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Do antispasmodics affect the body composition and basal metabolic rate in patients with cerebral palsy?

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The aim is to describe differences in the basal metabolic rate, anthropometric and body composition measurements between cerebral palsy (CP) patients treated and not treated with antispasmodic agents. Children diagnosed with CP and a healthy control group were included in the study. Patients were divided into two groups: patients currently treated with antispasmodics (group 1) and patients without antispasmodic treatment (group 2). There were 34 children with CP, mean age 7.57±3.62 years. Although weight and height measurements were significantly reduced in patient groups compared to the healthy control group, there was no significant difference between group 1 and group 2. Body mass index, triceps and subscapular skinfold thickness, arm circumference, and waist/hip ratio were not statistically different between group 1 and group 2. Although there was significant reduction in lean mass, dry mass, body cell mass, basal metabolic rate and fat free mass index in patient groups as compared to control group, there was no significant difference between group 1 and group 2 according to fat percentage, fat mass, total body water, body fat mass index, lean mass, dry mass, body cell mass, basal metabolic rate, fat free mass index, and basal metabolic rate/body weight. In conclusion, additional studies are needed to detect the exact effect of antispasmodic drugs on body composition in CP.

Keywords: cerebral palsy; parasympatholytics; body composition; basal metabolism; child, preschool; child

INTRODUCTION

Children with cerebral palsy (CP) generally have low body weight and growth retardation. The most common reasons for malnutrition are feeding dysfunction, gastroesophageal reflux, aspiration pneumonia and endocrinological abnormalities (1). Basal metabolic rate (BMR) is the energy that is needed to sustain the involuntary activities of our body. These involuntary activities include muscle tone and activities of the visceral organs (2). Therefore, spasticity and immobility may affect body composition.

Many CP patients suffer from marked decrease in anthropometric measurements including body weight, height and skinfold measurements. Skinfold thickness is used in determination of body fat, but this technique requires an experienced observer and has poor reliability. On the other hand, multifrequency bioelectrical impedance analysis (MFBIA) is a simple method that can be used to determine body composition. It is less dependent on the observer's experience and is easy to use in children. MFBIA provides a more appropriate tool for assessing body composition than skinfold measurements (1, 3).

Some drugs used in the treatment of CP patients may affect the patient weight status. Weight gain is the most common adverse effect of valproic acid treatment, and in contrast, topiramate may decrease appetite (4, 5). Although there are few studies investigating the relationship between the spasticity, BMR and body composition, there is no study assessing the effects of antispasmodic drugs on body composition in CP patients (2). In this cross sectional study, we

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aimed to describe differences in BMR, anthropometric and body composition measurements between CP patients treated and not treated with antispasmodic agents.

METHOD

This study was conducted at Pediatric Neurology Department, Dokuz Eylül University, İzmir, Turkey between March 2011 and July 2012. Children older than three years and diagnosed with CP were included in the study. Patients diagnosed with neurometabolic disorders and children with chronic illness affecting weight gain other than CP were excluded.

All patients were evaluated by anthropometric measurements, MFBIA and laboratory examinations. Motor limitations of the patients were classified according to the Gross Motor Function Classification System (GMFCS) and muscle tone was evaluated by modified Ashworth scale (6, 7). Daily caloric intake of the patients and caloric intake that healthy children should take according to the same age were calculated. Current antiepileptic and baclofen treatment and history of botulinum toxin type A injection in the past six months were recorded. The dosage of baclofen and botulinum toxin type A injection was also recorded. All evaluations were done between 8 and 10 AM to avoid bias due to diurnal variation. Patients were divided into two groups, as follows:

Group 1

- patients currently treated with baclofen oral tablet
- patients currently treated with baclofen oral tablet and with a history of botulinum toxin type A injection in the past six months
- patients with a history of botulinum toxin type A injection in the past six months

Group 2

- patients without antispasmodic treatment

Results were compared with the age- and sex-matched healthy control group. An informed consent was obtained from each patient. The study was approved by the Ethics Committee of Dokuz Eylul University, Izmir, Turkey.

BODY COMPOSITION AND ANTHROPOMETRIC MEASUREMENTS

Skinfold and body measurements

Body mass was determined on a digital scale (Hamburg, Germany) to the nearest 0.1 kg, with subjects dressed in a light t-shirt and shorts. Body height of the patients was recorded on a stadiometer with the subject standing to the nearest 0.1 cm using a Harpenden fixed stadiometer (Holtain Ltd., Crymych, Dyfed, Britain). In disabled patients, body height was measured with the patient lying supine. Body mass index (BMI) was calculated as weight/height^2 (kg/m^2). Skinfolds (triceps and subscapular), circumferences (arm, waist, hip) were measured. The waist/hip ratio was also evaluated.

Multifrequency bioelectric impedance analysis

On MFBIA, an alternating electrical current of constant frequency with low intensity is applied to the body. Body composition and body water compartment analysis were assessed by determining the resistance, reactance, and impedance with a Bodystat Qudscan 4000 bioimpedance analyzer (Bodystat Ltd., British Isles). Current-detecting electrodes were placed between the styloid processes of the right radius and ulna and between the medial and lateral malleoli of the right ankle. Current-introducing electrodes were then placed on the respective dorsal surfaces of the metacarpals and metatarsals, 5 cm distally to the proximal electrodes. Total body water (TBW), fat percentage (%), fat mass, lean mass, dry mass, body fat mass index (BFMI), fat free mass index (FFMI) and BMR were evaluated.

LABORATORY ANALYSIS

After at least 10-12 hour fast, blood levels of total cholesterol, triglycerides (TG), low-density and high-density lipoprotein cholesterol (LDL-C, HDL-C) and fasting glucose levels were assessed quantitatively. Fasting plasma glucose, serum TG, total cholesterol and HDL-C concentrations were measured enzymatically using DP Modular Systems (Roche Diagnostic Corp., Indianapolis, IN, USA). LDL-C levels were calculated using the Friedewald formula when plasma TG were <400 mg/dL.

Statistical analysis

Data were analyzed with Statistical Package for the Social Sciences (SPSS), Version 15.0. Means were calculated for continuous variables and frequency was measured for categorical variables. Comparisons were made by Kruskal-Wallis and Mann-Whitney U tests. A p-value <0.05 was considered statistically significant.

RESULTS

There were 34 children with CP, mean age 7.57±3.62 (range 3.0-16.4) years, 11 (32.4%) female and 23 (67.6%) male patients. Quadriplegic type CP was present in 24 (70.6%), diplegic type CP in four (11.8%), hemiplegic type CP in four (11.8%) and monoplegic type CP in two (5.8%) patients. Control group included 25 (8 female and 17 male) non obese age- and sex-matched healthy children (mean age 9.38± 4.59) (p=0.11).

The etiology of CP was hypoxic ischemic encephalopathy (14 cases), periventricular-intraventricular hemorrhage (10 cases), prematurity and neonatal hypoxia (five cases), traumatic brain injury (two cases), brain damage due to meningitis (two cases) and brain damage due to encephalitis (one case). Of the 34 patients, 16 (47.1%) were level V, three (8.8%) were level IV, five (14.7%) were level III, five (14.7%) were level II and five (14.7%) were level I according to the GMFCS. The mean Ashworth scores of the patients were 1.8±1.6 points in upper extremities (1.4±1.1 in group 1 and 1.9±1.7 in group 2, p=0.02) and 2.3±1.46 points in lower extremities (1.9±1.3 in group 1 and 2.5±1.6 in group 2, p=0.03).

Of the 34 patients, five (14.7%) were currently treated with baclofen oral tablet (mean dosage 1.6 mg/kg/day), seven (20.6%) were currently treated with baclofen oral tablet (mean dosage 1.7 mg/kg/day) and ten (29.4%) had a history of botulinum toxin type A injection in the past six months (four patients received it 2 times and six patients 3 times). Twelve (35.3%) patients did not receive any antispasmodic agents. In group 1, 14/22 (63.6%) patients (carbamazepine monotherapy in six patients, valproate and levetiracetam polytherapy in four patients, levetiracetam monotherapy in two patients, and carbamazepine and clonazepam polytherapy in two patients) and 3/12 (25%) group 2 patients (valproate and levetiracetam polytherapy in two patients and carbamazepine and clonazepam polytherapy in one patient) were treated with antiepileptic drugs.

Of the 34 patients, 32 (94.1%) were orally fed and two (5.9%) were fed by percutaneous gastroenterostomy. The mean ratio of the caloric intake during a day *per* caloric intake that healthy children should take according to the same age was 67.1±25.9% in group 1 and 58.1±24.3 in group 2 (p=0.37).

Anthropometric measurements

Although weight measurements were significantly reduced in patient groups (group 1 and group 2) as compared to control group (p=0.007), there was no significant difference between group 1 and group 2 (p=0.44). Height measurements were significantly reduced in patient groups (group 1 and group 2) as compared to control group (p=0.007), but there was no significant difference between group 1 and group 2 (p=0.55). BMI, triceps and subscapular skinfold thickness, arm circumference, and waist/hip ratio were not statistically different between group 1 and group 2 (p=0.14, p=0.12, p=0.18, p=0.07 and p=0.08, respectively). Anthropometric measurements are summarized in Table 1.

Results of multifrequency bioelectrical impedance analysis

Multifrequency bioelectric impedance analysis showed similar values of fat percentage, fat mass, TBW and BFMI in patient groups (groups 1 and 2) and control group (p=1.0, p=0.27, p=0.92 and p=0.81, respectively). There was significant reduction in lean mass, dry mass, body cell mass (BCM), BMR and FFMI in patient groups (groups 1 and 2) as compared to control group (p=0.005, p=0.007, p=0.01, p=0.03 and p=0.03, respectively). On the other hand, BMR/BW ratio was significantly increased in patient groups (groups 1 and 2) as compared to control group (p=0.002). There was no significant difference between group 1 and group 2 according to fat percentage (p=0.7), fat mass (p=0.3), TBW (p=0.35), BFMI (p=0.4), lean mass (p=0.6), dry mass (p=0.42), BCM (p=0.56), BMR (p=0.17), FFMI (p=0.26), and BMR/BW (p=0.46). MFBIA results are summarized in Table 2.

TABLE 1. Anthropometric measurements of the patients and controls

	Group 1 n=22	Group 2 n=12	Control n=25	p
Weight (kg)	35.8±3.4	35.8±2.3	38.1±3.9	0.007
Height (cm)	112.4±18.3	117.7±22.2	132.6±23.5	0.007
BMI	15.5±4.7	15.6 ±3.01	17.5±3.01	0.14
Triceps ST (mm)	8.9±6.0	7.8 ±3.5	11.0±4.1	0.12
Subscapular ST (mm)	6.9±4.9	6.5±3.4	9.1±5.1	0.18
Arm circumference (cm)	17.2±4.5	17.2±3.3	19.7±4.0	0.07
Waist/hip ratio	0.87±0.05	0.88±0.05	0.84±0.05	0.08

Group 1 = patients treated with antispasmodics; group 2 = patients without antispasmodic treatment; BMI = body mass index; ST = skinfold thickness

TABLE 2. Multifrequency bioelectric impedance analysis results in patients and controls

	Group 1 n=22	Group 2 n=12	Control n=25	p
Fat percentage (%)	19.6±12.9	19.7±15.9	19.6±6.2	1.0
Fat mass (kg)	4.7±5.2	4.5±3.9	6.6±4.0	0.27
TBW (%)	62.4±10.7	61.6±12.2	61.3±4.8	0.92
BFMI	3.8±2.8	3,3±2,9	3.5±1.4	0.81
Lean mass (kg)	16.3±7.8	17.9±8.7	26.3±12.8	0.005
Dry mass (kg)	3.8±1.9	4.3±2.4	6.4±3.4	0.007
BCM	13.5±4.8	13.7±5.3	17.9±5.9	0.01
BMR (cal)	963.9±229.2	994.9±229.1	1164.4±288.2	0.03
FFMI	12.0±2.9	11.6±4.0	14.0±2.3	0.03
BMR/BW ratio	52.2±13.5	48.7±10.0	39.8±10.2	0.002

Group 1 = patients treated with antispasmodics; group 2 = patients without antispasmodic treatment; TBW = total body water; BFMI = body fat mass index; BCM = body cell mass; BMR = basal metabolic rate; FFMI = fat free mass index; BMR/BW ratio = basal metabolic rate/body weight ratio

Laboratory investigations

There were no statistically significant differences in total protein, albumin, total cholesterol, TG, LDL-C, HDL-C, hemoglo-

TABLE 3. Laboratory results of patients and controls

	Group 1 n=22	Group 2 n=12	Control n=25	p
Total protein (g/dL)	7.0±0.47	7.1±0.57	7.2±0.45	0.37
Albumin (g/dL)	4.2 ±0.42	4.2±0.40	4.3±0.31	0.59
Total cholesterol (mg/dL)	166.6±38.9	149.1±30.2	151.2±22.5	0.21
TG (mg/dL)	78.8±49.8	69.5±17.9	70.1±18.7	0.66
LDL-C (mg/dL)	98.6±32.0	92.1±29.6	86.4±20.9	0.40
HDL-C (mg/dL)	49.9±13.9	43.0±8.2	50.5±27.7	0.53
Ferritin (ng/mL)	32.6±55.8	27.8±15.8	34.7±18.4	0.86
Hemoglobin (g/dL)	12.3±1.2	12.3±0.81	13.1±1.3	0.09
Hematocrit (%)	35.8±3.4	35.8±2.3	38.1±3.9	0.073

Group 1 = patients treated with antispasmodics; group 2 = patients without antispasmodic treatment; TG = triglycerides; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol

bin, hematocrit and ferritin levels between patient groups (groups 1 and 2) and control group. There was no significant difference between group 1 and group 2 according to total protein, albumin, total cholesterol, TG, LDL-C, HDL-C, hemoglobin, hematocrit and ferritin levels either. Laboratory results of the patients are summarized in Table 3.

DISCUSSION

Patients with CP generally have decreased anthropometric measurements including body weight, height and skinfold thickness, which are usually associated with nutritional factors (1, 8, 9). Feeding dysfunction leads to poor health and abnormal anthropometry (10). Non-nutritional factors including frequent infections, chronic illness affecting weight gain other than CP, and poor socioeconomic status may also negatively influence growth and nutritional status (11). *Tomoum et al*. conclude that growth, body composition and nutritional status are significantly altered in CP patients, especially in those with severe motor impairment and oral-motor dysfunction (1). Measuring techniques that evaluate the anthropometry and nutritional status of CP patients are controversial. Weight for height or skinfold thickness measurements may help evaluate the anthropometry; however, severe neurologic impairment and abnormal fat distribution may make these procedures less accurate (12). In our study, although patients with CP had lower height and weight measurements than controls, there were no significant differences in BMI, triceps and subscapular skinfold thickness, arm circumference and waist/hip ratio. We also suggest that measurements other than weight and height may not be so accurate to evaluate the nutritional status of CP patients.

It is well known that there is a positive correlation between energy expenditure and physical activity (13). *Monroe et al*. showed that patients with spinal cord injury had lower daily energy expenditure than healthy controls, which may be associated with the decreased physical activity (9). In contrast to this finding, patients with increased muscle tone may have higher energy expenditure, which may lead to decreased anthropometric measurements. Patients with muscle paralysis also show various types of body composition changes including decreased lean mass and increased fat mass (14, 15). In contrast, *Tomoum et al*. report that patients with CP had lower fat mass, fat percentage and BMR than healthy controls (1). These differences may be associated with increased energy expenditure related to spasticity. In our study, lean mass, dry mass, BCM, FFMI and BMR values were significantly lower in CP patients when compared with healthy controls. The BMR/BW ratio was also significantly increased in CP patients. Based on the hypothesis that increased spasticity may increase energy expenditure, thus leading to changes in body composition, we compared the MFBIA results between patients treated with antispasmodics (group 1) and without antispasmodic therapy (group 2). Although there was a significant difference in spasticity according to upper and lower extremities between groups 1 and 2, we could not find significant difference between groups 1 and group 2 according to fat percentage, fat mass, TBW, BFMI, lean mass, dry mass, BCM, BMR, FFMI and BMR/BW.

Biochemical abnormalities including significantly decreased levels of hemoglobin, ferritin, total protein and albumin are usually detected in patients with CP (1). Abnormalities of these parameters may reflect the malnutrition and anemia status of CP patients. The presence of anemia may reduce caloric intake by decreasing appetite (16). In our study, we could not detect any significant differences in total protein, albumin, total cholesterol, TG, LDL-C, HDL-C, hemoglobin, hematocrit and ferritin levels between patient groups (groups 1 and 2) and control group.

CONCLUSION

In conclusion, patients with CP had significantly reduced weight and height measurements as compared to healthy controls. Lean mass, dry mass, BCM, FFMI and BMR were decreased and BMR/BW ratio was significantly increased in patients with CP. Additional studies are needed to identify

the exact effect of antispasmodic drugs on body composition in CP.

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SAŽETAK

Utječu li antispazmodici na tjelesni sastav i stopu bazalnog metabolizma u bolesnika s cerebralnom paralizom?

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Cilj rada je opisati razlike u stopi bazalnog metabolizma, antropometrijskim mjerama i tjelesnom sastavu između bolesnika s cerebralnom paralizom (CP) na terapiji antispazmodičnim lijekovima i bez ove terapije. U studiju su bila uključena djeca s dijagnosticiranom CP i kontrolna skupina zdrave djece. Bolesnici su podijeljeni u dvije skupine: bolesnici na terapiji antispazmodicima (skupina 1.) i bolesnici bez terapije antispazmodicima (skupina 2.). Bilo je 34 djece s CP srednje dobi 7,57±3,62 godine. Iako su mjere tjelesne mase i visine bile značajno niže u skupinama bolesnika u usporedbi s kontrolnom skupinom zdrave djece, nije bilo značajne razlike među skupinama 1. i 2. Među ovim skupinama nije bilo statistički značajne razlike ni u vrijednostima indeksa tjelesne mase, kožnog nabora tricepsa i subskapularnog kožnog nabora, obujma nadlaktice i omjera obujma struka i bokova. U skupinama bolesnika zabilježene su značajno niže vrijednosti krte mase, suhe mase, tjelesne stanične mase, stope bazalnog metabolizma i indeksa bezmasne mase u usporedbi s kontrolnom skupinom, nije bilo značajne razlike između skupina 1. i 2. prema postotku masti, masi masti, ukupnoj tjelesnoj vodi, indeksu tjelesne masne mase, krtoj masi, suhoj masi, tjelesnoj staničnoj masi, stopi bazalnog metabolizma, indeksu bezmasne mase i omjeru stope bazalnog metabolizma/tjelesne mase. Zaključuje se da su potrebna daljnja ispitivanja kako bi se utvrdio stvarni učinak antispazmodičnih lijekova na tjelesni sastav kod CP.

Ključne riječi: cerebralna paraliza; antispazmodični lijekovi; antropometrijske mjere; bazalni metabolizam; dijete, predškolsko; dijete