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Research article

Significance of inflammatory biomarkers in assessment of weight reduction in obese children with Down syndrome

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Key words: Secondary obesity, diet intervention, physical therapy, Down syndrome, inflammatory biomarkers.

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Abstract

Objectives: The present study is designed to evaluate the effect of diet alone or in combination with physical therapy in obese children with Down syndrome. **Material and Methods:** 60 obese children (30 males+30 females) with Down syndrome (DS) before diet and therapy was subjected to clinical examination. They were divided into three groups matched in age and sex, group I (control), included 20 of them. The other 40 were divided into 2 groups, group IIA and group IIB, each of them 20. Group IIA was subjected to diet intervention program only while group IIB was subjected to both diet and physical therapy programs. Blood samples were obtained from all groups before and after therapy. Plasma levels of leptin, IL-1 and IL-6 were determined. **Results:** The study found significant weight reduction in both groups favoring combined diet and physical activity. Diet lowered but not significantly the plasma levels of leptin hormone, IL-1 and IL-6. While the diet and physical therapy in combination reduced significantly the plasma levels of leptin, IL-1 and IL-6. **Conclusions:** The combination of physical activity with nutritional intervention is an effective method for weight reduction in obese children with DS. One of the most objective parameter for the benefit of weight reduction is the inflammatory biomarkers, leptin, IL-1, and IL-6 in the early school age (6-9 years).

Introduction

In several developing and developed countries, the obesity prevalence has been steadily increasing over the past few decades. Obesity is a complex physiologic state associated with multiple molecular changes [1].
Mental health consequences of obese childhood were examined by little research relatively, although the physical health consequences of them are well described. While rates of prevalence continue to rise, and the childhood overweight has become pandemic [2], much less examined these consequences in obese children with DS. While obesity is the fifth leading risk factor for global deaths, it is of special concern for those with disabilities. According to data from the National Health and Nutrition Examination Survey (NHANES), 16% of children without disabilities compared to 22.5% of children with disabilities are obese [3].
Researches, also, indicates that obesity is related directly to cognitive abilities including reception, processing of environmental information and behavior. The main cognitive domains affected by obesity include executive functions, memory, and processing speed [4]. Reduced executive function, mental rotation, attention, reading achievement and mathematics are related to overweight in childhood [5]. Also, overweight in adolescents have deficits in cognitive functions and attention [6].
Troubles in swallowing or chewing can lead the children with Down syndrome (DS) to eat more processed and softer foods. In addition, children with DS suffer from deficits in sensory that make coordination and balance more difficult, leading to decreased physical activity. When the parents attempt to push the children with DS to healthy foods or exercise, the children have a tendency to be noncompliant or oppositional and may also have poor impulse control [7]. In humans, 1 of 800-1000 births suffers from DS, which is the most common chromosomal abnormality. Chromosome 21 triplication causes DS, which is an autosomal disorder [8].
Children with DS show strengths in social functioning and they may use relative strengths in social skills to compensate for other weaknesses of other adaptive domains. Individuals with DS may also show relative competence in forming relationships with others [9]. In the body, most cells produce small proteins are called cytokines, which promote cell-cell interaction through multiple biological activities. Many biological processes are participated by cytokines including regulation of

inflammatory and immune responses [10]. In DS, the cytokine role is still unclear, despite a growing interest in the immune system contribution [11].

Smigielska-Kuzia, *et al.* found significantly differences in mean serum IL-1α and IL-6 concentrations between the DS group and controls [11]. In adults with DS, no changes in plasma levels of IL-6 [12]. Adipocytes secrete a leptin hormone that plays an important role in the food intake regulation by promoting energy and stimulating satiety via energy expenditure. Typically, increased levels of the hormone correlate with obesity, due to leptin resistance. Studies suggest that pre-pubertal overweight DS children have high levels of leptin, which correlates with increased body mass index and degree of adiposity [13].

In obesity, circulating levels of leptin increase proportionally to total adipose tissue, has been characterized as a key member of the molecular network [1]. Exercise is extremely important in reducing body weight as it provides a decrease in body fat. Therefore children with DS should be encouraged to practice physical exercises to promote the development of lean mass and help in caloric expenditure [14].

The aim of this study was to determine the reduction in BMI after the diet intervention alone or when combined with physical therapy in obese children with Down syndrome, and also the significance of inflammatory biomarkers in assessment of weight reduction.

Materials & methods

Participants and materials

The study included 60 obese children (30 males+30 females) with DS. They were recruited from outpatient clinic, Center of Clinical Research Excellence, National Research Center, Faculty of Physical Therapy, Cairo University. The inclusion criteria were meeting the diagnostic according to the criteria of DSM-5 for DS, with age range from 6 to 9 years according to eligibility criteria, while their BMI will be not less than 34.9 kg/m^2 or (95%) on BMI percentile obesity class I [15]. Parents or care givers of all participants already signed informed legal consents. The study was approved by the medical ethics committee of the National Research Centre, Cairo, Egypt.

Standard Weight-Height scale: (Seca apparatus "SMIG") is a metal device was used to measure weight and height for all children before and after diet and physical therapy [16]. Body mass index (BMI) was calculated as BMI= kg/ m^2 (Whole body vibration device and balance board) as vestibular system stimulators, (electric treadmill and stepper exercise) as weight bearing exercise were used for physical treatment. A diet intervention program was applied according to [17].

Methods

The DS group before diet and therapy was subjected to clinical examination after reporting a full medical history. They were divided into three groups matched in age and sex, group I (control), included 20 of them. The other 40 were divided into 2 groups, group IIA and group IIB, each of them 20. Venous blood samples were collected (from all participants before diet intervention and physical therapy) into 5-ml vacutainer tubes containing potassium EDTA and mixed by gentle inversion. Each sample was centrifuged and processed within thirty minutes from sample collection to separate plasma, these plasma samples were kept at -20ºC until using. Group IIA was subjected to diet intervention program only, nutritional requirements were measured according to the method which is commonly used to estimate energy requirements for children is based on age: basal daily needs for all children= 100 kcal; added to the basal needs 125 kcal x age in years for boys and 100 kcal x age in years for girls. Add up to 20% more kcal for very active children. Children daily eating patterns generally include 3 meals and 2 or 3 snacks, depending on length of time between meals, age of child and level of physical activity [17]. While group IIB was subjected to both diet and physical therapy programs, aiming at significant weight reduction for both groups. Whole body vibration exercise was administered for 3 series lasting for 3 minutes, followed by 3-min pause between each series [18]. Each level was controlled by the patient before starting the next level of balance board exercise, exercise was repeated five times per session each time lasted one minute [19]. Treadmill exercise was applied three times weekly for a total period of treatment for 12 weeks and 30 minutes for every session [20]. 30 minutes (20 minutes each with a 10 minutes rest in-between) for each patient in stepper exercise [21]. After the end of diet intervention and physical therapy, another venous blood samples from group IIA and group IIB were obtained into 5-ml vacutainer tubes containing potassium EDTA for plasma isolation. Plasma leptin measuring was performed according to the method described by [22, 23]. The IL-1 and IL-6 measuring was determined using ELISA kits (Nova, China). All tests were performed for each case before and after 12 weeks of diet intervention and physical rehabilitation program.

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Statistical analysis

All the values were presented as means ± standard error of the means (SE). Comparisons between different groups were carried out using one way analysis of variance (ANOVA) followed by Tukey´s HSD test for multiple comparisons. Difference was considered significant when $p < 0.0001$. Graph Pad prism® software (version 5) was used to carry out these statistical tests.

Results

The study found significant weight reduction in both groups favoring combined diet and physical activity. We can conclude the combination of physical activity with nutritional intervention is an effective method for weight reduction in obese children with DS. BMI was significantly reduced after the combination between diet and physical therapy (Table 1).

Biochemical results

Diet lowered but not significantly the plasma levels of leptin hormone, IL-1 and IL-6, while the diet and physical therapy in combination reduced significantly the plasma levels of leptin, IL-1 and IL-6 (Table 1).

Table 1. Comparison between control, diet intervention alone and diet intervention in combination with physical therapy on body mass index (BMI), plasma leptin level, interleukin-1 (IL-1) and interleukin-6 (IL-6) in obese children with Down syndrome.

	Control (G I) Before treatment	After diet intervention alone (group II A)	After diet intervention and physical therapy (group II B)
BMI (kg/m^2)	36.8 ± 2.5	36.3 ± 1.9	35.2 ± 1.8[a]
Leptin (ng/ml)	18.4 ± 1.1	14.9 ± 0.9	11.6 ± 0.8[a]
IL-1 (pg/ml)	1.4 ± 0.8	1.2 ± 0.6	0.9 ± 0.3[a]
IL-6 (pg/ml)	8.1 ± 0.8	6.1 ± 0.6	4.5 ± 0.6[a]

Data were expressed as mean ± SE (n = 20). Statistical analysis was carried out by one-way ANOVA followed by Tukey's HSD test for multiple comparisons. [a] significantly different from control at $p<0.0001$.

Discussion

When they are born, children with DS have anatomical and structural differences that make them susceptible to potential food problems. Some of these differences are: reduced production of saliva, macroglossia, small oral cavity, poor coordination for sucking and swallowing, among others. It is also very common to present periodontal disease and consequent loss of dentition. In this sense, the first intervention at nutritional level should be the detailed research of the main difficulties that the DS patients present in their diet, adapting the diet, if necessary [24].

Also, Wong *et al.* suggested that population with DS need help to keep their weights at healthy levels [25]. In the population of DS, the prevalence of obesity and overweight are higher in other population [26]. Studies suggest that euthyroid DS children body at rest burns less amount of calories than their counterparts, and may contribute to the development of obesity [27]. Obesity as a singular disease is one of the greatest actual challenges and to achieve success in its treatment the set of scientific data and the patient individualization are needed. This is not different in DS children population that with proper exercise and nutrition-based interventions may have a greater chance to live a better and healthier life [14].

Overweight and obesity are usually related to poorer cognition across lifespan [28]; however, the association between BMI and cognitive function is less significant in adults [29], partly due to inaccurate measurement of body fat. Indirect evidence has shown an association between western high fat diet and impaired cognitive functions [30]. Overweight is identified by metabolically active and reprogrammed fat tissue that enhances local alteration and inflammation of cytokine levels [31].

Our data showed that the serum levels of IL-1 and IL-6 were significantly increased in patients with DS. These findings are in accordance with Carta et al. who reported that levels of cytokines in DS patients were higher [32]. Our results showed that the physical therapy reduced but not significantly the leptin hormone, IL-1 and IL-6 levels in obese children with Down syndrome, while the physical therapy and diet significantly lowered the leptin hormone, IL-1 and IL-6. These findings are in agreement with Servidi *et al.* who reported that obesity are an essential reason for diabetes, hypertention, coronary, artery disease. Hence, the dietary modification and the lifestyle modification are important to keep the health. The serum leptin levels and its relation with existing obesity can be used as a predictor for obesity in children with DS [33].

Other than BMI, obesity is also related to cognitive performance and structural brain alterations. Obesity and fat content is inversely related to attention and verbal memory and is found to be associated with smaller hippocampus and larger ventricular volume. There is also a negative correlation between waist-to-hip ratio and hippocampal volume and a positive correlation between waist to- hip ratio and white matter hyperintensities [34].

Conclusions

Obesity or even being overweight is a common disorder among children with DS in the early school age (6-9 years). The combination of physical activity with nutritional intervention is an effective method for weight reduction in obese children with DS. One of the most

objective parameter for the benefit of weight reduction is the inflammatory biomarkers, leptin, IL-1, and IL-6.

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Conflict of interest

The authors declare that they have no conflict of interests.

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