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The Role of Adiponectin in The Immunopathogenesis of Multiple Sclerosis

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ÖZET

Multipl skleroz immünopatogenezinde adiponektinin rolü

Amaç: Adipositokinlerden olan adiponektin nöroinflamasyon, nöroimmunoendokrin sistem modülasyonu ve immun sistem regülasyonunda rol oynar. Antienflamatuar ve protektif etkileri vardır. Fonksiyonlarını, proinflamatuar sitokinler, vazoaktif peptidler ve kompleman proteinleri ile etkileşerek periferik ve santral mekanizmalar aracılığı ile gösterir. Nöroinflamasyon ve nörodejenerasyon ile ilerleyen multipl sklerozun immunopatogenezi ile ilişkili çalışmalar immun hücreler, sitokinler, kemokinler, membran proteinleri, adhezyon molekülleri ve gen polimorfizmi üzerinde odaklanmaktadır. Son yıllarda adipoz dokunun immünolojik fonksiyonlar üzerindeki etkisine dikkat çekilmekte olduğundan, MS immunopatogenezinde adiposit ilişkili adiponektinin rolünü belirlemeyi planladık.

Gereç ve Yöntem: Atak ve atak sonrası dönemlerde MS hastalarından alınan serum örnekleri kontrollerin serum örnekleri ile ELISA yöntemi ile, karşılaştırmalı olarak ölçüldü. İstatistiksel analiz için Student's t test kullanıldı. $p<0.05$ anlamlı kabul edildi.

Bulgular: Adiponektin düzeylerinin MS hastalarında, atak sırasında, kontrollere göre ve ataktan sonraki döneme göre anlamlı şekilde daha düşük olduğu gözlendi.

Sonuç: Bulgularımız, immünolojik fonksiyonları olan adiponektinin MS immunopatogenezinde rolü olacağı düşüncesini ve sinyal transdüksiyon yolakları ve gen ekspresyon regülasyonunun, gelişen nanoteknolojisi yardımı ile yeni bir tedavi hedefi olabileceği görüşünü desteklemektedir.

Anahtar kelimeler: Multipl skleroz, adiponektin, nöroinflamasyon

ABSTRACT

The role of adiponectin in the immunopathogenesis of multiple sclerosis

Objective: Adiponectin from adipocytokines plays role in neuro-inflammation, neuroimmunoendocrine system modulation and immune system regulation and has anti-inflammatory and protective effects. It functions by interacting pro-inflammatory cytokines, vasoactive peptides and complement proteins through peripheral and central mechanisms.

The studies related to immunopathogenesis of Multiple Sclerosis (MS) progressing with neuroinflammation and neurodegeneration are focused on immune cells, cytokine, chemokines, membrane proteins, adhesion molecules and gene polymorphisms. We planned to determine the role of adipocyte related adiponectin in MS immunopathogenesis since the immunological functions of adipose tissue has drawn attention in the last years.

Material and Methods: Adiponectin levels were comparatively measured with serum samples of MS patients taken during and after attacks and control samples by using ELISA method. Student's t-test was used for statistical analysis. $p<0.05$ was accepted as significant.

Results: It was observed that adiponectin levels were extremely decreased in MS patients during attack compared to control group and the period after attack.

Conclusion: Our findings give rise to the thought that adiponectin which has immunological functions may play a role in immunopathogenesis of MS and its signal transduction pathways and gene expression regulation may be a new target in treatment with the help of developing nano technology..

Key words: Multiple sclerosis, adiponectin, neuroinflammation

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INTRODUCTION

Adiponectin from adipocytokines resulted from adipocytes plays role in neuroinflammation, neuroimmunoendocrine system modulation and immune system regulation and has anti-inflammatory and protective effects. In addition to adiponectin, adipocytokines such as resistine, visfatine and TNF alpha, IL-6, IL-1, CCL2 and complement factors are also excreted from adipose tissue and interact each other (1-3). These molecules may cause local or generalized inflammation by effecting immune cells. They may also affect endothelium functions by modulating nitric oxide and superoxide release. They also suppress the phagocytic activities of macrophages and monocytes. Its level decreases when endocannabinoid system is activated and increases when it is inhibited (4).

Adiponectin functions by interacting with proinflammatory cytokines, vasoactive peptides and complement proteins through peripheral and central mechanisms (5). It is activated with inflammatory stimulus and has two receptors such as Adipo R1 ve Adipo R2 (6). It inhibits the effects of resistine. Resistine increases the expression of ICAM-1 and VCAM-1 by directly affecting endothelium cells whereas adiponectin decreases (7).

The studies related to immunopathogenesis of Multiple Sclerosis (MS) progressing with neuroinflammation and neurodegeneration are focused on immune cells, cytokine, chemokines, membrane proteins, adhesion molecules and gene polymorphisms (8-19). Although cytokines and chemokines such as TNF alpha, IL-12, MIF, IFN gama, IL-4, IL-10, IL-17, IL-18, CCL2, CXCL8, CXCL10, CX3CLI has been studied, there has been still no study related to adiponectin.

In our study, we comparatively measured the adiponectin levels in 45 RRMS patients during attack and in control group after attack with the aim to analyze the role of adiponectin in MS immunopathogenesis which has not been analyzed yet.

MATERIAL AND METHODS

45 patients with RRMS who applied to Gazi University Medical Faculty, MS Polyclinic and diagnosed according to the McDonald's criteria between the ages of 20-38 (avr. 26±6.4), EDSS 3.1±1.9 being 31 females (68%) and 14 males (32%) and 20 control individuals were included in the study (8).

3 cc serum was taken from all individuals during and after the attack and stored at -20°C.

Adiponectin levels were measured with ELISA (Enzyme Linked Immuno Sorbent Assay). Standard solutions including adiponectin were diluted and incubated in micro plates together with serum samples and finally their absorbance values were measured at 450 nm at subsequent to several steps. Student's t-test was used for statistical analysis. $p<0.05$ was accepted as significant.

RESULTS

Serum adiponectin levels of patients with RRMS and control group during attack are shown in Figure 1. The serum adiponectin levels of patients were significantly lower than the control group during attack ($p<0.05$).

Serum adiponectin levels of patients with RRMS and control group after attack are given in Figure 2. The difference between groups was not found significant ($p>0.05$).

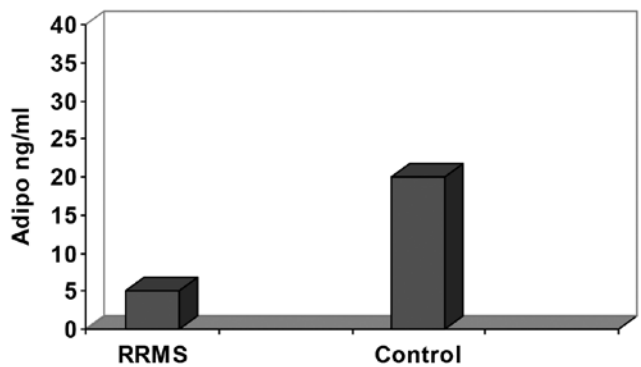

Figure 1: Serum adiponectin levels of RRMS patients during attack

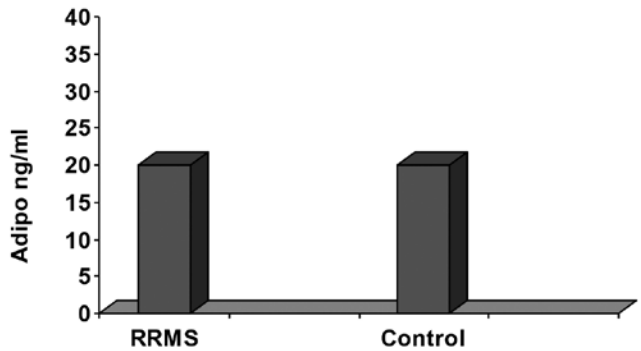

Figure 2: Serum adiponectin levels of RRMS patients after attack

Table 1: Serum adiponectin levels of RRMS patients during and after attack

	Adiponectin (ng/ml) (During attack)	**Adiponectin (ng/ml) (After attack)**
RRMS (n=45)	5.7±2.3	12.0±5.2
Control (n=20)	14.0±6.7	14.0±6.7

Serum adiponectin levels of patients with RRMS during and after attack are given in Table 1. According to this table, the difference of serum adiponectin levels during and after attack was not found significant (p>0.05).

DISCUSSION

Within the last years, neuroinflammation draws attention in MS immunopathogenesis and cytokine, chemokine and peptides which are considered to play a role has been intensively researched (9-22). Having anti-inflammatory and protective characteristics which have not been analyzed yet, adiponectin plays a role in immunoinflammation by interacting other cytokines and chemokines and can be activated through inflammatory stimulus (5,6,23). The immunological functions of adipose tissue and adipocytokines have recently taken the attention. The facts that adipocytes excrete cytokines such as TNF alpha, IL-6, IL-1, CCL2, chemokines besides adipocytokines and regulate monocyte/macrophage functions and express Toll-like receptors indicate that it is a new member of adipose tissue and immune system (24,25).

In our study, the decreasing levels of adiponectin in RRMS patients during attack were considered to be as a result of its interaction with proinflammatory cytokines and chemokines and resistine from adipocytokines (7). These findings give rise to the thought that adiponectin which immunological functions has not been known until recently and which has not been analyzed in MS patients before may play a role in immunopathogenesis and its signal transduction pathways and gene expression regulation may be a new target in treatment with the help of developing nanotechnology by considering its anti-inflammatory and protective characteristics.

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