

Serum leptin levels among 6-16-year-old children with asthma and obesity

Astım ve obezitesi olan 6-16 yaş arası çocuklarda serum leptin düzeyi

Ayşe YENİGÜN¹, Özgün UYGUR², Dilek YILMAZ¹, Aslıhan KARUL BÜYÜKÖZTÜRK³

¹ Department of Children's Health and Diseases, Faculty of Medicine, Adnan Menderes University, Aydın, Turkey
Adnan Menderes Üniversitesi Tıp Fakültesi, Çocuk Sağlığı ve Hastalıkları Anabilim Dalı, Aydın, Türkiye

² Department of Children's Health and Diseases, Faculty of Medicine, Ege University, Izmir, Turkey
Ege Üniversitesi Tıp Fakültesi, Çocuk Sağlığı ve Hastalıkları Anabilim Dalı, İzmir, Türkiye

³ Department of Biochemistry, Faculty of Medicine, Adnan Menderes University, Aydın, Turkey
Adnan Menderes Üniversitesi Tıp Fakültesi, Biyokimya Anabilim Dalı, Aydın, Türkiye

ABSTRACT

Objective: The incidence of asthma is slightly increasing. In regions where prevalence of asthma is getting higher, there is a tendency for an increase in obesity. The aim of this study is to evaluate the relation between serum leptin levels, pulmonary function tests and serum total IgE levels among 6-16-year-old-children with asthma and obesity.

Materials and Methods: There were 44 children included in the study (mean age 10.2 ± 2.36 years). Totally 11 asthmatic (3 female, 8 male), 12 asthmatic obese (3 female, 9 male) and 9 obese (7 female, 2 male) children were selected. Control group was consisted of 12 healthy (6 female, 6 male) children. Body mass index, pulmonary function tests, serum total IgE levels and serum leptin levels were calculated.

Results: Interestingly; there was a significant relation between PEF levels and serum leptin levels ($p=0.016$) but no relation was found between leptin levels and FEV₁, FVC, FEV₁/FVC. In the study; no positive effect of inhale steroid on leptin was present ($p>0.05$).

Conclusion: Every new study about leptin brings together new data about the subject. In this point

ÖZ

Giriş: Astım insidansı giderek artmaktadır. Astım prevalansının daha fazla olduğu bölgelerde, obezitede de artma eğilimi vardır. Bu çalışmada 6-16 yaş arası astım ve obezitesi olan çocuklarda, serum leptin düzeyi ile solunum fonksiyon testleri ve serum IgE düzeyleri arasındaki ilişkinin araştırılması amaçlanmıştır.

Gereç ve Yöntem: Çalışmaya 11'i astımlı (K/E = 3/8), 12'si astımlı obez (K/E = 3/9), dokuzu obez (K/E = 7/2) ve 12'si sağlıklı (K/E = 6/6) toplam 44 çocuk alındı. Beden kitle indeksi, solunum fonksiyon testleri, serum IgE ve leptin düzeyleri ölçüldü.

Bulgular: PEF düzeyleri ile serum leptin düzeyleri arasında anlamlı ilişki ($p=0.016$) olmasına rağmen, leptin düzeyi ile FEV₁, FVC, FEV₁/FVC arasında herhangi bir ilişki saptanmadı. Bu çalışmada inhaler steroidin leptin üzerine pozitif etkisi saptanmadı ($p>0.05$).

Sonuç: Leptinle ilgili yapılan her yeni çalışma bize yeni bilgiler kazandırmaktadır. Serum leptin düzeyi ile PEF arasında pozitif ilişki olmasından dolayı, akut ve kronik astım tedavisi sırasında PEF'in yanında serum leptin düzeyinin de ölçülmesi gerekmektedir.

Yazışma Adresi/Address for Correspondence

Uzm. Dr. Dilek YILMAZ

Adnan Menderes Üniversitesi Tıp Fakültesi, Çocuk Sağlığı ve Hastalıkları Anabilim Dalı, Aydın, Türkiye
e-posta: dr.dlkylmz@gmail.com

of view because of the positive relation between PEF and serum leptin levels, it would be necessary to measure serum leptin level beside PEF in acute and chronic asthma therapy.

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INTRODUCTION

The prevalence of asthma is continuously increasing through the world^[1]. In regions where prevalence is getting higher, there is a tendency for an increase in obesity. A positive association has been reported between asthma symptoms and obesity^[2,3]. Studies show that body mass index (BMI) has a relation with the clinic of asthma^[3,4]. Leptin is a proteohormone produced by adiposities and it is thought to act through specific receptors in hypothalamus. Leptin receptors also exist in human lung tissue and have a proliferative effect on cell proliferation. Although asthma and obesity appears because of inflammation and leptin affects asthma through macrophages, TNF- α , IL-6 and IL-12; still very little is known about the role of leptin on asthma^[5]. From another point of view, asthmatic children becomes obese children especially because of the parents' over reactivity to physical activities.

On the other hand, during the past years, the factors leading to asthmatic response are evaluated. The effect of parental smoking, birth weight, birth types (especially the role of cesarean section plays a role in asthma) and parental atopy are investigated for the development of asthma and obesity.

In this study, serum leptin levels were determined in randomly selected asthmatic, obese, obese asthmatic and healthy children in the same age group. Besides prenatal and antenatal history, risk factors, success of treatment, laboratory findings were compared.

MATERIALS and METHODS

This study was performed at the outpatient clinic of department of pediatric allergy. Totally

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44 children were included in the study (mean age 10.2 ± 2.36 years). Eleven asthmatic (female/male = 3/8), 12 asthmatic obese (female/male = 3/9), nine obese (female/male = 7/2) and 12 healthy (female/male = 6/6) children were selected. Informed consent was previously obtained from all the children's parents.

Asthmatic and asthmatic obese children were selected randomizingly from our outpatient clinic of department of pediatric allergy. These children were previously diagnosed as asthma according to the Global Strategy for Asthma Management and Prevention Classification^[6]. To these children, skin prick tests were performed previously using a panel of common allergens (Stallergenes, Paris, France). Children with a history of an attack requiring systemic corticosteroid treatment during the six months were excluded from the study. The only obese children and the control group were selected from the children who referred to our general pediatrics outpatient clinic for detailed investigation with no history of wheezing or any recurrent airway disease.

Standing height was measured using a portable direct reading stadiometer in the outpatient clinic. Weight was measured in children without coats and shoes using a calibrated electronic scale. BMI was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). To assess the effect of puberty on leptin levels, the children were grouped according to their pubertal development stage.

Blood samples were obtained in the morning by standard venopuncture technique. After clotting the samples at 4°C , the serum was separated by centrifugation and stored at -70°C until assay.

Fasting serum leptin concentration were measured with Biosource Leptin EASIA kit (Cat. No: KAP2281; Biosource Europe S.A.; Nivelles, Belgium) which is a solid phase enzyme amplified sensitivity immunoassay (EASIA) on microtiter plate. The assay uses monoclonal antibodies againsts distinct epitopes of human leptin^[7]. Also leptin shows a significant diurnal variation and reaches peak levels during the night. In this study, to avoid this variation, blood samples were collected from each individual child in the morning hours before lunch. Pulmonary function tests were performed using spirometry. Minato auto spiropal was used for spirometric measurements. Some of the children were not able to cooperate the spirometry because of the profile of the age group. By the spirometry, besides PEF, FEV₁, FVC and FEV₁/FVC levels were determined.

Serum total IgE levels were determined in the microbiology department using immunoblot technique. Birth delivery, breast feeding, family history about atopy, passive smoking and other factors related with asthma and obesity were questioned.

In this study, the results were presented as means \pm SD. Paired Student's t test were used for comparison of the data and Mann Whitney-U test for comparison of the data for the groups. Values of $p < 0.05$ were considered significant. Statistical analysis was performed with the SPSS software, version 10.0 for Windows.

RESULTS

Totally 44 children participated in the study and the mean age was 10.2 ± 2.36 years. The clinical characteristics of these patients are summarized in Table 1. Although BMI scores of the obese children were significantly higher ($p < 0.001$) than the control and the only asthmatic patients, also the mean age of the obese children were significantly higher from non-obese children ($p = 0.029$). Interestingly, asthmatic obese patients' birth weight was significantly lower than the other three groups ($p = 0.04$) and although this group had a lower breast feeding time, no significant difference was found between the four groups ($p > 0.05$). Passive smoking ratio was higher in the control group and the asthmatic obese group, but no significant difference was detected between the groups.

In our study, among all the patients, no association was found between BMI, serum leptin and IgE levels. When the leptin levels were analyzed in obese and non-obese groups, leptin levels were considerably higher in obese (13 ± 9.36 ng/mL) children than non-obese (3.79 ± 2.89 ng/mL) children ($p < 0.001$) as expected. There were no significant difference between asthmatic and non-asthmatic patients' serum leptin levels ($p = 0.83$). When the obese and non-obese children in the asthmatic group were compared, significantly higher BMI scores, PEF and serum leptin levels were determined ($p = 0.000$, $p = 0.04$, $p = 0.007$, respectively), but

Table 1. Clinical characteristics of the children

| Characteristics | Asthmatic (n= 11) | Asthmatic obese (n= 12) | Obese (n= 9) | Control (n= 12) | p |
|--|-------------------|-------------------------|------------------|-------------------|-------|
| Age (year) (mean \pm SD) | 9.45 \pm 2.06 | 10.33 \pm 2.42 | 11.78 \pm 1.92 | 9.58 \pm 2.54 | |
| Gender (male/female) | 8/3 | 9/3 | 2/7 | 6/6 | |
| Body mass index (kg/m ² \pm SD) | 18.36 \pm 3.39 | 25.28 \pm 2.60 | 26.67 \pm 3.42 | 19.21 \pm 2.72 | 0.001 |
| Birth weight (g \pm SD) | 3500 \pm 479 | 2766 \pm 1336 | 3066 \pm 1263 | 3505 \pm 525 | 0.04 |
| Breast feeding (months \pm SD) | 11.77 \pm 8.83 | 8.83 \pm 7.84 | 10.56 \pm 7.42 | 13.25 \pm 14.07 | NS |
| Passive smoking (%) | 36.4 | 58.3 | 44.4 | 58.3 | NS |
| Familial atopy (%) | 100 | 50 | 55.6 | 16.6 | |

SD: Standard deviation, NS: Not significant.

no statistically significant difference was found in IgE levels. Leptin levels are shown as a diagram in Figure 1. The leptin levels were also grouped for puberty. Prepubertal and pubertal patients' mean serum leptin levels were found 5.1 (0.7-38.18) and 11.94 (1.12-26.20) ng/mL, respectively. When the leptin levels were grouped according to gender, the mean serum leptin level was 6.37 (1.78-28.15) ng/mL in girls and 5.2 (0.7-38.18) ng/mL in boys ($p > 0.05$). No significant sex difference was detected in leptin levels of both asthmatic and obese groups. The total laboratory results are summarized in Table 2.

Among the four groups, significantly higher IgE levels were detected in asthmatic obese patients ($p = 0.009$). The IgE levels of asthmatic children were also significantly higher than the

control group and only obese group ($p = 0.02$). Spirometric tests were performed to all the patients and PEF values were significantly lower only in asthmatic patients ($p = 0.004$). When the FEV_1 and FEV_1/FVC values were analyzed, no significant difference was found between the groups.

Also among the four groups, possible relation was investigated between leptin levels and IgE levels. No significant relation was found between the groups. Also no significant difference was determined between serum leptin levels and breast-feeding, birth weight, passive smoking, need of corticosteroid treatment and bronchial hyperreactivity. Need of treatment was not effective in the leptin levels among the patients in four groups ($p = 0.96$).

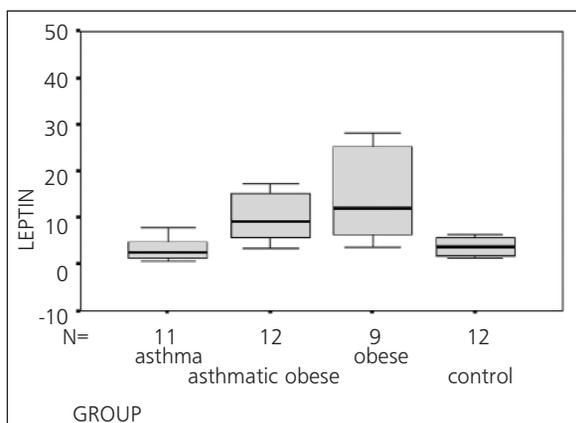


Figure 1. Serum leptin levels.

DISCUSSION

The increasing prevalence of asthma with increasing BMI, together with the increase in risk of developing asthma with weight gain is suggestive for the causality of asthma-obesity relationship^[8]. There are many suggestions to enlighten the relationship. Mechanical effects of obesity have important side effects on lung function. Because of that, weight reduction is a therapeutic goal in the management of asthma with obesity.

Childhood obesity has become a major problem in the last decades^[9]. Parallel to this

Table 2. Laboratory results of the patients

| Laboratory results | Asthmatic (n= 11) | Asthmatic obese (n= 12) | Obese (n= 9) | Control (n= 12) | p |
|--------------------------------|-------------------|-------------------------|-----------------|-----------------|---------|
| IgE (IU/L) | 378.05 ± 413.66 | 908.15 ± 1206.72 | 143.09 ± 221.45 | 144.23 ± 143.16 | 0.009* |
| PEF | 294.55 ± 51.26 | 379.58 ± 118.92 | 368.89 ± 39.90 | 330.42 ± 41.20 | 0.004* |
| PIF | 80.91 ± 25.28 | 96.25 ± 37.73 | 86.67 ± 19.53 | 71.25 ± 31.92 | |
| FEV ₁ predicted (%) | 1.49 ± 0.32 | 1.92 ± 0.89 | 1.63 ± 0.97 | 1.62 ± 0.53 | NS |
| FVC predicted (%) | 1.77 ± 0.51 | 2.29 ± 1.10 | 1.98 ± 1.20 | 1.89 ± 0.63 | NS |
| FEV ₁ /FVC (%) | 85.72 ± 7.39 | 77.42 ± 25.55 | 65.23 ± 38.00 | 78.67 ± 25.93 | |
| Leptin (ng/mL) | 3.29 ± 2.58 | 12.05 ± 9.44 | 14.27 ± 9.67 | 4.25 ± 3.19 | 0.001** |

* Among the four groups.

** Between obese and non-obese group.

PEF: Peak expiratory flow, NS: Not significant.

problem, many researches focus on leptin and its effects on obesity. In our study, serum leptin levels were higher in obese children as expected. But this group's mean age was higher than non-obese group. Because of that, age factor could not be ruled out in this study.

Although studies about the relation between the serum leptin levels and asthma continues, more leptin is produced as body weight increases. Although there is evidence of both asthma and obesity appears because of inflammation and leptin affects asthma through T cells, macrophages, TNF- α , IL-6 and IL-12; still very little is known about the role of leptin in asthma^[10]. But in our study, there were no significant difference between asthmatic and non-asthmatic patients' serum leptin levels, but serum IgE levels of asthmatic children were significantly higher compared to non-asthmatic children as expected ($p=0.018$).

In a study of Carroll et al., obese children with asthma admitted to intensive care unit with status asthmaticus required more intensive treatment and longer duration of therapy than children with normal weight^[11]. Also these children were more likely to have persistent asthma. Heuck and Wolthers stated that serum leptin levels are not affected by inhaled budesonide with a dose of 800 μg ^[12]. Thus in this study, no effect of treatment in the past twelve months was detected on serum leptin levels of children.

Serum leptin level is also affected by age and puberty. Garcia-Mayor et al. stated that leptin levels change according to pubertal changes^[13]. In their study, also at any stage, leptin levels were lower in boys. Yılmaz et al. investigated serum leptin levels in children and although an increase was observed in both sexes with puberty, leptin levels were higher in girls with no statistically different BMI scores^[14]. In our study, there was no significant difference in pubertal leptin levels between the two sexes.

Guler et al. have investigated the role of leptin in childhood asthma and found that asthmatic boys have higher levels of leptin^[15]. In

contrast to this study, we found that asthmatic girls have higher levels of leptin in the same age group, but no significance was present. And there was no difference in age between these two groups.

To determine the association of BMI with respiratory allergens and total or specific IgE levels, information was collected from 15.454 young adults in the European Community Respiratory Health Survey and no association was found between BMI and total or specific IgE levels^[16]. In our study, no association was found between BMI and IgE levels, either.

Similarly to the study of Guler et al. there was no correlation between the serum leptin levels and the spirometric results^[15]. In our study interestingly; there was a significant relation between PEF levels and serum leptin levels ($p=0.016$, $Z=0.453$) but no relation was found between leptin levels and FEV₁, FVC, FEV₁/FVC.

In conclusion, further studies with larger series are needed to evaluate the relation between PEF and leptin levels in asthma and obesity.

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