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BRIEF DEFINITE REPORT

Serum adipokine levels in patients with systemic lupus erythematosus

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Abstract
In patients with systemic lupus erythematosus (SLE) metabolic alterations are often observed, which may be due to either the disease, the genetic background or the treatment. We studied the serum levels of the adipokines leptin, adiponectin, resistin, visfatin and ghrelin in patients with SLE and controls. Leptin levels were lower and adiponectin, ghrelin and visfatin levels were higher in the patients. No significant differences were encountered for resistin. The values of adipokines were independent of treatment, even after correction for body mass index. Inverse correlations were found among leptin and adiponectin, ghrelin and visfatin. We conclude that adipokines are involved in the metabolic imbalance of patients with SLE.

Keywords: *Adipokines, leptin, adiponectin, ghrelin, resistin, visfatin*

Introduction

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease with multiple cellular and serological alterations. Genetic background, disease activity and treatment may play a major role in this imbalance [1–3]. Systemic inflammation has been shown to modulate adipocyte metabolism and consequently adipokines levels [4–7]. Steroids and other immune suppressors may be in part responsible for insulin resistance, alterations in circulating lipoproteins, as well as other hormones that consequently alter adipocyte metabolism and function [4–7]. Thus, the aim of the study was to assess adipokine levels and the possible role of treatment for the levels of these cytokines in patients with SLE.

Materials and methods

Blood samples were obtained from 60 SLE patients and 60 controls (see manuscript of Liliana Rivas this issue). The patients were divided according to the pharmacological treatment: (i) no treatment, (ii) steroids, (iii) steroids plus immune modulators, and (iv) steroids plus immune modulators and immune suppressers. Treated patients were on steroid therapy for more than 3 years. None of the patients was diabetic nor had moderate or severe kidney disease; SLE disease activity index (SLEDAI) index was moderate for all patients. The control collective was negative for infectious, autoimmune and lipid disorders. All patients and controls gave their written consent; The study was approved by the Ethical Committee of the Institute.

We employed commercial tests as described by the manufacturers for: (i) High sensitive C-reactive protein (CRP; Diagnostic Systems Laboratories, Webster, TX, USA), (ii) leptin and (iii) adiponectin (R&D systems, Minneapolis, MN, USA), (iv) ghrelin (Diagnostic Systems Laboratories, Webster, TX, USA) and (v) visfatin (BioVision, Mountain View, CA, USA). Unpaired Students' *t*-test, analysis of variance (ANOVA) analysis and Pearson's coefficient was assessed.

Results and discussion

Leptin levels were significantly lower in patients with SLE (4.1 ± 2.3 vs. 9.8 ± 2.4 ng/ml; $p < 0.005$).

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Table I. Patient groups and serum paramaters.

	NHD ($n = 60$)	Group 1 ($n = 22$)	Group 2 ($n = 17$)	Group 3 ($n = 14$)	Group 4 ($n = 7$)
Age (years)	32 ± 12	35 ± 5	34 ± 15	36 ± 6	36 ± 6
Female (%)	90	82	88	86	86
BMI	22 ± 2.0	25 ± 2.5	28 ± 5.2	24 ± 2.7	29 ± 8.1
p	–	0.003	0.0001	0.005	0.006
SLEDAI	–	4.5 ± 1.5	5.5 ± 3.5	6.8 ± 3.3	5.9 ± 2.8
p	–	–	0.3	0.1	0.2
CRP (mg/dl)	0.7 ± 0.3	2.8 ± 1.4	1.9 ± 1.2	1.7 ± 0.6	2.5 ± 1.3
p	–	0.001	0.001	0.01	0.0001
AN (ng/ml)	11 ± 4.7	18 ± 3.1	22 ± 3.8	19 ± 4.1	22 ± 4.2
p	–	0.001	0.0001	0.001	0.001
Ghrelin (ng/ml)	0.3 ± 0.1	0.5 ± 0.2	0.6 ± 0.2	0.5 ± 0.1	0.7 ± 0.2
p	–	0.05	0.01	0.01	0.001
Leptin (ng/ml)	9.8 ± 2.4	7.1 ± 2.6	5.1 ± 2.0	5.6 ± 3.2	4.5 ± 2.5
p	–	0.01	0.001	0.001	0.001
Resistin (ng/ml)	6.6 ± 3.2	6.9 ± 1.6	6.1 ± 2.5	6.3 ± 1.2	5.8 ± 2.9
p	–	0.8	0.8	0.8	0.5
Visfatin (ng/ml)	15 ± 2.8	21 ± 2.2	27 ± 3.2	22 ± 4.2	25 ± 8.2
p	–	0.001	0.001	0.001	0.001

AN, Adiponectin; 1, non-treated patients; 2, steroids; 3, steroids plus immune modulators and 4, steroids plus immunomodulators and immune suppressers. *p* values were calculated with respect to the controls.

In contrast, adiponectin, ghrelin and visfatin levels were higher in patients (19.3 ± 4.1 vs. 10.8 ± 4.7 ng/ml; $p < 0.005$, 0.5 ± 0.1 vs. 0.3 ± 0.1 pmol/l; $p < 0.005$ and 22.3 ± 1.9 ng/m vs. 15.2 ± 2.8 ng/ml, $p = 0.001$). No significant differences were detected for resistin (5.9 ± 2.8 vs. 6.6 ± 3.2 ng/ml). The difference in persisted even when values were corrected for body mass index (BMI). The differences were independent of CRP levels ($p > 0.2$) and did not correlate ($p > 0.6$) to CRP, BMI, SLEDAI index and treatment (Table I). Interestingly, even non treated patients had similar values as treated patients.

The levels of leptin were correlated with adiponectin, ghrelin and visfatin levels ([4,9]; Figure 1). An inverse correlation was found in all adipokines: for adiponectin ($r = -0.7$, $p < 0.005$), for ghrelin ($r = -0.6$, $p < 0.005$) and for visfatin ($r = -0.75$, $p < 0.001$). As suggested previously, systemic inflammation may be responsible for the decrease of leptin and the concomitant increase of adiponectin, ghrelin and visfatin [5–8].

There are other groups confirming decreased leptin levels in patients with SLE [10,11]. Opposite results are reported by Garcia-Gonzalez et al. [9], the only group observing increased leptin levels in SLE. The differences between all the reports may be due to differing disease severity and treatment modalities. The levels of resistin were similar among the different groups suggesting a complex control of insulin metabolism in these patients. Most probably, the

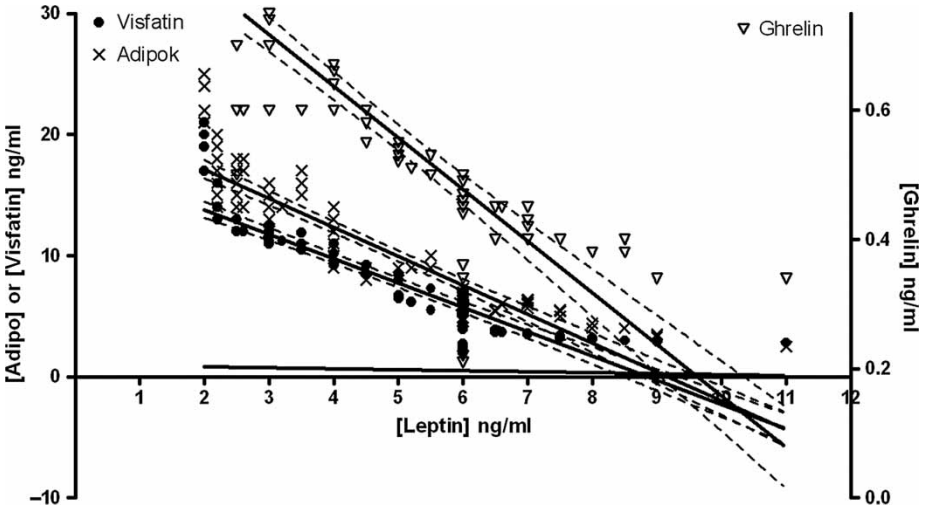

Figure 1. Correlation between leptin and adiponectin, ghrelin and visfatin

modulations of adipokine levels may also be related to other metabolic conditions influenced by the hypothalamic–adrenal–pituitary axis.

Our results regarding leptin and adiponectin levels differ slightly from those of Sada et al. [11], since no diabetic patients were enrolled in the study and even though we did not assess the homeostasis model assessment (HOMA) index, no major differences were encountered between the different patients. The lack of difference between patients and controls further support this finding.

Even though we did not encounter any association between the levels of these adipokines with the SLEDAI index ($p > 0.3$ for all parameters), a study involving defined subgroups of SLE and further parameters like insulin and sex hormones will be important to ascertain the effect of the inflammatory response. Treatment, an important and complexly interacting variable of adipokine metabolism, did not associate with adipokine levels in this small group of patients with low SLEDAI indices.

To our knowledge, there are no reports that have assessed adipokine levels in non treated patients with SLE. Furthermore, no study analyzed five adipokines. Genetic background seems not to be predominant in this context since Mestizo or Caucasian patients did not differ significantly. We propose that the chronic inflammatory status of the patients may be responsible for altered adipokine levels.

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