Eating Behaviors 15 (2014) 244–251

Contents lists available at ScienceDirect

Eating Behaviors

The prediction role of indexes of circulating adipokines for common anthropometric and nutritional characteristics of obesity in the obese Central European population

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ARTICLE INFO

Article history:
Received 12 September 2013
Received in revised form 25 January 2014
Accepted 4 March 2014
Available online 15 March 2014

Keywords:
Obesity
Nutrition
Adipokine
Leptin
Index
Correlation

ABSTRACT

Aims: This study was designed to investigate the relationship between 8 selected adipokines (leptin, leptin receptor, adiponectin, agouti-related peptide, omentin, visfatin, adipsin and resistin), dietary composition and anthropometric parameters found in the Central European obese population.
Methods: A total of 65 unrelated obese Central European Caucasian individuals were recruited for the study. Phenotypic measurements included weight, height, BMI, lean body mass, fat mass, body fat, waist and hip circumference, waist–hip ratio (WHR) and skinfold thickness. Participants completed standardized self-reported 7-day food records. Plasma levels of leptin, leptin receptor, adiponectin, agouti-related peptide (AgRP), resistin, adipsin, omentin and visfatin were examined using ELISA.
Results: Multiple associations (weight, height, percentage of body fat, waist circumference, hip circumference, WHR and sum of skinfold thickness) with the circulation levels of the investigated adipokines were identified. Leptin-Leptin receptor (L-LR) levels were found to correlate with total energy intake and macronutrients while adipsin was found to strongly correlate with multiple adipokines. Furthermore, the L-LR index was found to constitute a more accurate description of the relationship between BMI and body weight than individual measurements and the Ag–LR index was found to strongly correlate with both anthropometric and dietary characteristics.
Conclusion: Following confirmation on larger population samples and on samples of different ethnicities, the reported adipokine indexes could become a useful tool for estimating nutritional status and predicting the body composition of specific patient groups.

1. Introduction

The worldwide pandemic of obesity has brought considerable attention to research focused on the metabolic activity of white adipose tissue. Obesity has become a major worldwide health problem, especially as it is closely linked to a number of comorbidities including cardiovascular diseases, type 2 diabetes and hypertension; moreover, it also reduces life expectancy and has enormous economic and societal consequences (Ouchi, Parker, Lugus, & Walsh, 2011).

The discovery of leptin in 1994 (Zhang et al., 1994) changed the general perception of white adipose tissue to that of a major endocrine organ — in addition to its lipid storage function, responsible for maintaining and releasing energy-rich substrates (Berg & Scherer, 2005; Ouchi, Kihara, Funahashi, Matsuzawa, & Walsh, 2003). Since then, a continuous search for new molecules produced by adipose tissue, known as "adipokines", constitutes an important direction in obesity research (Bluher, 2012). Adipokines play a pivotal role in the regulation of appetite and satiety control, regulation of fat distribution, insulin sensitivity and insulin secretion, energy expenditure, inflammation, blood pressure, hemostasis, and endothelial function (Bays, 2009; Bluher, 2010; Bluher et al., 2012; Flier, Cook, Usher, & Spiegelman, 1987; Siiteri, 1987; Wajchenberg, 2000). Thus far, over 600 adipokines were identified; together, they comprise the so-called adipokinome of the fat tissue (Lehr, Hartwig, & Sell, 2012) and exert enormous systemic effects on various target organs including the brain, liver, ovaries, muscle, vasculature, heart and pancreatic β-cells (Bluher, 2012).

Recent data indicate that adipokines comprise a complex interconnected network, mediating an intense crosstalk between various

Abbreviations: BMI, body mass index; WHR, waist–hip ratio; AgRP, agouti-related peptide; M, male; F, female; SD, standard deviation; POMC, proopiomelanocortin.

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http://dx.doi.org/10.1016/j.eatbeh.2014.03.001
1471-0153/

tissues (Bays, 2009; Breitling, 2009; Sell, Dietze-Schroeder, & Eckel, 2006), and that the role these new chemical substances play in inflammation, metabolism, satiety and energy balance regulation has paved the way for new research and theories examining their effects on obesity.

Although a great deal of information regarding the individual effects of single adipokines is available from experimental models, not much is known about the actual relationships and synergy/antagonism of adipokines in human subjects and about their associations with other parameters — such as nutrition. Several recently published works indicated that using the ratio of two adipokines may reflect nutritional status more precisely that circulating level of just one adipokine (Labruna et al., 2011; Lau & Muniandy, 2011; Rubio-Guerra et al., 2013). This study therefore aims to investigate the relationship between 8 selected adipokines (leptin, leptin receptor, adiponectin, agouti-related peptide, omentin, visfatin, adipsin and resistin), measured at the same point in time in relation to the recorded dietary composition of a Czech obese population.

2. Materials and methods

2.1. Subjects

A total of 65 unrelated obese Central European Caucasian individuals of Czech origin were recruited for the study in a mass media campaign targeting the South Moravia region of the Czech Republic (n = 65, 12 M/53 F, BMI > 30 kg/m^2; mean BMI 45.12 (SD 5.75) kg/m^2; median age 42.70 years; age range 31.30–61.30 years). Inclusion and exclusion criteria were derived from a study conducted by Ma et al. (Ma et al., 2003). The study was conducted according to the guidelines set out in the Declaration of Helsinki and all procedures involving human subjects were approved by the Committee for Ethics of Medical Experiments on Human Subjects, Faculty of Medicine of Masaryk University (Brno, Czech Republic). Written informed consent was obtained from all subjects and is archived.

All individuals participating in the study were available for plasma analyses of all eight investigated peptides/proteins.

2.2. Anthropometric characteristics

All phenotypic measurements were performed by experienced specialists and included weight, height, BMI, lean body mass, fat mass, body fat, waist and hip circumferences, waist–hip ratio and skinfold thickness. Body composition was assessed by bioelectrical impedance analysis using the InBody 230 bioimpedance analyzer (Biospace Co Ltd., 518-10 Dogok 2-dong, Gangnam-gu, Seoul, Korea) with the subject in a standing position.

2.3. Dietary intake

Participants were advised to complete standardized self-reported 7-day food records. Food intake data obtained from the subjects were submitted for further analysis: the percentage of daily energy intake from carbohydrates, fat and protein as well as total energy and macronutrient intake were calculated using Nutrimaster Diet Analysis software modified for the Czech population (Abbott Laboratories, Abbott Park, IL, USA).

2.4. Biochemistry

Plasma levels of leptin, leptin receptor, adiponectin, AgRP, resistin, adipsin, omentin and visfatin were investigated using an ELISA-based methodology. Blood samples for plasma analyses were collected after overnight fasting and were immediately centrifuged at 1700 *g* for 20 min and then stored at −80 °C until analysis.

Plasma leptin, soluble leptin receptor, adipsin, AgRP and resistin levels were measured by commercially available sandwich ELISA (R&D Systems, Minneapolis, MN, USA). Plasma samples for analyses of leptin, leptin receptor, adipsin and resistin were diluted with calibrator diluent immediately before the assay in a ratio of 1:100, 1:5, 1:400 and 1:5, respectively. Intra-assay precision (expressed as CV) was less than 3.3, 6.1, 5.9, 5.5 and 5.3% while inter-assay precision (CV) was less than 5.4, 8.6, 6.9, 7.7 and 9.2% for the assays of leptin, leptin receptor, adipsin, AgRP and resistin, respectively.

Plasma adiponectin levels were measured by a commercially available ELISA (RayBiotech, Norcross, GA, USA). Samples were diluted 50,000 times in a singlet to assay range (4.1–1000 pg/ml) with a standardized assay diluent. The intra- and inter-assay CVs were less than 10 and 12%, respectively.

Plasma omentin-1 concentrations were measured by a commercially available ELISA (BioVendor, Modřice, Czech Republic). Samples were diluted 40 times with a dilution buffer immediately before the assay. The intra- and inter-assay CVs were less than 4.1% and 4.8%, respectively.

Intra- and inter-assay coefficients of variation for the visfatin in serum were <4.5% and <5.9%, respectively.

2.5. Statistics

Where applicable, it was first determined whether a variable presented a normal distribution using the Shapiro–Wilk test; in cases of skewed variables, logarithmic transformation was performed and normal distribution was tested again. For descriptive purposes, mean values are presented using untransformed values. Results are expressed as mean values and standard deviations unless otherwise stated.

The Pearson correlation coefficient (r) was utilized in the case of data which represented normal distribution while the Spearman correlation coefficient (R) was used in all other cases. Similarly, the *t*-test was used for the comparison of groups when data exhibited normal distribution, while the Mann–Whitney test was used in all other cases.

In order to identify variables which may contribute to predicting anthropometric or nutritional phenotypes, a backward stepwise logistic regression was carried out, i.e. a sequential procedure omitting one input variable at a time to build up a regression model in which the dependent variable is represented as the linear combination of independent variables (anthropometric and nutritional parameters).

Data analysis was performed using the R version 2.15.2 program package. Consensual values of $p < 0.05$ were considered statistically significant.

3. Results

A basic description of clinical data obtained from the study subjects is provided in Table 1.

3.1. Correlation of investigated adipokines with anthropometric parameters (Table 2)

In the univariate regression modeling across the entire cohort of obese individuals, independently of gender, significant correlations were observed between age and leptin receptor levels ($r = 0.398$, $p = 0.001$), adipsin levels ($r = 0.310$, $p = 0.014$), omentin levels ($r = 0.494$, $p < 0.001$) and visfatin levels ($r = 0.275$, $p = 0.027$). Weight correlated with leptin levels ($r = 0.254$, $p = 0.048$), leptin receptor levels ($r = -0.292$, $p = 0.022$) and adipsin levels ($r = 0.275$, $p = 0.031$), while height correlated only with soluble leptin receptor levels ($r = -0.276$, $p = 0.031$). Further correlations were established between BMI and leptin ($R = 0.378$, $p = 0.003$) and adipsin ($R = 0.450$; $p < 0.001$) levels, between waist circumference