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Plasma levels of adipokines in systemic lupus erythematosus patients

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ABSTRACT

Objective: To evaluate the plasma levels of six adipokines, including chemerin, omentin-1, lipocalin-2, cathepsin-S, cathepsin-L and adipsin, in patients with SLE.
Methods: Ninety SLE patients and ninety control subjects were recruited, plasma adipokines levels were measured by enzyme-linked immunosorbent assay, and their associations with major clinical and laboratory indexes were analyzed.
Results: There were no significant differences in plasma chemerin, omentin-1, lipocalin-2, cathepsin-S, cathepsin-L and adipsin levels between SLE patients and controls. Further subgroup analyses by major clinical and laboratory indexes showed that plasma omentin-1 level was significantly lower in SLE patients without nephritis when compared with those patients with nephritis ($P = 0.002$). Plasma chemerin, cathepsin-S levels in SLE patients without nervous system disorder were significantly lower in comparison with SLE patients with nervous system disorder ($P = 0.035$, $P = 0.029$). No significant associations of other adipokines with any major clinical and laboratory indexes were observed.
Conclusions: Plasma levels of chemerin, omentin-1, lipocalin-2, cathepsin-S, cathepsin-L and adipsin in SLE patients were not markedly different from the normal controls. The presence of nephritis was connected with higher plasma omentin-1 levels in SLE patients, and the presence of nervous system disorder was associated with higher plasma chemerin, cathepsin-S levels in SLE patients. However, functional studies are awaited to further explore the potential roles of these cytokines in SLE.

1. Introduction

Systemic lupus erythematosus (SLE) is a chronic, recurrent, potentially fatal inflammatory connective tissue disorder characterized by the loss of self-immune tolerance, autoantibody production, formation of immune complexes, tissue inflammation in multiple organs, with high levels of pro-inflammatory cytokines in blood [1]. SLE patients have increased risk for cardiovascular events, metabolic syndrome caused by insulin resistance, and are associated with the development of obesity [2–4]. Adipose tissue has already been identified as a storage depot for body energy, but it is now also recognized as a key, complex endocrine organ by secreting a large number of mediators, including leptin, chemerin, resistin, omentin-1, etc., known as adipokines that have pro-inflammatory or anti-inflammatory effect [5]. These adipokines could affect metabolism, inflammation, and are responsible for pathological changes associated with obesity, metabolic syndrome, cardiovascular disease [6], as well as play significant roles in inflammatory, autoimmune and rheumatic diseases [5,7].

Numerous studies have focused on the expression and pathogenic roles of several adipokines in autoimmune diseases like SLE [8–12]. For instance, leptin has been suggested to have a role in pathogenic process of SLE, in particular modulating the cardiovascular risk of SLE patients. One study suggested that the leptin receptor gene Q223R polymorphism and increased serum leptin levels were significantly associated with increased SLE risk [8]. Meanwhile, two contradictory findings that serum leptin levels were significantly lower in SLE patients compared to the controls, and there was no significant difference in plasma leptin levels between SLE patients and controls were also reported [9,10]. Our recent study by meta-analysis also shows no significant difference in plasma/serum leptin levels between the SLE patients and

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controls [13]. Another study has demonstrated plasma adiponectin levels were increased in SLE patients with lupus nephritis (LN) in comparison with normal controls and SLE patients without LN [10,11]. Another adipokine, resistin has also been involved in SLE but with contradictory results [14]. In addition to leptin, adiponectin and resistin, there are also other adipokines, such as chemerin, omentin-1, lipocalin-2, etc., but very little is known about the expression level and pathogenic role of these adipocytokines in SLE. Therefore, in the present study, we evaluated the plasma chemerin, omentin-1, lipocalin-2, cathepsin-S, cathepsin-L and adipsin levels and their clinical associations in patients with SLE.

2. Subjects and methods

2.1. Study subjects

This study comprised of 180 subjects including 90 SLE patients and 90 control subjects. SLE patients were recruited from the Department of Rheumatology and immunology at the First Affiliated Hospital of Anhui Medical University and Anhui Provincial Hospital. The sex- and age-matched controls were selected from healthy blood donors of the same hospitals. All the patients were defined according to the 1997 revised American College of Rheumatology (ACR) classification criteria [15]. LN was diagnosed in accordance with the ACR criteria, any one of the following: persistent proteinuria $\geqslant$0.5 g/day; the presence of active cellular casts; biopsy evidence of LN [16]. Individual disease activity was evaluated using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score [17]. The SLEDAI score was evaluated at the time of the blood draw. Based on the SLEDAI score, the SLE patients were classed as more active (SLEDAI score $\geqslant$ 10), less active (SLEDAI score < 10) [18]. Body mass index (BMI) is defined as the patient's body weight divided by the square of his or her height, and the formula universally used in medicine produce a unit of measure of kg/m^2. Based on the BMI, SLE patients were divided into two groups: overweight or obese was defined as BMI $\geqslant$ 24 kg/m^2 while normal weight or underweight was defined as BMI < 24 kg/m^2 [19]. The controls were included as the general population, with no history of SLE, other rheumatologic conditions. All subjects signed their written informed consent before study, and this protocol conform to the provisions of the World Medical Association Declaration of Helsinki.

2.2. Collection of Sample, Clinical features, and enzyme-linked immunosorbent assay (ELISA)

In this study, plasma obtained from 5 ml peripheral blood of SLE patients and controls were prepared from EDTA-anticoagulated blood by Ficoll-Hypaque density gradient centrifugation, and stored at −80 °C until processed. Plasma chemerin, omentin-1, lipocalin-2, cathepsin-S, cathepsin-L, adipsin concentrations were determined by ELISA kits according to the manufacturer's instruction (Abcam, Inc.), and the results were expressed as nanogram per milliliter. The Clinical features of SLE such as nephritis, arthritis, serositis, alopecia, tetter, myositis, oral ulcers, and nervous system disorder, the laboratory features including anti-Sm, anti-SSA, anti-SSB, anti-dsDNA, etc., were collected from hospital records.

2.3. Statistical analysis

Statistical analysis was performed by using the Statistical Package for the Social Sciences (SPSS) statistical software for Windows, version 10.01 (SPSS Inc., IL, USA). Numerical data in normal distribution were expressed as mean ± SD, Nonparametric distribution data were described as median (interquartile range, IQR). The difference in categorical data between two groups was tested using the chi-square or Fisher's exact test. Difference in plasma concentration among groups was compared with Mann–Whitney rank sum test. A two-sided P value of less than 0.05 was considered as significant.

3. Results

In this study, the demographic characteristics of all subjects were shown in Table 1, there were no significant differences in age and gender distribution between SLE patients and health controls. The plasma chemerin, omentin-1, lipocalin-2, cathepsin-S, cathepsin-L and adipsin levels of SLE patients and controls were summarized in Table 2. There were no significant differences regarding plasma chemerin, omentin-1, lipocalin-2, cathepsin-S, cathepsin-L and adipsin levels between SLE patients and controls. No significant differences were found in plasma chemerin, omentin-1, lipocalin-2, cathepsin-S, cathepsin-L and adipsin levels between different BMI groups in SLE patients. The associations of plasma chemerin, omentin-1, lipocalin-2, cathepsin-S, cathepsin-L and adipsin levels with major clinical and laboratory features of SLE patients were shown in Tables 3 and 4. The plasma omentin-1 level was significantly decreased in SLE patients without nephritis when compared with those patients with nephritis (P = 0.002), and the higher chemerin, cathepsin-S levels were associated with the presence of nervous system disorder in SLE patients (P = 0.035, P = 0.029).

4. Discussion

Adipokines include a variety of pro-inflammatory and anti-inflammatory peptides, and these adipokines appear to represent a new family of compounds that can be considered as key players of the complex network of soluble mediators involved in the pathogenesis of rheumatic diseases, include SLE. In this study, we investigated the plasma expression of six adipokines (chemerin, omentin-1, lipocalin-2, cathepsin-S, cathepsin-L, adipsin) in SLE and healthy controls, and analyzed their relations with clinical and laboratory features. However, we found that there was no significant difference in plasma levels of chemerin, omentin-1, lipocalin-2, cathepsin-S, cathepsin-L, adipsin between SLE patients and controls; no significant difference of the plasma adipokines levels, except omentin-1, was found between SLE patients with nephritis and these patients without nephritis.

Omentin is a newly identified secretory protein and omentin-1, as another novel adipokine, has been shown to be the major circulating isoform in human serum. Our results revealed that omentin-1 levels were significantly higher in the plasma of SLE patients with nephritis compared with SLE patients without nephritis. Similarly, a previous study reported that patients with end stage renal disease who were in haemodialysis have increased levels of omentin-1 when compared with controls, and those patients with diabetes mellitus have decreased levels than patients with end stage renal disease on haemodialysis without diabetes mellitus

Table 1
The demographic characteristics of study subjects.

Characteristics	SLE patients (n = 90)	Normal controls (n = 90)	P value
Age (years)	37.85 ± 13.98	36.26 ± 11.82	0.408
Sex (male/female)	8/82	8/82	1.000
Active (SLEDAI $\geqslant$ 10)	49/41	NA	NA
Nephritis (yes/no)	33/57	NA	NA

SLEDAI: SLE disease activity index; NA: not applicable.