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Original article

Serum potassium level is associated with metabolic syndrome: A population-based study

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SUMMARY

Background & aims: Evidence has suggested that low serum potassium concentration or low dietary potassium intake can result in many metabolic disorders. Our objective was to evaluate the association between serum potassium level and risk of prevalent metabolic syndrome.
Methods: We conducted a cross-sectional study in 10,341 participants aged 40 years or older. Metabolic syndrome was defined according to guidelines from the National Cholesterol Education Program with modification.
Results: The prevalence rate of metabolic syndrome was 51.7% in participants with hypokalemia and 37.7% in those with normokalemia. With the reduction of serum potassium quartiles, participants were tended to have higher level of triglycerides and uric acid, lower level of high-density lipoprotein cholesterol (HDL-C), larger waist circumference and more severe insulin resistance. Serum potassium level significantly decreased with the increasing number of metabolic syndrome components. Compared with subjects in the highest quartile of serum potassium level, multivariate adjusted odds ratios for prevalent metabolic syndrome in the lowest quartile was 1.48 (95% confidence interval, 1.16–1.87). Moreover, compared with subjects without central obesity, hypertriglyceridemia, low HDL-C and elevated fasting plasma glucose, those with each of these metabolic syndrome components have lower level of serum potassium after adjusted for age and sex.
Conclusions: Low serum potassium level significantly associated with prevalence of metabolic syndrome in middle-aged and elderly Chinese.

1. Introduction

Metabolic syndrome is highly prevalent in Chinese adults[1] which can lead to increased risk for all causes mortality.[2] Metabolic syndrome is consists of abdominal obesity, dyslipidemia, hypertension, insulin resistance and hyperglycemia.[3] Additionally, nonalcoholic fatty liver disease (NAFLD) has been regarded as a hepatic manifestation of metabolic syndrome.[4]

A low serum potassium concentration may be the most usual electrolytic disorder encountered in clinical practice.[5] Relatively small change in the concentration of extracellular potassium could greatly affect the extracellular homeostasis and result in many metabolic disorders. Adults with lower serum potassium level and lower dietary potassium intake are at higher risk for incident diabetes.[6] Recently, C. Meisinger et al. found that serum potassium levels were inversely associated with prevalent prediabetes.[7] In addition, patients with central obesity have lower plasma potassium level compared with non-obese patients during diuretic therapy.[8] Higher prevalence of NAFLD and more serious insulin resistance are found in primary aldosteronism patients with potassium depletion than those with normokalemia.[9] Aside from the association of serum potassium level with glucose and lipids metabolism, the relationship of potassium with metabolic syndrome is also of interest. Aldosterone over production and

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concurrent hypokalemia can impair the insulin action, which seem to be the major contributors to the high prevalence of metabolic syndrome in patients with primary aldosteronism.[10] Reungjui et al.[11] proposed that potassium depletion might has a pivotal role in the exacerbation and worsening of the metabolic syndrome in response to thiazides. They also claimed that controlling serum potassium level to a normal range could reduce the risk of metabolic syndrome.

Further clarify the relationship between serum potassium level and metabolic syndrome would be conducive to the prevention and treatment of the disease. However, to our knowledge, studies that investigated the association in a general population were not available. Therefore, we analyzed data from a Chinese population to explore the possible association between serum potassium level and risk of prevalent metabolic syndrome.

2. Subjects and methods

2.1. Study population and design

We performed a population-based cross-sectional study in a community of Jiading District, Shanghai, China from March to August, 2010.[12] During the recruiting phase, a total of 10,569 residents who aged 40 years and older were invited to participate by examination notice and home visits. Totally, there were 10,375 subjects signed the consent form and agreed to take part in the survey, with a participation rate of 98.2%. Subjects who missed information on metabolic syndrome status ($n = 29$) were excluded from analysis. Subjects were also excluded if their serum potassium level greater than 5.5 mmol/L ($n = 5$).[6] Eventually, a total of 10,341 eligible individuals were included in the data analyses. The study protocol was approved by the Institutional Review Board of the Rui-Jin Hospital affiliated to Shanghai Jiao-Tong University School of Medicine and was in accordance with the principle of the Helsinki Declaration II. Written informed consent was obtained from each participant before data collection.

2.2. Clinical and biochemical measurements

We collected information on lifestyle factors, medical history, sociodemographic characteristics and family history by using a standard questionnaire. Smoking or drinking habit was classified as 'never', 'current' (smoking or drinking regularly in the past 6 months) or 'ever' (cessation of smoking or drinking more than 6 months).[13] A short form of the International Physical Activity Questionnaire (IPAQ) was used to estimate physical activity at leisure time by adding questions on frequency and duration of moderate or vigorous activities and walking.[14] Separate metabolic equivalent hours per week (MET-h/week) were calculated for evaluation of total physical activity.

All participants completed anthropometrical measurements with the assistance of trained staff by using standard protocols. Three times consecutively blood pressure measurements by the same observer with 5 min interval were obtained by an automated electronic device (OMRON Model HEM-752 FUZZY, Omron Company, Dalian, China). The average of three measurements of blood pressure was used for analysis. Body height and body weight were recorded to the nearest 0.1 cm and 0.1 kg while participants were wearing light indoor clothing without shoes. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Obesity was defined as BMI equal or greater than 28 and overweight was defined as BMI equal or greater than 24. Waist circumference (WC) was measured at the umbilical level with participant in standing position, at the end of gentle expiration.

Venous blood samples were collected for laboratory tests after an overnight fasting of at least 10 h. Measurement of serum potassium, fasting serum insulin, fasting plasma glucose (FPG), triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and creatinine was done using an autoanalyser (Beckman CX-7 Biochemical Autoanalyser, Brea, CA, USA). Hemoglobin A1c (HbA1c) was assessed by high-performance liquid chromatography (Bio-Rad, Hercules, CA). The abbreviated Modification of Diet in Renal Disease (MDRD) formula recalibrated for Chinese population was used to calculate estimated glomerular filtration rate (eGFR) expressed in mL/min per 1.73 m^2: eGFR $= 186 \times$ [serum creatinine $\times$ 0.011]$^{-1.154} \times$ [age]$^{-0.203} \times$ [0.742 if female] $\times$ 1.233, where serum creatinine was expressed as μmol/L and 1.233 was the adjusting coefficient for Chinese population.[15] The insulin resistance index (homeostasis model assessment of insulin resistance, HOMA-IR) was calculated as fasting insulin (μIU/ml) $\times$ fasting glucose (mmol/L)/22.5.[16] Insulin resistance was defined as HOMA-IR index in the top quartile (more than 2.5 in the present study).[17] Diabetes was diagnosed according to the 1999 World Health Organization diagnostic criteria. Prevalence of diabetes was calculated on both questionnaire and baseline blood sample test while anti-diabetic medications use was collected by questionnaire.

2.3. Definition of metabolic syndrome

According to the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III; ATP III) criteria,[2] metabolic syndrome was defined as the presence of three or more of the following abnormal factors: 1. Central obesity: WC greater than 102 cm in men and 88 cm in women, respectively; 2. Hypertriglyceridemia: serum triacylglycerol concentration of 1.69 mmol/L or greater; 3. Low HDL-C level: HDL-C concentration of less than 1.03 mmol/L in men or less than 1.29 mmol/L in women; 4. Hyperglycemia: fasting glucose concentration greater than 6.1 mmol/L or previous diagnosis of diabetes; 5. Elevated blood pressure: blood pressure of 130/85 mm Hg or greater. However, previous studies suggested that the ATP III criteria for WC might not be appropriate for Asian populations. Therefore, analyses of the prevalence of the metabolic syndrome in this study were done based on a more accurate cutoff for WC, which was equal to or greater than 90 cm for men and 80 cm for women.[1]

2.4. Statistical analysis

Statistical analysis was performed using SAS version 9.2 (SAS Institute Inc, Cary, NC, USA). Continuous variables were presented as means ± standard deviation (SD) except for skewed variables, which were presented as medians (interquartile ranges). Categorical variables were expressed as numbers (proportions). FPG, TG, HbA1c, HOMA-IR, eGFR and MET-h/week were logarithmically transformed before analysis due to a non-normal distribution. The study population was divided into quartiles on the basis of serum potassium distribution: quartile 1 (2.54–3.85 mmol/L), quartile 2 (3.86–4.11 mmol/L), quartile 3 (4.12–4.39 mmol/L) and quartile 4 (4.40–5.50 mmol/L). Linear regression analysis was used to test for trend across serum potassium quartiles. Differences among groups were tested by one-way ANOVA and *post hoc* comparisons were performed by using Bonferroni correction. Comparisons between categorical variables were performed with the χ^2 test. Hypokalemia was defined as serum potassium less or equal than 3.5 mmol/L.

We analyzed the impact of serum potassium level on the prevalence rates of metabolic syndrome and its related components. The unadjusted and multivariate adjusted logistic regression analysis was used to assess the risk of prevalent metabolic syndrome for each quartile of serum potassium compared with the