Original Research

Association of Biomarkers of Inflammation and Endothelial Dysfunction with Fasting and Postload Glucose Metabolism: A Population-Based Prospective Cohort Study among Inner Mongolians in China

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ARTICLE INFO

ABSTRACT

Objective: To examine the associations between elevated levels of C-reactive protein (CRP), soluble intercellular adhesion molecule-1 (sICAM-1) and soluble E-selectin (sE-selectin) with fasting and 2-hour postload glucometabolic status among Inner Mongolians in China.
Methods: Based on a cross-sectional survey of patients during 2003, 2260 participants were reinvestigated between 2013 and 2014. We categorized the participants into 3 subgroups according to fasting and postload glucose levels, respectively. The associations between biomarkers of inflammation and endothelial dysfunction and deterioration of fasting and postload glucometabolic status were examined by ordinal logistic regression analysis.
Results: We found 142 and 49 persons who had impaired fasting glucose (IFG) levels and type 2 diabetes in the fasting state and 335 and 50 persons who had impaired glucose tolerance (IGT) and type 2 diabetes in the postload state. After multivariable adjustment, elevated CRP and sICAM-1 levels were associated with deterioration of fasting glucometabolic status from normal fasting glucose to IFG and type 2 diabetes (odds ratio [OR] 1.73 [95% CI 1.18 to 2.54] for elevated CRP levels, OR 1.86 [95% CI 1.30 to 2.66] for elevated sICAM-1 levels). Elevated sE-selectin levels were associated with deterioration of postload glucometabolic status from normal glucose tolerance to IGT and type 2 diabetes (OR 1.34 [95% CI 1.01 to 1.77]) in the multivariable-adjusted model.
Conclusions: Biomarkers of inflammation and endothelial dysfunction were separately associated with fasting and postload glucose metabolism among Inner Mongolians.

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RÉSUMÉ

Objectif : Examiner les associations entre des niveaux élevés de protéine C-réactive (CRP), de la fraction soluble de la molécule d'adhésion intercellulaire de type 1 (sICAM-1), et de la fraction soluble de la E-sélectine (sE-sélectine) avec le statut gluco-métabolique à jeûn et 2 heures postprandial chez une population de Mongolie Intérieure en Chine.
Méthodes : Basé sur une enquête transversale sur des patients en 2003, 2260 participants ont été ré-évalués entre 2013 et 2014. Nous avons classé les participants en 3 sous-groupes en fonction des niveaux de jeûne et de glycémie postprandiale, respectivement. Les associations entre les biomarqueurs de l'inflammation et la dysfonction endothéliale, ainsi que la dégradation des statuts gluco-métaboliques à jeun et postprandial ont été examinés via une analyse par régression logistique ordinale.

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Résultats : Nous avons trouvé 142 et 49 personnes qui avaient des niveaux de glucose à jeun altérés (IFG) et un diabète de type 2 lors du jeûne, et 335 et 50 personnes qui avaient une intolérance au glucose (IGT) et un diabète de type 2 à l'état postprandial. Après ajustement par analyse multivariée, des niveaux élevés de CRP et de sICAM-1 ont été associés à une altération du statut de l'état gluco-métabolique lors du jeûne d'une glycémie à jeun normale à un IFG et un diabète de type 2 (odds ratio [OR] 1,73 [IC 95% 1.18 à 2,54] pour les niveaux de CRP élevés, OR 1,86 [IC 95% atteindre 1,30 à 2,66] pour les niveaux élevés de sICAM-1). Dans le modèle multivarié ajusté, des niveaux élevés de sE-sélectine ont été associés à une altération de l'état gluco-métabolique postprandial d'une normo-tolérance au glucose à une IGT et un diabète de type 2 (OR 1,34 [IC 95% 1,01 à 1,77]).

Conclusions : Les biomarqueurs de l'inflammation et de la dysfonction endothéliale ont été séparément associés au métabolisme du glucose à jeun et en état postprandial parmi la population de Mongolie Intérieure.

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Introduction

Type 2 diabetes results in devastating consequences to quality of life and is a leading cause of morbidity and mortality (1). In China, the prevalence of prediabetes and diabetes is high and is increasing (2,3), a development that has followed rapid economic growth and changes in lifestyle. China has the highest prevalence of diabetes in Asia and has the largest absolute disease burden of diabetes in the world (4). Inflammation and endothelial dysfunction are related to obesity and high glucose levels, suggesting that activation of the inflammatory response plays an important role in the pathogenesis of type 2 diabetes. Several prospective studies have showed that high baseline levels of C-reactive protein (CRP) are associated with the increased risk for type 2 diabetes (5,6). However, most of these studies were conducted in Western populations, and the roles of inflammation and endothelial dysfunction in the risk for fasting and/or postload glucose metabolic disorders have been poorly studied.

Additionally, there are inconsistencies in the literature regarding the relationship between soluble plasma adhesion molecules, such as E-selectin (sE-selectin) and intracellular adhesion molecule-1 (sICAM-1) and glucose metabolic disorders (7–9). For example, a cohort study of 1455 participants suggested that sE-selectin, but not sICAM-1, was associated with type 2 diabetes (8). In a multiethnic cohort of persons in the United States, higher levels of sE-selectin and sICAM-1 were consistently associated with increased risk for diabetes (9).

Epidemiologic studies demonstrated that impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) defined distinct populations, with only partial overlap (10), suggesting that different pathophysiologic metabolic disturbances lead to each state. It has been proposed that biomarkers of inflammation and endothelial dysfunction secreted by adipose tissue exert an endocrine effect, conferring insulin resistance in liver, skeletal muscle and vascular endothelial tissue, ultimately leading to the clinical expression of fasting or postload glucose metabolic disorders. In the present study, we examined the associations of elevated levels of CRP, sICAM-1 and sE-selectin with the deterioration of fasting and 2-hour postload glucometabolic status based on a more than 10-year follow-up study in an Inner Mongolian population from China.

Methods

Study participants

This study was established to evaluate potential risk factors for chronic diseases in a rural population of 32 villages in 2 townships, Kezuohou Banner (county) and Naiman Banner, Inner Mongolia, China, during the period between July 2002 and September 2003. The methods of recruitment of study participants and baseline data collection have been described before (11,12). In brief, 2589 Mongolian people 20 years of age or older were recruited from Inner Mongolia. All of the participants signed informed consent forms and completed the standard questionnaire at baseline. Individuals with cardiovascular diseases, endocrine diseases, infectious diseases in the past 2 weeks and antihypertensive drug users were excluded. In addition, 182 persons with prediabetes, 94 patients with diabetes and 53 without complete key variables were excluded in the present study. Finally, 2260 individuals were included in this study at baseline. The study was approved by the ethics committee at Soochow University in China.

Data collection

The trained staff interviewed participants using a standard questionnaire to obtain information about demographic characteristics and lifestyle risk factors. Cigarette smoking was defined as having smoked at least 1 cigarette per day for 1 year or more. Alcohol drinking was defined as having consumed at least 50 grams of alcohol per day for 1 year or more. Three sitting blood pressure measurements were taken for each participant by using a mercury sphygmomanometer according to a standard protocol. The mean of the 3 blood pressure measurements was used in the analysis. The waist circumferences were measured at the level of halfway between the iliac crest and the last rib.

Blood samples were collected in the morning after at least 8 hours of fasting. Plasma and serum samples were frozen at –80°C. Fasting plasma glucose levels were examined using a modified hexokinase enzymatic method. Total cholesterol, high-density lipoprotein cholesterol and triglyceride levels were analyzed enzymatically on a Beckman Synchrony CX5 Delta Clinical System (Beckman Coulter, Fullerton, California, USA) using commercial reagents. Low-density lipoprotein cholesterol concentration was calculated by means of the Friedewald equation for participants who had less than 400 mg/dL triglycerides (13). Concentrations of CRP were determined by an immunoturbidimetric assay on a Beckman Synchrony CX5 Delta Clinical System using commercial reagents. sE-selectin and sICAM-1 were measured by an ELISA assay (R&D Systems, Minneapolis, Minnesota, USA), which employs the quantitative sandwich enzyme immunoassay technique (14,15). Elevated levels of CRP, sICAM-1 and sE-selectin were defined as ≥9.55 mg/L, ≥381.88 ng/mL and ≥23.84 ng/mL (the upper quartile), respectively.

Follow up and outcome definitions

Cohort members were reinvestigated between 2013 and 2014. If participants reported that type 2 diabetes had occurred during the period between baseline survey and follow up, the staff contacted the subjects' general practitioners and reviewed records or death certificates to confirm. All other participants alive were instructed to maintain their usual physical activity and diet (more than 150 grams of carbohydrates per day) for at least 3 days before the oral glucose tolerance test according to a standard protocol. After