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ORIGINAL ARTICLE

Role of multifunctional Chemerin in obesity and preclinical diabetes

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Summary
Background: ''Chemerin'' is a multifuntional peptide involved in lipid and glucose metabolism. Elevated levels of this peptide have been associated with insulin resistance and systemic inflammation. This study aims to identify whether Chemerin along with other inflammatory markers (TNFα and hsCRP) can discriminate subjects with subclinical diabetes.
Methodology/findings: Fifty-two asymptomatic healthy volunteers and 22 chronic diabetics (T2DM) were enrolled in a cross sectional study design. They were subjected to a 75 g oral glucose tolerance test [OGTT (2-h glucose > 200 mg/dL)] and were then classified as either newly diagnosed diabetics (NDM) ($n = 23$) or healthy controls ($n = 29$). Our results showed a higher Chemerin level in NDM ($p < 0.01$; MWU) compared to controls and previously diagnosed DM. Using ROC analysis, Chemerin level in NDM and T2DM had AUC of 0.963 and 0.764 respectively, compared to healthy controls. We suggest that the cut off of 13.7 ng/ml of Chemerin can discriminate 73% of NDM subjects with impaired glucose level with 91% and 96% of sensitivity and specificity respectively. Elevated serum Chemerin in NDM group is a surrogate of impairment in glucose metabolism in obese individual.

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Conclusions: Chemerin along with other inflammatory biomarkers suggest an ongoing inflammatory process in a high risk obese group that indicates a pre-diabetic state.

Introduction

The prevalence of diabetes in Pakistani population has been reported to be 10% and twofold increase in cases is projected by the year 2030 [1,2]. Chemerin is a multifunctional protein, primarily known for its adipokine and chemotactic activities. The circulating concentration of Chemerin in humans was initially reported as 3—4.4 nM in blood [3,4]. However, no cut off value or population dependent reference ranges are available. Elevated levels of this peptide have also shown to be associated with disruption of normal insulin function and systemic inflammation [5]. Among pro-inflammatory cytokines, TNFα contributes in developing low grade inflammation in obese individuals [6] and link between visceral white adipose tissue (vWAT) and TNFα have been reported to cause increased insulin sensitivity [7,8]. Studies on genetic association of type II diabetes mellitus with TNFα polymorphism further confirms the role of cytokine and its association with diabetes [9]. Human C reactive protein (hsCRP) is another marker of inflammation, the possible link of hsCRP and Chemerin is the hepatic origin or synthesis of both proteins in liver. High level of Chemerin has been reported in cases with liver fibrosis or chronic liver disease [10,11]. Moreover, hepatic Chemerin production and expression was also confirmed by delivery of this adipokine in liver [12,13]. We therefore suggest an indirect relationship of Chemerin with hsCRP in T2DM. Since adipokine are thought to have a role in metabolic disorders, so Chemerin may act as a causal factor between obesity and development of T2DM [14]. In our study, the elevated level of Chemerin and other related inflammatory markers identify individuals with subclinical diabetes, which was also confirmed by conventional screening test such as OGTT. Such systemic inflammation in at risk obese individuals may lead to impairment in glucose metabolism, and increases the susceptibility to type II diabetes.

Methods

In a cross sectional study, we recruited 52 asymptomatic volunteers and 22 known cases of T2DM. All the asymptomatic subjects were subjected to an oral glucose challenge test (OGTT) (75-g glucose load in fasting state) and screened for nascent diabetes according to WHO criteria [15]. The subjects with 2 h glucose levels > 200 mg/dl were classified as newly diagnosed diabetics (NDM, $n = 23$), whereas remaining subjects with normal glucose levels were considered as control group ($n = 29$). Body fat was measured using Diagnostic Scale BG55 (Beurer Germany) and body mass index (BMI, kg/m^2) was calculated [16]. Blood samples were centrifuged within 1 h of collection and plasma was stored at −80 °C till further testing. Cytokine/adipokine levels in plasma samples were determined using commercially available sandwich ELISA kits, Chemerin (Glory Bioscience, USA, cat #11406), hsCRP (Dia Source, Immunoassay SA, Belgium). Serum TNFα level was measured by sandwich ELISA using pairs of monoclonal antibodies (Thermo Scientific, USA). All assays were performed according to manufacture instructions. The inter-assay coefficient of variation was less than 10%, and the within-assay coefficient of variation was less than 5%. Data was entered and analysed using SPSS 19.0 software (IBM, USA). Significant difference between the groups were tested by Mann Whitney *U* and *p* value <0.05 was considered significant. Receiver operating characteristic (ROC) curves was plotted for calculating sensitivity and specificity of markers to discriminate DM and NDM from controls. Rationale cut-offs were determined by MedCalc 13.3 software (Ostend, Belgium).

Ethics statement

The research protocol was approved by Basic Medical Sciences Institute research ethics committee (14/2/11/SSF/BMSI). All study subjects gave written informed consent before participation in the study. Study protocol was briefly explained for minimal risk of procedure and any possible adverse effects.

Results

Characteristics of study subjects

Table 1 shows the demographics of the study participants in controls, T2DM and NDM groups. The mean age of total participant was 41.5 ± 8.09 years, mean weight was 71.57 ± 13.27 kg, BMI 26.2 ± 4.46 kg/m^2, BF% 26.73 ± 7.06%. NDM group had significantly higher BMI and BF% ($p < 0.001$) compared to controls. The mean Fasting Blood Glucose (FBG) in NDM was slightly lower compared to T2DM but significantly higher ($p < 0.001$) compared to controls.

Biomarkers assessment in study subjects

Within biomarkers, Chemerin, TNFα and hsCRP were compared among three groups (Table 1). Mean level of Chemerin was highest in NDM group, followed by T2DM and control group. NDM had significantly higher