Available online at www.sciencedirect.com
ScienceDirect
Metabolism Clinical and Experimental 58 (2009) 270 – 274
Metabolism
Clinical and Experimental
www.metabolismjournal.com

Adipogenic risk factor differences between Korean and white adults—potential role of plasma free fatty acid and adiponectin

Sangyeoup Lee[a,b], Michael D. Jensen[b,*]

[a]Center for Obesity, Nutrition and Metabolism and Department of Family Medicine, Pusan National University Hospital and Medical Education Unit, Pusan National University School of Medicine, and Medical Research Institute, Pusan National University, Busan 602739, South Korea
[b]Endocrine Research Unit, Mayo Clinic, Rochester, MN 55905, USA

Received 31 July 2008; accepted 11 September 2008

Abstract

Asian adults are at greater risk for metabolic abnormalities (insulin resistance, dyslipidemia) at the same body mass index (BMI) than are whites. Elevated free fatty acids (FFA) and decreased adiponectin are linked with these same metabolic abnormalities. We tested the hypothesis that fasting plasma FFA are greater and adiponectin concentrations are lower in Korean than white adults matched for age, sex, and BMI. Plasma FFA and adiponectin concentrations were analyzed using a microfluorometric assay and radioimmunoassay, respectively. Fasting plasma FFA concentrations were not different (P = .51) between Korean and white subjects (208 [183-232] vs 215 [168-262] μmol/L, median and 95% confidence interval). Despite similar body composition in the 2 groups, the plasma adiponectin concentrations in Koreans were significantly lower than those in whites in men, women, and total subgroups (adjusted mean ± SEM: 4.9 ± 0.8 vs 9.1 ± 0.8 μg/mL, P = .004; 8.9 ± 1.0 vs 13.2 ± 1.0 μg/mL, P = .006; and 6.5 ± 0.6 vs 11.1 ± 0.6 μg/mL, $P \leq .001$, respectively) after adjustment for differences in height, weight, and fat-free mass as covariates. Men had lower plasma adiponectin concentrations than women in both Korean (P = .041) and Western adults ($P < .001$). Plasma adiponectin levels are lower in Korean than age-, sex-, and body mass index–matched white adults, whereas fasting plasma FFA are not different. To the extent that adipogenic factors account for ethnic differences in metabolic disease risk, our data suggest that differences in the regulation of adiponectin may predispose toward greater metabolic abnormalities in Asians than whites at comparable BMI levels.

1. Introduction

Different cut points have been suggested for the diagnosis of obesity and upper-body obesity according to race or sex [1] because the risk of comorbidities is greater for Asians than whites at comparable body mass index (BMI), waist circumference (WC), and intraabdominal fat [2-5]. It is not yet known why Asians are more vulnerable to obesity-related diseases at similar BMI as whites as regards potential pathophysiologic mechanisms.

Excess free fatty acids (FFA) are thought to contribute to at least some of the metabolic abnormalities associated with central or upper-body obesity, including dyslipidemia and insulin resistance [6]. Unfortunately, although the ethnic differences in amounts of visceral adipose tissue had been already evaluated, direct comparison of plasma total FFA concentrations in different ethnic groups has not yet been reported. Kamei et al [7] reported no significant difference in fasting FFA concentration between native Japanese and Japanese Americans. Japanese Americans in this study, however, were older, had higher BMI, and had higher percentage of body fat than native Japanese. Adiponectin is another adipogenic factor linked to metabolic outcomes in obesity, metabolic syndromes, and cardiovascular complications of these disorders [8]. In general, whites seem to have greater plasma concentrations of adiponectin than other ethnic populations [9-14]; and Kadowaki et al [9] showed that, although American men were heavier, they had higher adiponectin concentrations than Japanese men. We could find no direct comparison of plasma FFA and adiponectin concentrations between white and Asian men and women who are matched for BMI and percentage of body fat.

* Corresponding author.
E-mail address: jensen@mayo.edu (M.D. Jensen).

0026-0495/$ – see front matter
doi:10.1016/j.metabol.2008.09.024

We hypothesized that plasma total FFA and adiponectin concentrations are different in Asians and whites after matching for age, sex, and BMI. We tested whether plasma FFA concentrations would be greater and adiponectin concentrations would be less in matched Korean and white adults.

2. Research design and methods

2.1. Subjects and experimental design

Forty-seven healthy Koreans and 47 age-, sex-, and BMI-matched whites with a BMI ranging from 18.9 to 30.3 kg/m^2 participated in this study, which was approved by both the Pusan National University Institutional Review Board and the Mayo Clinic Institutional Review Board. Height and weight were measured by an automatic height-weight scale to the nearest 0.1 cm and 0.1 kg, respectively; and BMI was calculated by dividing weight (in kilograms) by height squared (in meters^2). Percentage of body fat and total fat mass were measured by bioelectric impedance analysis (Inbody 3.0; Biospace, Seoul, Korea) for Korean subjects and by dual-energy x-ray absorptiometry (DXA) (DPX-IQ; Lunar Radiation, Madison, WI) for white subjects. Venous blood samples were obtained from each subject after a 12-hour fast.

2.2. Analytical methods

Total plasma FFA concentrations were measured using automated enzymatic techniques on the Cobas Fara centrifugal analyzer (Cobas Mira; Roche Diagnostics, Indianapolis, IN) at 340 nm (for FFA: FFA-C test kit; Wako Chemicals, Neuss, Germany). The FFA standard curve was prepared in our laboratory, containing 22% linoleic acid, 28% oleic and palmitic acid, 6% stearic and myristic acid, and 3% each of elaidic acid, palmitoleic acid, linolenic acid, and arachidonic acid bound to fatty acid–free bovine serum albumin. This was because the oleic acid standard provided with the kit resulted in total FFA concentrations 30% below those measured by high-performance liquid chromatography, likely because the kinetics of the reaction differ between different FFA species. All samples were analyzed in the same assay; and standards were run at the beginning, middle, and end of the run. Samples from Korean and white volunteers were intermixed to avoid potential ordering effects. Plasma adiponectin concentration was determined with a double-antibody radioimmunoassay kit (Linco Research, St Charles, MO). Intraassay coefficient of variation was 23%, 6.6%, and 5.1% at 2.8, 28.5, and 64.1 ng/mL, respectively.

Table 1
Characteristics of Korean and white groups

	Korean (n = 47)	White (n = 47)	P value
Age (y)	39.8 ± 6.9	38.7 ± 6.7	.140
Sex (M/F)	26:21	26:21	1.000
Height (cm)	164.9 ± 8.0	174.2 ± 10.8	<.001
Weight (kg)	63.4 ± 11.0	70.7 ± 15.1	<.001
BMI (kg/m^2)	23.1 ± 2.8	23.1 ± 2.9	.344
Body fat (%)	24.3 ± 4.3	25.7 ± 7.4	.079
Fat-free mass (kg)	44.3 ± 8.3	52.3 ± 12.7	<.001
Total plasma FFA (μmol/L)	208 (183-232)	215 (168-262)	.563
Adiponectin (μg/mL)	7.1 ± 4.1	10.8 ± 4.4	<.001

Data are expressed as mean ± SD except for sex (number) and total plasma FFA (median and 95% confidence interval). By paired *t* test except the McNemar test for sex and the Wilcoxon signed-rank test for total plasma FFA comparison.

Table 2
Correlation coefficients (*r*) of plasma adiponectin levels vs BMI, percentage of body fat, fat-free mass, and total plasma FFA in both races with adjustment for age and sex

Variables	Korean (n = 47)		White (n = 47)	
	r	*P* value	*r*	*P* value
BMI (kg/m^2)	−0.34	.028	−0.36	.018
Body fat (%)	−0.20	.209	−0.15	.351
Fat-free mass (kg)	−0.37	.017	−0.29	.065
FFA (μmol/L)	0.17	.277	0.05	.733

Statistics were tested by partial correlation analysis.

2.3. Statistical analysis

The mean and standard deviation of fasting plasma FFA and adiponectin concentrations from previous studies were used to develop the statistical power for this study. To test the hypothesis that fasting plasma FFA and adiponectin concentrations would be at least 20% greater in Koreans than whites (1-sided test), a sample size of 47 subjects per group provides 94% power to detect this difference with an α of 5%. Relations between continuous variables were analyzed by means of the calculation of Pearson or partial correlation coefficients or multivariate analysis as appropriate. Results are presented as mean and SD, SEM, or median and 95% confidence interval, as appropriate. We used analysis of covariance (ANCOVA) to determine differences in adjusted mean adiponectin between Koreans and whites after controlling for several covariates. A *P* value less than .05 was deemed statistically significant. SPSS 11.0 for Windows (SPSS, Chicago, IL) was used for all statistical analyses.

3. Results

By design, there was no difference in age, sex, and BMI between Korean and white volunteers. Although Korean participants were shorter, weighed less, and had less fat-free mass compared with white subjects, the percentage of body fat was not different between the 2 groups (Table 1). Eighty percent of the volunteers were in the BMI range of 18.9 to 24.9 kg/m^2, 18% had a BMI of 25 to 29.9 kg/m^2, and only 2% of the subjects had a BMI of at least 30 kg/m^2.

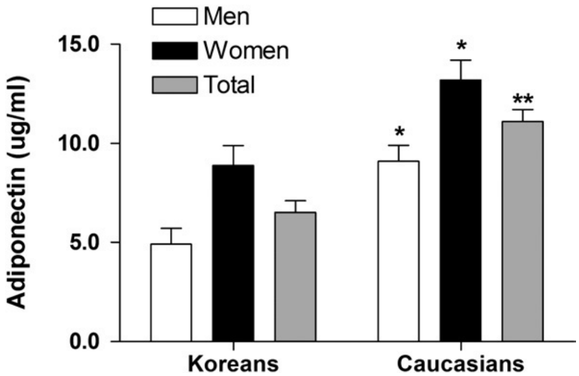

Fig. 1. Comparison of plasma adiponectin concentration in men (white bars), women (dark gray bars), and total (light gray bars) subjects between Koreans and whites. Values represent adjusted means ± SEM after adjustment for BMI and fat-free mass as covariates (additional adjustment for sex in total). **P* < .005, ***P* < .001 by ANCOVA.

Percentage of body fat was negatively correlated with height and fat-free mass (Table 2). Fat-free mass was positively correlated with height, weight, and BMI. Women had a tendency to have a higher body fat percentage and higher fat-free mass than men (data not shown).

We did not find a significant difference in plasma FFA concentrations between Korean and white subjects (Table 1, $P = .51$). We found no significant correlation between plasma FFA and BMI or percentage of body fat in either Korean or white people (data not shown).

Plasma adiponectin concentrations were lower in Korean than white adults ($P < .001$, Table 1). Men had lower adiponectin levels than women in both Korean ($P = .041$) and Western populations ($P < .001$, Fig. 1). By simple regression analysis, adiponectin was significantly and negatively correlated with BMI and free-fat mass ($P < .05$) in Korean adults and was negatively correlated only with BMI ($P < .05$) in white adults. No other variable was significantly associated with adiponectin. When the 2 groups were combined, ethnicity ($P = .001$) was the only independent predictor of plasma adiponectin in a multivariate analysis. The main effects of ethnicity on plasma adiponectin concentrations remained significant ($P < .001$) after controlling for height, weight, and fat-free mass as covariates with ANCOVA. The plasma adiponectin concentrations in Koreans were significantly lesser than with whites in men, women, and total subgroups (adjusted mean ± SEM: 4.9 ± 0.8 vs 9.1 ± 0.8 μg/mL, $P = .004$; 8.9 ± 1.0 vs 13.2 ± 1.0 μg/mL, $P = .006$; and 6.5 ± 0.6 vs 11.1 ± 0.6 μg/mL, $P \leq .001$, respectively).

4. Discussion

This is the first study, to our knowledge, to compare the concentration of 2 important adipogenic factors in metabolic disease—plasma FFA and adiponectin—directly among Koreans with similar age, sex, and BMI as whites. Previous studies indicate ethnic differences in the amount of intraabdominal fat, a factor associated with abnormal FFA and adipokines, between Asians and whites at the same WC levels [4,5]. A lower threshold of WC to define abdominal adiposity\disease risk has been proposed for South Asian populations compared with white populations [1]. It seemed likely to us that there might be differences in some key adipogenic factors that relate to metabolic complications of obesity. We found that, although fasting FFA concentrations were not different, adiponectin concentrations were lower in Korean than white men and women.

Plasma FFA, the major circulating lipid fuel in postabsorptive humans, originate from adipose tissue lipolysis. Adiponectin is an adipocyte-derived hormone that is thought to have anti-inflammatory and antiatherogenic effects [12,15] and is found at relatively high concentrations in human plasma ranging from 5 to 30 μg/mL. The adiponectin messenger RNAs and its plasma levels are reduced in obesity and its related comorbidities. Recently, racial and ethnic differences have been reported in plasma adiponectin levels between whites and other racial or ethnic groups [9-14]. To our knowledge, only a single study evaluated ethnic difference in adiponectin concentration between Eastern Asians who remain in their country of origin and whites [9]. However, this study reported results only for men, unmatched for age and BMI. Other studies have included mainly overweight/obese men or women or patients with diabetes mellitus or coronary artery disease [10-14]. Therefore, we hypothesized that racial difference in fasting plasma FFA or adiponectin concentrations could partially explain why Asians generally tended to have a higher risk of metabolic abnormalities at a lower WC and BMI than whites.

Asians consume less fat and more carbohydrate than whites [16]. Our results suggest that there is maybe limited interracial variability in fasting plasma FFA concentrations between people with similar normal and overweight BMI. This suggests that the regulation of FFA availability may be similar in different ethnic groups, although food items or the amount of dietary composition consumed varies widely between populations. In this study, whites were taller, weighed more, and had more fat-free mass compared with Koreans for the same BMI as in previous studies [17].

We found that Korean adults had significantly ($P < .001$) lower adiponectin levels than whites even after adjustment for confounding covariates. The prevalence of hypoadiponectinemia (<4.0 μg/mL) was 23.9% in Korean adults, which was higher than that in white adults (6.5%). In addition, we observed that women had higher adiponectin levels than men in both Korean and Western population. These findings are consistent with those of most [12,18], but not all [19], studies. Some of these sex differences in adiponectin may result from differences in the numbers and sizes of fat cells or sexual hormone [18,19]. In addition, we found that fat-free mass, not body fat percentage, was negatively correlated with plasma adiponectin concentration. However, some studies have shown lower adiponectin levels in subjects with higher body fat percentage [20-22], whereas other studies did not show such a relationship [13,23,24], which are consistent with our study. This discrepancy may be attributed, in part, to the differences in BMI, comorbidity, age distribution, or sample size among the subjects of previous studies. Possible mechanisms underlying the ethnic difference in adiponectin concentrations include differences in fat distribution, genetic polymorphisms in genes regulating adiponectin synthesis, secretion or degradation, and diet [2,10,13,14,16].

Our study has some limitations, including the lack of information regarding visceral fat, which could be an important predictor of adiponectin. We used bioimpedance analysis for body composition for Koreans and DXA methods for whites in this study, although bioimpedance analysis has been shown to be accurate in comparison to DXA [25]. Although the generalizability of our study to all Asians and whites is uncertain (all of the participants were Koreans and Americans), nevertheless, recent reports of similar differences between whites and other ethnic groups [9-14] suggest that this phenomenon is not limited to Koreans and American whites. Finally, we do not know whether there are ethnic differences in postprandial FFA concentrations or differences in other adipokines between these populations.

In conclusion, we found significant difference in plasma adiponectin, but not total plasma FFA, concentrations between Koreans and whites at the same BMI. Our findings suggest that total FFA concentrations are well regulated within the reference range in the overnight postabsorptive state even in different ethnic groups consuming different diets. However, ethnic difference in adiponectin concentrations is consistent with the greater vulnerability of Asians to obesity-related diseases than whites [26].

Acknowledgment

We would like to thank Deborah Harteneck for technical assistance with this study. This study was supported by DK45343 and UL1 RR024150 from the US Public Health Service, by 7-07-DCS-03 from the American Diabetes Association, and by the Mayo Foundation.

References

[1] James WP. Assessing obesity: are ethnic differences in body mass index and waist classification criteria justified? Obes Rev 2005;6:179-81.

[2] Deurenberg P, Deurenberg-Yap M, Guricci S. Asians are different from Caucasians and from each other in their body mass index/body fat percent relationship. Obes Rev 2002;3:141-6.

[3] Lee SY, Park HS, Kim DJ, Han JH, Kim SM, Cho GJ, et al. Appropriate waist circumference cutoff points for central obesity in Korean adults. Diabetes Res Clin Pract 2007;75:72-80.

[4] Park YW, Allison DB, Heymsfield SB, Gallagher D. Larger amounts of visceral adipose tissue in Asian Americans. Obes Res 2001;9:381-7.

[5] Han JH, Park HS, Kim SM, Lee SY, Kim DJ, Choi WH. Visceral adipose tissue as a predictor for metabolic risk factors in the Korean population. Diabet Med 2008;25:106-10.

[6] Koutsari C, Jensen MD. Thematic review series: patient-oriented research. Free fatty acid metabolism in human obesity. J Lipid Res 2006;47:1643-50.

[7] Kamei N, Yamane K, Nakanishi S, Ishida K, Ohtaki M, Okubo M, et al. Effects of a westernized lifestyle on the association between fasting serum nonesterified fatty acids and insulin secretion in Japanese men. Metabolism 2005;54:713-8.

[8] Rabin KR, Kamari Y, Avni I, Grossman E, Sharabi Y. Adiponectin: linking the metabolic syndrome to its cardiovascular consequences. Expert Rev Cardiovasc Ther 2005;3:465-71.

[9] Kadowaki T, Sekikawa A, Okamura T, Takamiya T, Kashiwagi A, Zaky WR, et al. Higher levels of adiponectin in American than in Japanese men despite obesity. Metabolism 2006;55:1561-3.

[10] Weyer C, Funahashi T, Tanaka S, Hotta K, Matsuzawa Y, Pratley RE, et al. Hypoadiponectinemia in obesity and type 2 diabetes: close association with insulin resistance and hyperinsulinemia. J Clin Endocrinol Metab 2001;86:1930-5.

[11] Hulver MW, Saleh O, MacDonald KG, Pories WJ, Barakat HA. Ethnic differences in adiponectin levels. Metabolism 2004;53:1-3.

[12] Lim HS, Tayebjee MH, Tan KT, Patel JV, Macfadyen RJ, Lip GY. Serum adiponectin in coronary heart disease: ethnic differences and relation to coronary artery disease severity. Heart 2005;91:1605-6.

[13] Shand B, Elder P, Scott R, Poa N, Frampton CM. Comparison of plasma adiponectin levels in New Zealand Maori and Caucasian individuals. N Z Med J 2007;120:U2606.

[14] Martin M, Palaniappan LP, Kwan AC, Reaven GM, Reaven PD. Ethnic differences in the relationship between adiponectin and insulin sensitivity in South Asian and Caucasian women. Diabetes Care 2008;31:798-801.

[15] Gil-Campos M, Canete RR, Gil A. Adiponectin, the missing link in insulin resistance and obesity. Clin Nutr 2004;23:963-74.

[16] Ueshima H, Okayama A, Saitoh S, Nakagawa H, Rodriguez B, Sakata K, et al. Differences in cardiovascular disease risk factors between Japanese in Japan and Japanese-Americans in Hawaii: the INTERLIPID study. J Hum Hypertens 2003;17:631-9.

[17] Wang J, Thornton JC, Heymsfield SB, Pierson Jr RN. The relationship between body mass index and body cell mass in African-American, Asian, and Caucasian adults. Acta Diabetol 2003;40(Suppl 1):S305-8.

[18] Abbasi F, Chang SA, Chu JW, Ciaraldi TP, Lamendola C, McLaughlin T, et al. Improvements in insulin resistance with weight loss, in contrast to rosiglitazone, are not associated with changes in plasma adiponectin or adiponectin multimeric complexes. Am J Physiol Regul Integr Comp Physiol 2006;290(1):R139-44.

[19] Gavrila A, Chan JL, Yiannakouris N, Kontogianni M, Miller LC, Orlova C, et al. Serum adiponectin levels are inversely associated with overall and central fat distribution but are not directly regulated by acute fasting or leptin administration in humans: cross-sectional and interventional studies. J Clin Endocrinol Metab 2003;88:4823-31.

[20] Ryan AS, Berman DM, Nicklas BJ, Sinha M, Gingerich RL, Meneilly GS, et al. Plasma adiponectin and leptin levels, body composition, and glucose utilization in adult women with wide ranges of age and obesity. Diabetes Care 2003;26:2383-8.

[21] Silha JV, Nyomba BL, Leslie WD, Murphy LJ. Ethnicity, insulin resistance, and inflammatory adipokines in women at high and low risk for vascular disease. Diabetes Care 2007;30:286-91.

[22] Hara T, Fujiwara H, Nakao H, Mimura T, Yoshikawa T, Fujimoto S. Body composition is related to increase in plasma adiponectin levels rather than training in young obese men. Eur J Appl Physiol 2005;94:520-6.

[23] Kim C, Park J, Park J, Kang E, Ahn C, Cha B, et al. Comparison of body fat composition and serum adiponectin levels in diabetic obesity and non-diabetic obesity. Obesity 2006;14:1164-71.
[24] Sobngwi E, Effoe V, Boudou P, Njamen D, Gautier JF, Mbanya JC. Waist circumference does not predict circulating adiponectin levels in sub-Saharan women. Cardiovasc Diabetol 2007;6:31.
[25] Bolanowski M, Nilsson BE. Assessment of human body composition using dual-energy x-ray absorptiometry and bioelectrical impedance analysis. Med Sci Monit 2001;7:1029-33.
[26] Okamoto Y, Kihara S, Funahashi T, Matsuzawa Y, Libby P. Adiponectin: a key adipocytokine in metabolic syndrome. Clin Sci 2006;110:267-78.