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ORIGINAL ARTICLE

Correlation of serum resistin level with insulin resistance and severity of retinopathy in type 2 diabetes mellitus

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Abstract Resistin is an adipocyte secreted hormone, to investigate the relationship between levels of serum resistin and C-reactive protein (as an inflammatory marker) together with insulin resistance and the presence of retinopathy in type 2 diabetes mellitus in Egyptian subjects, we measured fasting serum resistin and CRP levels in thirty obese diabetic subjects (with different grades of retinopathy: ten diabetic patients without retinopathy, ten diabetic patients with non-proliferative retinopathy and ten diabetic patients with proliferative retinopathy) and compared them with the results of ten obese non diabetic subjects and ten non obese healthy volunteers. Insulin resistance was assessed using the homeostasis model assessment for insulin resistance (HOMA-IR). All subjects were investigated to analyze the change in their total cholesterol, HDL-C, LDL-C, and triglycerides levels. Fasting glucose and insulin resistance were significantly higher ($P < 0.05$) in diabetic compared with non diabetic subjects. Fasting Serum resistin and CRP were highly significantly different among the groups of study ($P < 0.001$). Fasting serum resistin concentration showed highly significant positive correlation with CRP, BMI (body mass index), serum insulin, HOMA-I.R, and FBS (fasting blood sugar) and it was significantly positively correlated with waist, hip circumferences and triglycerides levels, while it was significantly negatively correlated with HDL-C. Serum resistin was associated with the presence of retinopathy in T2DM.

1. Introduction

Resistin is a member of a secretory protein family, known as resistin-like molecules (RELMs) (Steppan and Lazar, 2004). It was originally named for its resistance to insulin (Steppan et al., 2001). Resistin is expressed in white adipose tissue with the highest levels in female gonadal adipose tissue (Steppan and Lazar, 2002), besides adipose tissue, human resistin is also expressed in other varieties of human tissues. Real-time PCR showed that human resistin was expressed at the highest level

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in the bone marrow followed by the lung (Patel et al., 2003). Human resistin mRNA has also been detected in the nonfat cells of adipose depots (Fain et al., 2003).

Resistin was identified as a possible link between obesity and insulin resistance (Chen et al., 2002). Insulin resistance is a fundamental aspect of the etiology of type 2 diabetes and is also linked to a wide array of other pathophysiologic sequels including hypertension, hyperlipidemia, atherosclerosis and polycystic ovarian disease (Reaven, 1995). A specific complication of diabetes, microangiopathy, includes retinopathy, nephropathy, and neuropathy (Mabley and Soriano, 2005). The development or progression of diabetic microangiopathy could be affected by serum resistin (Osawa et al., 2007a).

Several recent human studies have supported the concept of inflammatory cytokine mediation of resistin (Mattevi et al., 2004), however, resistin associations with inflammatory markers appear to be independent of BMI, suggesting that resistin may have a direct proinflammatory role or mediate its effects via yet to be discovered obesity-independent mechanisms(Greeshma et al., 2004), C-reactive protein (CRP) is an inflammatory biomarker (Sun et al., 2005), involved in endothelial dysfunction and atherogenesis (Torzewski et al., 2000). Inflammation as measured by serum C-reactive protein has been shown to be increased in people with diabetes who have macro vascular complications (Zhao et al., 2011), and microangiopathy (Matsumoto et al., 2002).

In view of this, we investigated the correlation between serum resistin level and insulin resistance in obesity and type 2 diabetes mellitus together with serum resistin and CRP levels in relation to the presence of diabetic retinopathy in fifty Egyptian subjects.

2. Materials and methods

The study was conducted on fifty unrelated Egyptian subjects divided into three groups: group1 (control group) consists of ten non obese non diabetic healthy volunteers, group 2 consists of ten obese, non diabetic subjects and group 3 consists of thirty obese, diabetic subjects divided into 3 subgroups:

- Group 3a: includes ten patients without diabetic retinopathy.
- Group 3b: includes ten patients with non proliferative diabetic retinopathy.
- Group 3c: includes ten patients with proliferative diabetic retinopathy.

Diabetes mellitus was diagnosed based on the American Diabetes Association criteria, as reported in 1998. All subjects were informed of the purpose of the study and their consent was obtained. Physical data for each subject, including weight, height, waist and hip circumferences were recorded. Non diabetic volunteers were judged to be in good health according to their medical history and their fasting blood glucose level (<100 mg/dL).The subjects in group 3 were subjected to fundus examination for detection of the presence of retinopathy and laboratory investigations including, fasting blood glucose level by colorimetric method and fasting serum insulin level (Pal et al., 2008). Insulin resistance was measured using the homeostasis model assessment of insulin resistance (HOMA-IR), a reliable marker for insulin resistance, was calculated as fasting insulin × glucose level/22.5 (Katz et al., 2000). Serum resistin was measured using a human resistin ELISA kit (Bender Medsystems, Inc) (Greeshma et al., 2004). Subjects also were assayed for C-reactive protein (Ridker et al., 2002), and Lipid profile (Al-Omar et al.,2010) & (Mehrotra et al.,2009).

2.1. Statistical analysis

The collected data were tabulated and analyzed using SPSS version 16 software. Categorical data were presented as number and percentages, Chi square test (X2) was used as a test of significance while quantitative data were expressed as mean and standard deviation. Comparison of variables among groups of the study was made by one way analysis of variance (ANOVA). The Student "t" test was used to compare the means for pairs of groups. Correlation between serum resistin and other parameters of the subjects was determined by Pearson's Product correlation coefficient (r) to test the strength of association between serum resistin and other variables. Bonferroni's correction was also applied to analyses. Differences were considered statistically significant at $P < 0.05$ and highly significant at $P < 0.01$, to examine the relationship between serum resistin and retinopathy, simple regression analysis involving retinopathy stage as a dependent variable and serum resistin as an independent variable was performed. The receiver operating characteristic (ROC) curve was used to evaluate the performance of fasting serum resistin level as an indicator of developing retinopathy in diabetic subjects, specificity and sensitivity of different cut off values were estimated. An area under the ROC curve of 1.0 indicates perfect discrimination, whereas an area of 0.5 indicates that the test discriminates no better than chance (Zweig and Campbell, 1993).

3. Results

Fasting glucose and insulin resistance, as assessed using the homeostasis model of insulin resistance ratio (HOMA-IR), were similar in non obese and obese subjects, but significantly higher ($P < 0.05$) in diabetic compared with non diabetic subjects.

Fasting serum resistin was highly significantly ($P < 0.01$) different among the five groups (Table 1), mean serum resistin concentration increased in ascending manner in the five groups, showing the highest level in subjects with proliferative diabetic retinopathy. Bonferroni adjustment revealed that there was a significant difference between diabetic non retinopathy subjects and subjects with proliferative diabetic retinopathy.

The serum C-reactive protein levels showed a high significant difference between non diabetic and diabetic groups ($P < 0.01$), the comparison between diabetic non retinopathy group (DNR), and non-proliferative diabetic retinopathy group (NPDR) showed a high significant difference too ($P < 0.01$), so it appears that CRP concentrations were significantly associated with the presence of retinopathy.

Fasting serum resistin concentrations were not correlated with those of LDL-C, whereas there was a highly significant positive correlation between serum resistin concentrations and triglycerides, CRP, serum insulin and FBS concentrations, the same results were seen with BMI and HOMA-R. Serum