Obesity Research & Clinical Practice (2014) 8, e271—e282

ORIGINAL ARTICLE

Comparison of serum ferritin and oxidative stress biomarkers between Japanese workers with and without metabolic syndrome

Suketaka Iwanaga[a], Noriko Sakano[b], Kazuhisa Taketa[c], Noriko Takahashi[d], Da-Hong Wang[d], Hidekazu Takahashi[d], Masayuki Kubo[d], Nobuyuki Miyatake[b], Keiki Ogino[d,*]

[a] *Department of Public Health, Faculty of Medicine, Kyoto University, Kyoto, 606-8501, Japan*
[b] *Department of Hygiene, Faculty of Medicine, Kagawa University, Kagawa, 761-0793, Japan*
[c] *Geriatric Health Service Facility, Niwanosato Home, Mihara, Hiroshima, 729-1321, Japan*
[d] *Department of Public Health, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, 2-5-1 Shikata-cho, Okayama, 700-8558, Japan*

Received 18 August 2012; received in revised form 10 December 2012; accepted 9 January 2013

KEYWORDS
Oxidative stress;
Ferritin;
8-Hydroxy-2′-deoxyguanosine (8-OHdG);
Hydrogen peroxide (H_2O_2);
Metabolic syndrome

Summary
Objective: Metabolic syndrome (MS) is closely associated to life-style and is characterized by central obesity causing severe diseases such as diabetes mellitus (DM) or atherosclerosis. This study investigates the role of oxidative stress and inflammation in MS.
Subjects: Total of 685 workers stratified by gender (293 men and 392 women) with a mean age of 41.2 ± 10.4 in different offices in a city in Japan.
Methods: Fasting blood and urine tests for MS, oxidative and/or inflammatory biomarker analysis and blood pressure (BP) measurement were performed. MS was defined on the basis of the Japanese criterion.
Results: Serum ferritin and urinary hydrogen peroxide (H_2O_2) levels were significantly higher in subjects with MS than those without. Ferritin was positively correlated with 8-hydroxy-2′-deoxyguanosine (8-OHdG) in all subjects and it was negatively correlated with 8-isoprostane and H_2O_2 in men. In addition, there was a significant positive correlation between ferritin and homeostasis model assessment (HOMA-R) in men. By using multiple regression analysis, ferritin was closely correlated with HOMA-R, γ-GT, 8-OHdG, smoking value and amount of alcohol ingestion in men, and it was correlated with 8-OHdG, γ-GT, HOMA-R in women under 50 years old.

* Corresponding author. Tel.: +81 86 235 7184; fax: +81 86 226 0715.
E-mail address: kogino@md.okayama-u.ac.jp (K. Ogino).

1871-403X/$ — see front matter
http://dx.doi.org/10.1016/j.orcp.2013.01.003

Conclusions: Ferritin is a useful marker of MS including insulin resistance, reflecting the importance of oxidative stress as a cause of MS, especially in men.

Introduction

Metabolic syndrome (MS) is a condition related to life-style and characterized by central obesity leading to pathological conditions such as diabetes mellitus (DM) or atherosclerosis. Oxidative stress appears to be involved in this process and we have investigated several oxidative stress biomarkers in Japanese workers with and without MS and have shown that the urinary concentrations of 8-hydroxy-2′-deoxyguanosine (8-OHdG) and 8-isoprostane are useful prospective biomarkers of lifestyle-related disease risks [1]. We have also reported that 3-nitrotyrosine is related to exercise habits among healthy Japanese [2], and high-sensitivity C-reactive protein (hs-CRP) appears to mediate the smokers' renal dysfunction [3].

In addition to the above mentioned nitric oxide system for 8-isoprostane formation as well as the inflammatory process causing hs-CRP elevation, iron is also involved in oxidative stress by forming superoxide anion from hydrogen peroxide (H_2O_2) and Fe^{++} by the Fenton reaction. Serum ferritin level represents the amount of stored body iron and is regarded as one of the oxidative stress marker by forming Fe^{++} for the Fenton reaction. Total iron-binding capacity (TIBC) in serum is in reciprocal relationship with ferritin level and its increase represents the reduction in stored body iron. Serum iron level and its change are marker of chronic inflammation independent of serum ferritin or TIBC. Therefore, it is interesting to evaluate these markers of iron metabolism together with other oxidative stress markers and hs-CRP in MS in considering the effect of oxidative stress on life-related diseases.

Oxidative stress is defined as a situation in which an increased level of reactive oxygen species, such as superoxide anion and H_2O_2, overwhelms the antioxidative defense capacity, resulting in oxidative damage to lipids, DNA and proteins [4]. Thus, the determination of reactive oxygen species or the above mentioned oxidative stress markers in subjects with MS provide useful strategy in public health field [5].

In the present study, biomarkers of oxidative stress, including urinary 8-OHdG, 8-isoprostane, H_2O_2, hs-CRP, and serum ferritin were determined and compared among Japanese workers with and without MS.

Methods

Subjects

Data were obtained from a worksite lifestyle intervention study in six offices in a city in Japan in which 847 individuals were participated. For the purpose of this study, we excluded 162 subjects who had any history of cancer, stroke, DM, ischemic heart disease or asthma, and who were taking any medicines. Seven subjects were also excluded because their urinary concentrations of oxidative stress biomarkers and serum ferritin were under the limit of detection. Therefore, we finally used data for 685 subjects (293 men and 392 women). All subjects had been instructed to overnight-fast and not to consume any beverage and food except plain water before the sample collection.

The ethics committee of Okayama University approved the study, and written informed consent was obtained from all the subjects.

Health assessment

Health assessment was performed from September to December, 2007 by collecting blood samples after overnight fasting for at least 10 h. Serum and plasma samples were preserved at 4 °C for the measurement of aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ-glutamyltranspeptidase (γ-GT), triglycerides (TG), high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), fasting glucose, fasting insulin, hemoglobin A1c of NGSP (HbA1c), and hs-CRP. In addition, ferritin, Fe and unsaturated iron-binding capacity (UIBC) were determined in serum samples stored at −80 °C until analyses, because there was a time delay until measuring these markers. Serum ferritin was measured by iatro ferritin kit (Mitsubishi Chemical Medience Corporation, MBC, Tokyo, Japan) using automated analyzer (HITACHI 7700). Serum Fe was analyzed by colorimetric assay using iatro FeII kit (MBC, Tokyo, Japan), and UIBC was measured by colorimetric assay using iatro LQ UIBCIIkit (MBC, Tokyo, Japan). So, TIBC was calculated as TIBC = UIBC + Fe, and