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Original Article

The effect of nutritional support treatment on growth factors in nutritional short stature adolescents: result of long-term follow-up

Nutrisyonel boy kısalığı olan adolesanlarda nutrisyonel destek tedavisinin büyüme faktörleri üzerine etkisi: uzun süreli izlem sonuçları

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ABSTRACT

Aim: Long-term insufficient nutrition intake in childhood affects height gain negatively. This study was designed to analyze the effect of oral nutritional support product (ONSP) treatment on growth velocity (GV) and growth factors (GF) in adolescents who were diagnosed nutritional short stature (NSS).

Material and Methods: Sixteen adolescents diagnosed NSS were involved. Patients recorded their dietary intake. Caloric deficiencies were calculated and fulfilled with ONSP. Effects of nutritional support treatment on GV, GF and growth parameters were analyzed on 0th, 6th, and 12th months.

Results: The increment of the height of the cases on 6th and 12th months, increment of IGFBP3 on 6th month, and the increment of IGF-1 levels, body mass index and weight SDS of the cases on 12th month were statistically significant ($p < 0.05$).

Conclusion: Long-term ONSP treatment, which is given to the adolescents with NSS, increases the growth factors. The increment of IGF-1 levels was in-between secure limits.

Keywords: nutrition therapy, short stature, adolescents

ÖZ

Amaç: Uzun süreli yetersiz nutrisyon alımı çocukluk çağında boy kazanımını negatif olarak etkiler. Bu çalışmanın amacı nutrisyonel boy kısalığı (NBK) tanısı alan adolesanlarda oral nutrisyonel destek ürününün (ONDÜ) büyüme hızı (BH) ve büyüme faktörleri (BF) üzerine olan etkisini incelemektir.

Gereç ve Yöntemler: NBK tanısı alan 16 adolesan çalışmaya dahil edildi. Hastalar oral beslenme ile alımlarını kaydetti, kalori açıkları hesaplandı ve açıkları ONDÜ ile tamamlandı. Nutrisyonel destek tedavisinin BH, BF ve büyüme parametreleri üzerine etkisi 0, 6, 12. aylarda değerlendirildi.

Bulgular: Olguların 6. ve 12. aylardaki boy kazanımları; 6. aydaki IGF-BP3 artışı; 12. aydaki IGF-1, beden kitle indeksi ve vücut ağırlığı SDS artışı istatistiksel olarak anlamlı saptandı. ($p<0.05$).

Sonuç: Nutrisyonel boy kısalığı olan adolesanlara verilen uzun sureli ONDÜ tedavisi büyüme faktörlerini arttırmaktadır. IGF-1 seviyesindeki artış güvenli sınırlar içerisinde saptanmıştır.

Anahtar kelimeler: Nutrisyon tedavisi, boy kısalığı, adolesan

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Introduction

Growth is the main physiologic process of childhood, which is one of the most important criteria showing health of the child [1]. As known, genetic is the main factor for height gain and environmental factors have less effect on this process. Since it's possible to change the environmental factors, they become more important for increment of growth potential [2]. Nutrition comes first in-between these environmental factors.

The most common and important cause of growth failure in worldwide is malnutrition, which causes many macro and micro nutrition deficiencies. Decrement of growth velocity (GV) is the result of adaptation process of suboptimal nutrition intake; so nutritional short stature (NSS) patients equilibrate in-between their genetic potential and energy intake. Decrement of growth equilibrates nutritional needs with nutritional intake without affecting biochemical or functional homeostatic factors negatively. If nutritional deficiency increases or acute malnutrition superimposes on chronic suboptimal stage, changes showing malnutrition in biochemical parameters or anthropometric measurements may be observed [1]. The main clinical phenotype is growth arrest in the case of long-term suboptimal nutrition intake [3,4]. Oral nutritional support products (ONSP) involve macro nutrition (protein, carbohydrate and fat) and micro nutrition (vitamin, minerals and trace elements) [5]. As a matter of fact, its value in balanced nutrition cannot be denied. Adolescents are children who have naturally short period of time to grow after growth spurt. In addition with nutritional deficiency, final height of these children would be shorter and they would not reach their target height [3,4]. They need efficient and fast supportive treatment in this short period of time. According to this idea, we designed this study to evaluate the effect of nutritional support treatment (NST) on GV, growth parameters and growth factors of the malnourished adolescents diagnosed as NSS.

Material and methods

The Local Clinical Research Ethics Committee confirmed ethical approval of this study and written informed consent was obtained from all participants and/or their parents. Sixteen adolescents (7 girls and 9 boys) attending to pediatric endocrinology department with complaint of short stature (SS) were involved in the study. NSS criteria was defines as, weight and height below 3rd percentile, weight for height below 90%, GV below normal ranges according to patients age and gender, actual height percentile below target height (height of mother + height of father ± 13 / 2) percentile (showing inappropriate growth according to genetic potential), IGF-1, IGF-BP3 levels below 3rd percentile (- 2SD), delayed puberty, not having delayed bone age. Normal variant short stature patients (NVSS) (familial, constitutional and/or pathologic SS), pathological SS, patients with acute or chronic infections, patient with chronic diseases (diabetes mellitus, metabolic malnutrition, renal, hepatic or cardiovascular diseases, pancreatic insufficiency, cystic fibrosis, mental retardation or etc.) patients taking any kind of medicine, vitamin or nutritional support treatment (multivitamin preparations, iron supplementation or etc.), patients with disabilities and patients with eating disorders (anorexia nervosa, bulimia or etc.) were not involved in the study.

Anthropometric measurements (height, weight, body mass index (BMI), weight for height, height SDS), pubertal staging (Tanner stage), and bone age (Greulich-Pyle method) measurements were done for diagnosis of NSS. Laboratory tests (total blood count, biochemistry, thyroid function tests and serum zinc, ferritin, folic acid, vitamin B12, endomisial antibody, IGF-1, IGF-BP3 levels were obtained in the morning after at least 10 hours of overnight fasting. Growth factors were evaluated with chemiluminescence method. Measurements were done 3 times (0th, 6th, 12th months) during the study.

Weight and height of the adolescents were measured using a stadiometer appropriate to the standards with all their clothing removed except undergarments. BMI was calculated by dividing weight (kg) by height squared (m^2). Weight, height and BMI percentiles of the adolescent were determined according to World Health Organization (WHO) Growth Reference Data for 5-19 years in 2007 [6,7].

To calculate nutritional intake of the adolescents, they were asked to record all solid and fluid foods with their amounts intake for subsequent 3 days (2 weekdays, 1 weekend day). In order to obtain an accurate dietary intake list, proper education was given to parents by a dietician. Some foods were taken as samples (apple, cheese, bread, rice, etc.) and adequate measurement of the items were taught. Patients and parents were asked to fill the dietary intake list forms adequate to this education. According to these lists daily food intake (species and amount) was calculated. The sums of 3 days were divided into 3 and an average of daily energy and nutrients intake was identified. Energy and nutrients intake of the adolescents were calculated by the dietician, according to food consumption and portion ingredient by using 'Standardized Food Recipes', 'Samples From Turkish Cuisine', 'Food and Nutrition Catalogue' [8-10]. Percentage of Dietary Reference

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Intakes (DRI %) of the patients were calculated and compared with standardized age and gender specific daily consumption values in order to calculate the daily energy and nutrients insufficiencies of the patients [11, 12]. So, the daily energy and nutrients needs and how much of it was covered by normal daily nutrition of the patient was determined and a NSP covering 50% of the deficit was chosen and increased gradually in order to replace the daily energy and nutrients deficit of each patient. The product was chosen carefully as to be a 'nutritionally accurate product (enriched by macro nutritional elements, carbohydrates (oligosaccharides and polysaccharides), proteins (casein), fat (saturated, polyunsaturated, single fatty acids), vitamins and minerals (Na, K, Ca, P, Cl, Mg, Zn, Fe) with low solid load and a good taste that can be well tolerated by adolescents which was designed to fulfill the high energy intake need of them [5]. An education involving healthy nourishment and usage of the product was given to patient and his parents. The patients were called every month by phone and a constant consumption of the product for a year was estab-lished. On the 6th and 12th months of NST, anthropometric measurements were done, growth velocity was calculated and levels of growth factors were obtained.

Statistical analysis

A commercially available statistical software package (SPSS 21.0 for Windows, Chicago, Ill, USA) was employed for all statistical analyses. The values are presented as mean. Pre-treatment and post-treatment parameters were compared using Wilcoxon test. A p-value of less than 0.05 was considered statistically significant.

Results

Seven girls and 9 boys were involved in the study. Mean age was 14.6 ± 1.6 years. The anthropometric measurements, biochemical, hormonal parameters and growth factors results of the patients were given in Table 1. The mean height of the patients were 145.11 ± 7.31 cm, 147.73 ± 6.51 cm, 149.58 ± 9.67 cm; height SDS were -2.12 ± 0,54, -1.76 ± 0,86, -1.14 ± 0,59; and the mean weight of the patients were 36.13 ± 7.66 kg, 37.92 ± 7.13 kg, 39.66 ± 5.95 kg; on 0th, 6th, and 12th months. The increment of height and weight were statistically significant on 6th and 12th months ($p < 0.05$). The increment of BMI and height SDS on 12th was also statistically significant. Anthropometric measurements and growth factor levels of the patients were given in the Table 2 and alterations of IGF-1 and IGF-BP3 levels were given in Figure 1 and 2. Both IGF-1 and IGF-BP3 levels were increased during the NST. The increment of IGF-1 levels on 12th month and IGF-BP3 levels on 6th months were found statistically significant ($p < 0.05$).

Table 1. Anthropometric measurements and laboratory results of cases during initial stage

	Mean (SD)
Number of cases (n)	16
Age (years)	14,6 (1,6)
Weight (kg)	36,13 (7,6)
Height (cm)	145,11(7,31)
Height SDS	-2,12 (0,54)
BMI (kg/m²)	16,99(2,37)
Tanner	Stage 4
Bone age (years)	13,9(2,1)
Hemoglobin (g/dl)	13,9(1,1)
MCV (fL)	85,5(5,6)
Ferritin (pmol/L)	57.52(39,99)
Vitamin B12 (µmol/L)	219.7(89,0)
Folic Acid (nmol/L)	253,73(133,66)
Vitamin D (nmol/L)	72,38(41,43)
Zinc (µmol/L)	14,29(5,69)
sT4 (pmol/ml)	14,15(2,57)
TSH (µU/ml)	2,1(0,9)

Table 2. Follow up of anthropometric measurements and growth factors under treatment

	0. month	**6. month**	**12. month**
Weight (kg)	3613 (7,66)	37,92 (7,13)*	39,66 (5,95)*
Height (cm)	145, 11 (7,31)	147,73 (6,51)*	149,58 (19,67)*
Height SDS	-2,12 (0,54)	-1,76 (0,86)	-1,14 (0,59)*
BMI (kg/m²)	17,81 (2,03)	17,76 (1,58)	18,38 (1,67)*
Growth velocity (cm)		2,20 (2,00)	4,75 (2,46)
IGF-1 (ng/ml)	323,51 (140,13)	430,15 (282,84)	469,30 (151,59)*
IGF-1 minimum (percentile)	-3, -2.3	-3	-1, 0
IGF-1 maximum (percentile)	0, 1	3	1, 1.28
IGF-BP3 (µg/ml)	4,88 (0,88)	5,33 (0,70)*	6,69 (3,18)
IGF-BP3 minimum (percentile)	-3	-3	-1.28, -1
IGF-BP3 maximum (percentile)	2, 2.3	2.3, 3	3

*p<0.05

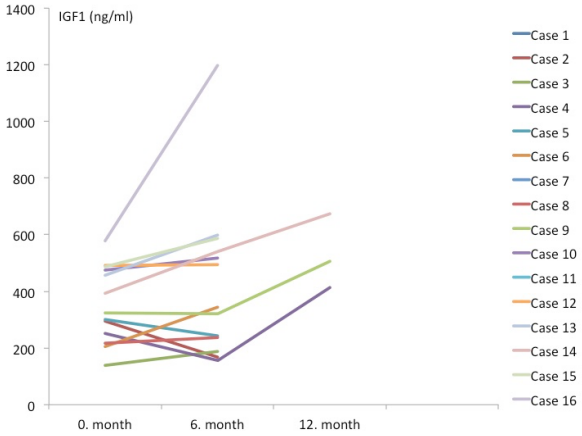

Figure 1. Alterations in IGF-1 levels

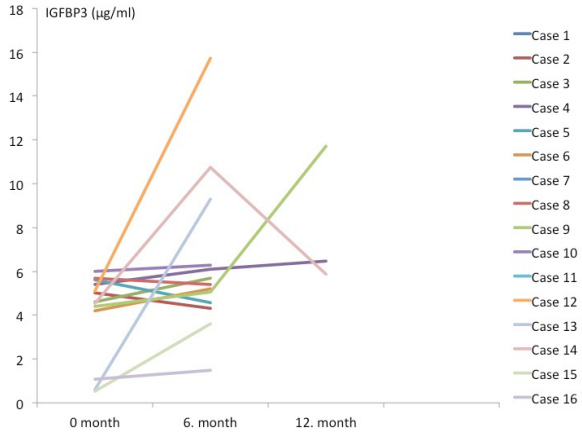

Figure 2. Alterations in IGF-BP3 levels

Discussion

Growth is a process, which is affected by genetics, nutrition, social and cultural factors. The most common measurements to assess the growth are weight for age, height and height for weight. Adolescence is the period of time in which physical, emotional, social development of the child occurs. In this period, growth spurt occurs and due to increment in growth, nutritional needs increase. If this higher energy need is not fulfilled by nutrition, a pause in the growth is seen which results as not being able to reach the genetic target height. Because of this reason this period is extremely important. Another important point is the possibility of not discriminating NSS adolescents with normal variant short stature (NVSS) adolescents because in both cases weight and height may be drowns back. GV is normal in NVSS cases but it is less in NSS cases. Family history is positive in familial SS. Bone age immaturity and delayed puberty may be seen in constitutional SS adolescents. In both cases decrement of GV is seen in first year of life. With all these differences NVSS may be distinguished from NSS [13]. Clinical studies emphasize that during nutritional rehabilitation of NSS cases, in order to protect patient's previous growth pattern, sufficient protein and micro nutritional intakes are satisfied [14,15]. It's necessary to determine nutritional deficiency of adolescents and to replace it. Additionally, it is important to remember that SS is an indicator of chronic malnutrition and a risk factor for obesity for future years. So, these cases may be not only SS adults but also be obese adults [16]. The effect of nutritional support treatment (NST) on growth is well known. A positive correlation between energy intake and GV was shown in the study of Zadik et al. [17]. Thus, there are some studies, which show height at 3 years of age is a good indicator of adolescence height [18,19]. In the study of Institute of Nutrition of Central America and Panama (INCAP), protein, and micro nutrition enriched NST was given to < 7 years old children. Decrement of infant death velocity, increment of GV in < 3 years old children were observed in the follow up. GV of children in between 3 to 7years of age was not changed in the long-term follow up. It was also observed that, women who took NST during childhood had increased height and fat free body mass, men who took NST in childhood had more work capacity, and in both men and women had higher intellectual performance than cases who did not take NST [20]. INCAP and Nutrition Collaborative Research Support Program (CRSP) studies are evaluated together and it was emphasized that growth failure and stunting develops in first 18 months in developing countries; interventions done after this period results in failure and permanent stunting and functional deficiencies develop [21]. However, studies showing the effect of NST on adolescents with growth failure in the literature are limited. In two different studies done in USA, it was emphasized that interventions done in later periods may affect growth and increment of height positively and total catch up may be obtained [22, 23]. Similarly, in our study the GV of the adolescents with growth failure were increased with NST. As a matter of fact, our study is quite remarkable.

In a study in between growth failure cases, it was shown that cases were very picky without having prominent malnourishment [24]. Additionally, some other studies point out that eating habits and attitudes of mother and family affect child's eating habits [25]. In our study patients and their families revealed similar stories, such as picky eating habits of patient and one of the parents. Besides, during follow-up these patients refused to consume their recommended age and gender specific personal diet lists.

Günöz et al. showed that the effect of both acute and chronic malnutrition decrease the effect of growth hormone and IGF-1 [26]. In our study, IGF-1 and IGF-BP3 levels were also decreased on the 0th month but they were increased gradually during NST.

As a result, in our study growth factors, and anthropometric measurements of adolescents who took NST were affected

positively. Besides, plasma IGF-1 level increments were in between confident levels during this improvement, which shows the NST, is safe for height increment of NSS adolescents. The limitation of the study is the small patient number. However, the remarkable point is there are not many studies in the literature, evaluating the effect of NST on growth pattern of adolescents. The other important point is that adolescents with nutritional short stature must be referred to a pediatric endocrinologist in order to be distinguished from normal variant and pathological SS. Afterwards, they must be referred to a dietician with his family to get an education for healthy nourishment and then treated and followed up in collaboration of pediatric endocrinologist and dietician.

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Declaration of conflict of interest

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