Clinica Chimica Acta 430 (2014) 104–108

Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/clinchim

High adiponectin level in late postmenopausal women with normal renal function

Sumika Matsui [a,*], Toshiyuki Yasui [b], Kaoru Keyama [a], Anna Tani [a], Takeshi Kato [a], Hirokazu Uemura [c], Akira Kuwahara [a], Toshiya Matsuzaki [a], Minoru Irahara [a]

[a] Department of Obstetrics and Gynecology, Institute of Health Biosciences, The University of Tokushima Graduate School, Japan
[b] Department of Reproductive Technology, Institute of Health Biosciences, The University of Tokushima Graduate School, Japan
[c] Department of Preventive Medicine, Institute of Health Biosciences, The University of Tokushima Graduate School, Japan

ARTICLE INFO

Article history:
Received 18 September 2013
Received in revised form 9 December 2013
Accepted 23 December 2013
Available online 2 January 2014

Keywords:
Adiponectin
Renal function
Late postmenopause
Insulin resistance
Lipid profiles

ABSTRACT

Background: We examined whether high circulating adiponectin level is associated with renal function and is favorable for lipid and glucose metabolism in late postmenopausal women with normal renal function.
Methods: We conducted a cross-sectional study in 115 postmenopausal women and divided the subjects into 2 groups (early postmenopausal women and late postmenopausal women). Serum levels of adiponectin, blood urea nitrogen, creatinine (Cr), glucose, insulin and lipid profiles were measured. Glomerular filtration rate (GFR) was estimated by age and Cr.
Results: Serum adiponectin level in late postmenopausal women was significantly higher than that in early postmenopausal women, and eGFR in late postmenopausal women was significantly lower than that in early postmenopausal women. Adiponectin level showed a negative correlation with eGFR and tended to have a negative correlation with eGFR after adjustments for age, BMI and bioavailable testosterone in all subjects, but adiponectin level did not show a significant correlation with eGFR in late postmenopausal women. Adiponectin level in late postmenopausal women showed a significant negative correlation with triglyceride (TG) and a positive correlation with high-density lipoprotein cholesterol (HDL-C) after adjustments for age and BMI.
Conclusion: In late postmenopausal women with normal renal function, high adiponectin level is associated with favorable lipid profiles. High adiponectin level may be involved in not only eGFR but also other factors in late postmenopausal women.

1. Introduction

Adiponectin, which is an anti-inflammatory protein mainly secreted by adipocytes, has been reported to play an important role in protection against insulin resistance and atherosclerosis [1,2]. It has been reported that hypoadiponectinemia was correlated with the clinical phenotype of metabolic syndrome such as hypertension, impaired glucose tolerance and dyslipidemia [3]. High-density lipoprotein cholesterol (HDL-C) level, which plays an important role in protection against atherosclerosis, has been reported to be positively correlated with adiponectin level [4]. Matsuura et al. reported that adiponectin protected against atherosclerosis due to increase in HDL assembly through enhancing the pathway of ATP-binding cassette transporters and apoA-1 synthesis in the liver [5].

Previous studies demonstrated that adiponectin level in postmenopausal women was higher than that in premenopausal women [6–9]. We also reported that total adiponectin level and high molecular weight (HMW) adiponectin level were increased in late postmenopausal women for whom >5 y had passed since menopause and adiponectin levels were associated with levels of free and bioavailable testosterone in postmenopausal women [10,11]. Since estrogen deficiency after natural and surgical menopause has been associated with increases in insulin resistance and dyslipidemia, high adiponectin level after menopause is paradoxical and its clinical significance has not been fully clarified.

On the other hand, an association of adiponectin with renal function has been demonstrated. It has been reported that serum adiponectin levels in hemodialysis patients and patients with chronic kidney disease (CKD) were elevated compared to the level in healthy subjects [4,12]. Adiponectin has been shown to be negatively correlated with estimated glomerular filtration rate (eGFR) in patients with early stages of CKD [13]. Therefore, high adiponectin level in postmenopausal women with renal dysfunction may be due to decrease in adiponectin clearance in the kidney. However, the relationship between adiponectin level and renal function in the healthy subjects without renal dysfunction has been controversial [14–16].

* Corresponding author at: Department of Obstetrics and Gynecology, Course of Human Development, Human Development and Health Science, Institute of Health Biosciences, The University of Tokushima Graduate School, 3-18-15 Kuramoto, Tokushima 770-8503, Japan. Tel.: +81 88 633 7177; fax: +81 88 631 2630.
E-mail address: matsui.sumika@tokushima-u.ac.jp (S. Matsui).

0009-8981/$ – see front matter © 2014 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.cca.2013.12.037

2. Subjects and methods

2.1. Subjects

The subjects of this study were recruited from patients visiting the outpatient clinic of the Department of Obstetrics and Gynecology, Tokushima University Hospital. We conducted a cross-sectional study in 115 postmenopausal women. Based on the 2001 Stages of Reproductive Aging (STRAW) criteria, early postmenopause was defined as a period of less than 5 years since menopause and late postmenopause was defined as a period of more than 5 years since menopause. We divided subjects into two groups based on previous study [17]. Sixty women in early postmenopause were women for whom <5 y had passed since menopause, and 55 women in late postmenopause were women for whom >5 y had passed since menopause.

Before recruitment in the study, women underwent gynecological and biochemical examinations. Reviews of medical histories and the results of physical examinations and blood chemistry tests showed that all of the women were in good health. Exclusion criteria in the study were a history of any cardiovascular disease, diabetes mellitus, CKD, or liver disease. CKD is defined as eGFR <60 ml/min/1.73 m^2 for 3 months or more regardless of the cause [18]. Women who had received hormone replacement therapy in the past and women taking any medication known to influence lipoprotein metabolism were not included in the study.

Venous blood samples for measurements of hormones were drawn into BD vacutainer tubes (Becton, Dickinson and Company, Franklin Lakes, New Jersey) between 8 AM and 10 AM after 12-h fasting. Blood samples obtained were frozen at −70 °C until used for analysis. Informed consent for participation in this study was obtained from each woman. The Ethics Committee of Tokushima University Hospital approved the study.

2.2. Measurement of serum adiponectin concentration

Serum total adiponectin concentration was measured by an enzyme-linked immunosorbent assay using a commercially available kit (Otsuka Pharmaceuticals, Tokyo, Japan) after the samples had been diluted 5100-fold with the sample buffer as previously reported [19]. Intra- and inter-assay CVs were <10.0%, and the sensitivity of the assay was 23.4 pg/ml.

2.3. Measurements of serum concentrations of hormones

Serum estradiol concentration was measured by a chemiluminescent immunoassay using a commercially available kit (Abbott Co., Tokyo, Japan). The intra- and inter-assay CVs were <7%, and the sensitivity of the assay was 10 pg/ml. Serum concentrations of luteinizing hormone and follicle-stimulating hormone were measured by a chemiluminescent immunoassay using a commercially available kit (Abbott Co.). The intra- and inter-assay CVs were <7% and <10%, respectively. Serum total testosterone level was measured by an electrochemiluminescence immunoassay using a commercially available kit (Roche Diagnostics). Intra- and inter-assay CVs were 2.2–3.2% and 3.6–4.6%, respectively. The sensitivity of the assay was 0.05 ng/ml. Serum SHBG concentration was measured by a solid-phase immunoradiometric assay (Siemens Medical Solutions Diagnostics). Intra- and inter-assay CVs were 2.8–5.3% and 7.9–8.5%, respectively, and the sensitivity of the assay was 1 nmol/l. Serum free testosterone and bioavailable testosterone were calculated using total testosterone, albumin and SHBG by a previously described method [20].

2.4. Measurement of renal function

Serum creatinine (Cr) and blood urea nitrogen (BUN) levels were measured by using an automated clinical analyzer system (Hitachi, Tokyo, Japan). Glomerular filtration rate was estimated using the following equation: $eGFR = 194 \times age^{-0.287} \times Cr^{-1.094} \times 0.739$ [21].

2.5. Measurements of concentrations of glucose, insulin and lipids

Plasma glucose level was measured by using the glucose oxidase method on an Automated Glucose Analyzer GA04 (A&T). The intra- and inter-assay CVs ranged from 0.8 to 1.3% and 0.6 to 1.3%, respectively. Serum insulin level was measured by using an enzyme immunoassay on AIA2000 (TOSOH Co., Tokyo, Japan). The intra- and inter-assay CVs ranged from 1.1 to 3.2% and 1.9 to 3.3%, respectively, and the sensitivity of the assay was 1.0 μIU/ml. Insulin resistance was evaluated with homeostasis model assessment of insulin resistance (HOMA-IR), which was calculated for all subjects by the following formula: fasting serum insulin (μIU/ml) × fasting plasma glucose (mg/dl) / 405. Serum total cholesterol (TC), HDL-C and triglyceride (TG) levels were measured by using a chemistry system (Hitachi, Tokyo, Japan). Low-density lipoprotein cholesterol (LDL-C) was estimated by the Friedewald equation (LDL-C = TC − TG / 5 − HDL-C).

3. Statistical analysis

Data are presented as medians with 25th to 75th percentile ranges. The Mann–Whitney *U* test was used to compare differences between the 2 groups. The Kruskal–Wallis rank test was used to compare differences between multi-groups. Correlations between variables were determined using Spearman's rank order analysis. Age and body mass index (BMI)-adjusted partial correlation analysis was performed to determine the relationships of serum adiponectin concentration with renal function, insulin resistance and lipid parameters. We also considered the effects of hormones including testosterone on the correlation between adiponectin and eGFR and the correlations between adiponectin and insulin resistance and lipid parameters because we previously reported that circulating adiponectin levels were associated with levels of free and bioavailable testosterone in postmenopausal women [10]. Age, BMI and bioavailable testosterone-adjusted partial correlation analysis was performed because bioavailable testosterone showed a significant and strong correlation with free testosterone ($r = 0.997$, $p < 0.001$). All statistical analyses were carried out using Statview ver 8.2 (SAS Institute Inc.) and SPSS statistics version 20.0 (IBM, Armonk). All p values reported were 2-sided and a $p < 0.05$ were considered statistically significant. We performed statistical analysis by using one-half of the value of sensitivity when the values were below the sensitivity level.

4. Results

4.1. Total adiponectin level and renal function

Background characteristics of all 115 subjects and those of early postmenopausal women and late postmenopausal women are shown in Table 1. Serum adiponectin level in late postmenopausal women was significantly higher than that in early postmenopausal women ($p = 0.009$). Serum levels of Cr and BUN in late postmenopausal women were significantly higher than those in early postmenopausal women ($p < 0.001$ and $p = 0.004$, respectively), and eGFR in late postmenopausal women was significantly lower than that in early postmenopausal women ($p < 0.001$).

4.2. Levels of glucose, insulin and lipid profiles

As can be seen in Table 1, lipid profiles did not show significant differences between the 2 groups. Plasma glucose level in late postmenopausal women tended to be higher than that in early postmenopausal women.