adjusted OR between Hcy and BP status after adjustment for covariates. Statistical significance was considered to be $P<.05$.

RESULTS

Baseline Characteristics

The population consisted of 451 individuals who were divided into two groups: 1) controls, non-hypertensive, $n=101$; 2) patients with hypertension, $n=350$. Average age for non-hypertensive patients was 55 years vs 62 years for hypertensives (Table 1). Differences in baseline characteristics were stratified by the presence of hypertension. In comparison with non-hypertensive participants, those with hypertension were more likely to be older, diabetic, alcohol users and smokers. We also found that hypertension was associated with elevated Hcy. Within each ethnic group, the mean Hcy was higher in the hypertensive patients compared to the non-hypertensive patients. Hcy levels of the Kazak group for both non-hypertensive and hypertensive patients were higher (11.9±9.8 vs 19.0±11.8,umol/L, respectively, unadjusted $P=.004$ and adjusted $P=.016$) than any other ethnic groups (data not shown).

Hypertension Risks in the Elevated Hcy by Different Ethnic Groups

Normal Hcy levels range from 5 to 15 umol/L. Levels between 16 to 30 umol/L are considered moderate elevations, 31 to 100 umol/L as intermediate, and greater than 100 umol/L as severe.[10] For the Xinjiang population, participants with a serum Hcy levels of 4.5–13.9 umol/L were considered within a normal range while Hcy levels >13.9 umol/L were considered elevated. Table 2 shows the relative odds ratios of hypertension by category of Hcy level. The hypertension risk in the

Table 2. Multinomial logistic regression modeling estimates the probability of the association of elevated Hcy and hypertension

	Unadjusted OR (95%CI)	*P**	Adjusted† OR (95%CI)	*P**
BP groups				
Nonhypertensive	1.00		1.00	
Hypertensive	3.5(2.2–5.4)	<.001	3.1(1.9–4.8)	<.001
Ethnic groups				
Han	2.8(1.2–6.5)	.021	2.9(1.2–7.1)	.020
Uygur	6.4(2.4–17.5)	.000	5.1(1.8–14.9)	.003
Kazak	3.9(1.2–13.2)	.024	3.8(1.1–13.5)	.041
Hui	2.1(0.5–9.4)	.336	2.7(0.5–15.9)	.260

* Multinomial logistic regression.
† Adjusted for age, sex, BMI, diabetes, alcohol use, smoking.
CI =confidence interval.

elevated Hcy group was 3.5 (95% CI, 2.2–5.4) times the normal Hcy group ($P<.001$). Even after adjustment for potential confounders, the ratio remained at 3.1 times higher (95% CI,1.9–4.9) ($P<.001$) (Table 2).

DISCUSSION

In our study, hypertension and SBP or DBP were associated with higher Hcy levels in 4 ethnic groups. The strength of the association varied across ethnic groups. There are two possible explanations for these results: 1) homocysteinemia may be promoted by genetic factors required for Hcy metabolism; or 2) the relationship between Hcy and hypertension in the ethnic populations may be a consequence of different dietary intakes of vitamins as well as other nutrients. The Dietary Approach to Stop Hypertension (DASH) study[11] demonstrated the BP reduction effect of a diet that was high in multiple nutrients achieved by increased intake of fruits, vegetables, and low-fat dairy products.

Previous studies have shown an association between BP and Hcy.[12,13] Lim et al reported that people in the highest quintile of plasma Hcy had a 2- to 3-fold increased prevalence of hypertension,[14] compared with those in the lowest quintile in the third National Health and Nutrition Examination Survey. Studies found that a 1 standard deviation increase in Hcy was associated with increases in SDP/DBP of 0.5/0.7 mm Hg, respectively, in men, and of 0.7/1.2 mm Hg in women.[14,15] There are a number of plausible mechanisms that could explain an association between Hcy and hypertension. It is possible that Hcy may reduce the bioavailability of nitric oxide, thereby decreasing vasodilatation.[16] Possible mechanisms include the effect on increased arterial stiffness, insulin resistance,[17,18] and reduced vasodilatory capacity.[19] However, Sundström et al[20] showed no major relation of Hcy levels to hypertension incidence in a large, community-based cohort of non-hypertensive individuals after adjustment for age, sex, and other important covariates. In addition, recently, prospective studies by Lonn et al[21] and Bonaa et al[22] demonstrated that, although folic acid and vitamin B supplements significantly lowered serum Hcy levels, no decrease in risk of cardiovascular disease was actually observed. The same may well be true for BP. A high blood Hcy association with hypertension does not necessarily mean that lowering blood Hcy will lower BP. Other studies showed that elevated Hcy levels can be lowered through relatively simple nutritional measures, such as increased use of folic acid supplements or fortification of foods with folic acid.[23,24] Therefore, although the use of folic acid supplements to decrease the risk of cardiovascular disease is debated,[25–28] consumption of fruits, vegetables, and fibers are recommended as part of cardiovascular disease prevention program.

In summary, we found a significant association between Hcy levels and hypertension in Chinese ethnic group populations and homocysteinemia appears to have a different effect on the risk of hypertension in different ethnic groups.

We found a significant association between Hcy levels and hypertension in Chinese ethnic group populations

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