Pediatric Neurology 51 (2014) 365–369

Contents lists available at ScienceDirect

Pediatric Neurology

journal homepage: www.elsevier.com/locate/pnu

Original Article

Serum, Urine, and Saliva Levels of Ghrelin and Obestatin Pre- and Post-treatment in Pediatric Epilepsy

Erdal Taskin MD [a,*], Bekir Atli MD [a], Mehmet Kiliç MD [a], Yusuf Sari MD [a], Suleyman Aydin PhD [b]

[a] *Firat University, Faculty of Medicine, Department of Pediatrics, Elazig, Turkey*
[b] *Firat University, Faculty of Medicine, Department of Biochemistry, Elazig, Turkey*

ABSTRACT

INTRODUCTION: In this study, we aimed to determine the serum, urine, and saliva levels of acyl ghrelin, des-acyl ghrelin, and obestatin in the newly diagnosed idiopathic generalized pediatric epilepsy patients in the pretreatment period and in the third month of valproic acid. **MATERIAL AND METHODS:** Thirty pre- and post-treatment cases of patients who were diagnosed with idiopathic generalized epilepsy and 30 control patients were included in this study. Serum, saliva, and urine levels of ghrelin were measured in epileptic group and in the control group in the pretreatment period and in the third month of the treatment. **RESULTS:** There were 14 females and 16 males. Mean age was 8.9 ± 2.5 years. Mean body mass index was 17.2 ± 2.3 in the patients and 16.6 ± 2.0 in the control group, whereas it was 16.8 ± 2.1 in the third month of the therapy ($P > 0.05$). Pretherapy serum, urine, and saliva levels of acyl ghrelin were 36.45 ± 9.93, 31.78 ± 12.87, and 34.23 ± 11.49 pg/mL, respectively in the patient group. Post-treatment serum, urine, and saliva levels of acyl ghrelin were 51.34 ± 12.01, 48.24 ± 16.76, and 44.90 ± 14.99 pg/mL in the patient group. Pretherapy serum, urine, and saliva levels of des-acyl ghrelin were 419.62 ± 75.63, 370.59 ± 60.11, and 396.28 ± 60.76 pg/mL, respectively in the patient group. Post-therapy serum, urine, and saliva levels of des-acyl ghrelin were 458.61 ± 87.10, 429.92 ± 55.81, and 449.48 ± 74.32 pg/mL, respectively in the patient group. Pretherapy serum, urine, and saliva levels of obestatin were 23.02 ± 3.15, 14.27 ± 4.22, and 29.52 ± 5.39 ng/mL, respectively. Post-therapy serum, urine, and saliva levels of obestatin were 24.30 ± 4.18, 15.27 ± 6.43, and 30.94 ± 7.42 ng/mL, respectively. **CONCLUSION:** There was a significant increase in the serum, urine, and saliva levels of acyl ghrelin and des-acyl ghrelin without an increase in post-therapy body mass index in idiopathic generalized epilepsy patients.

Keywords: Ghrelin, obestatin, epilepsy, childhood period

Pediatr Neurol 2014; 51: 365-369
© 2014 Elsevier Inc. All rights reserved.

Introduction

Ghrelin is a peptide of 28 amino acids that plays a role in the regulation of energy balance and food intake, in addition to having a growth hormone releasing effect.[1-3] A large amount of the ghrelin in the circulation is secreted by the stomach, and most of the remainder originates from the small intestine. There are two major forms of ghrelin in plasma and tissues, acyl ghrelin and des-acyl ghrelin, and both cross the blood-brain barrier.[4,5] There has recently been an increase in the number of publications investigating the relationship between ghrelin and epilepsy and reporting the neuroprotective and antiepileptic features of ghrelin.[6] Some studies have reported that ghrelin levels increase in epileptic patients, whereas others have reported that ghrelin levels decrease in these individuals.[7-10] Two hypotheses have been advanced in attempts to explain the reason for an increase in ghrelin levels in people with epilepsy. The first of these proposed that ghrelin increases with neuroprotective and antiepileptic effects in cellular stress situations due to epilepsy and protects the neurons against apoptosis, whereas the second hypothesis suggested that

Article History:
Received March 4, 2014; Accepted in final form May 5, 2014
* Communications should be addressed to: Dr. Taskin; Firat University, Faculty of Medicine, Department of Pediatrics, 23119 Elazig, Turkey.
E-mail address: erdaltaskin@gmail.com

0887-8994/$ - see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.pediatrneurol.2014.05.014

weight gain, which is observed as a side effect of antiepileptic drugs causes an increase in ghrelin levels.[11-15]

Obestatin is a peptide hormone that was discovered in 2005. It is coded by the same gene as ghrelin, and it suppresses weight gain. Obestatin has the opposite effect to ghrelin. Most of the previous obestatin studies have focused on weight gain and appetite,[16,17] and its role in epilepsy has not been extensively examined.

In this study, we aimed to determine the serum, urine, and saliva levels of acyl ghrelin, des-acyl ghrelin, and obestatin in people with newly diagnosed, idiopathic, generalized pediatric epilepsy in the pretreatment period and in the third month of valproic acid (VPA) treatment, as well as the possible relationship between epilepsy and these parameters.

Materials and Methods

Patient and control groups

This study included individuals who initially presented with seizures at the Pediatric Clinics at Firat University, Turkey, and who were subsequently diagnosed with idiopathic, generalized epilepsy, using clinical and laboratory methods. We included 30 prepubertal children aged between 4 and 11 years, and children with a body mass index (BMI) >25 were excluded. As antiepileptic therapy, patients received two daily doses of sodium valproate 10-15 mg/kg at the beginning of the study, and we increased these doses to a mean of 20-25 mg/kg/day. We measured serum drug levels in each patient in the third month of the treatment.

After taking a full blood count, and conducting biochemical analyses, electroencephalograph, cranial computed tomography, cranial magnetic resonance imaging, and the other necessary patient examinations, we enrolled only those diagnosed with idiopathic, generalized epilepsy according to International League Against Epilepsy (ILAE) 1989 classifications. We excluded patients who had an abnormal finding in a neurological examination, those with a structural or organic cerebral lesion detected on cranial computed tomography or cranial magnetic resonance, patients with a history of chronic diseases, such as those of the thyroid, heart, liver, and kidney, those having an endocrine disorder or a chromosomal aberration, and patients taking drugs for any reason.

The control group consisted of 30 healthy prepubertal children who had presented to the Firat University Medical Faculty Pediatric Clinic and who had no history of epilepsy in their family, no previous history of seizures or a previously known history of chronic disease, and who required a full blood count during their routine examinations. This study was approved by the Ethics Committee of Firat University. In addition, we obtained the necessary consent from the families of the patients and the individuals in the control group.

Collecting and analysis of the samples

We collected samples (blood, saliva, and urine) within the first 6 hours of seizure in the epilepsy group, to measure the acyl, des-acyl ghrelin, and obestatin levels. We repeated these measurements at the end of the third month of the treatment. We obtained corresponding measurements from the individuals in the control group at the time of inclusion. We measured acyl, des-acyl, and obestatin levels through 1 mL serum, 3 mL saliva, and 2 mL urine samples that remained from the blood analyses of all the patients. However, because peptides are easily broken in the cell by proteases, we added 20-30 μL of aprotinin, a protease inhibitor, to accurately measure the amount of ghrelin in serum, saliva, and urine. Furthermore, we added a 1/10 volume of 1 N HCl to the samples obtained after centrifugation at 3000 rpm for 5 minutes. Addition of *hydrochloric acid* leads to precipitation in the samples, without affecting peptides. We kept the samples between −20°C and −80°C. After we had collected all the samples, we dissolved those that were frozen in the correct manner and studied those using proper kits that were specified in the catalog of the producer.

We studied these two hormones using radioimmunoassay in the saliva samples, whereas we studied obestatin in the blood samples using the enzyme-linked immunosorbent assay method. We also used radioimmunoassay to study ghrelin in the urine samples.

Statistical analysis

We expressed descriptive data as mean ± standard deviation, and used the chi-square test in the analysis of categorical data. As a result of normal distribution of the continuous variables, we observed that some of these did not indicate a normal distribution; so we preferred a nonparametric method for their analysis. We used the independent samples *t* test and the Mann-Whitney *U* test to compare the two groups and used the paired samples *t* test and Wilcoxon test in the analysis of repeated measurements.

We performed statistical analysis using MedCalc v.11.1.0 package software and considered values of $P < 0.05$ to be statistically significant.

Results

The mean age of the patient group was 8.9 ± 2.5 (4-11) years (Table 1), and it consisted of 14 girls (46.6%) and 16 boys (53.4%). The mean age of the control group was 9.0 ± 2.2 (5-11) years, and this group comprised 13 girls (43.3%) and 17 boys (56.7%). No statistically significant difference was observed between the groups.

Pretreatment mean body weight of the patient group was 28.8 ± 9.1 kg and 29.5 ± 9.3 kg in the third month of the treatment, whereas mean body weight was 28.1 ± 5.1 in the control group. We found no statistically significant difference between the control group and the epilepsy group at the beginning of the study. Again, we found no statistically significant difference between the pretreatment and third month of treatment values in the epilepsy group in terms of body weight. BMI, which is more meaningful than body weight, was 17.2 ± 2.3 in the patient group in the pretreatment period and 16.6 ± 2.0 in the control group. BMI was 16.8 ± 2.1 in the third month of treatment. When we compared the groups in terms of BMI, we found no statistically significant difference ($P > 0.05$). Again, we observed no statistically significant difference between the initiation of therapy and the third month of treatment in the epilepsy group regarding BMI.

We measured ghrelin levels at the beginning of the treatment and in the third month of treatment in the three separate body fluids; serum, urine, and saliva (Table 1). The serum levels of acyl ghrelin were 44.09 ± 10.58 pg/mL in the control group at the beginning of the study, whereas these values were 36.45 ± 9.93 pg/mL in the pretreatment period

TABLE 1.
Levels of Serum, Urine, and Saliva Acyl Ghrelin

	Patient, N = 30	Control Group, N = 30	*P* Value
Serum (pg/mL)			
Pretreatment	36.45 ± 13.93*	44.90 ± 14.58	<0.05
Post-treatment	51.34 ± 18.01*		0.03*
Urine (pg/mL)			
Pretreatment	31.78 ± 12.87*	43.35 ± 8.63	0.001
Post-treatment	48.24 ± 16.76*		0.003*
Saliva (pg/mL)			
Pretreatment	34.23 ± 11.49*	39.77 ± 13.69	0.002
Post-treatment	44.90 ± 14.99*		0.002*

* *P* values were used to indicate the relationship between the pretreatment patient group and posttreatment patient group.

Download English Version:

https://daneshyari.com/en/article/3084624

Download Persian Version:

https://daneshyari.com/article/3084624

Daneshyari.com