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Original Article (Pages: 8101-8110)

The Effect of Educational Intervention on Body Mass Index and Thyroid Function Tests in Children and Adolescents with Obesity and Overweight

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Abstract

Background
Studies declare the possibility of thyroid abnormalities in the obese patients and return of normal thyroid activities after weight loss. Therefore in this study, the effect of educational intervention on body mass index (BMI) and thyroid function tests in obese children has been evaluated.

Materials and Methods: The current randomized clinical trial research included 126 overweight or obese children and adolescents with an age range of 7 to 18 years, form Birjand city (Iran), who were divided into two control and intervention groups for 6 months between 2015 and 2016. The educational intervention consisted of 1 session per month (each session was 60 minutes), which was done by the researcher. BMI, thyroid stimulating hormone (TSH), free triiodothyronine (FT3) and free thyroxine (FT4) in both groups were measured and compared before and after the intervention, and data were analyzed using SPSS software version 19.0.

Results: In the intervention group, the average of TSH and FT4 after 6 months of intervention showed both significant decreases and increases, respectively ($p=0.003$ and $p< 0.001$). In the control group, both THS and BMI average had a significant increase ($p<0.001$), and FT3 and FT4 significant decrease ($p=0.009$ and $p=0.001$, respectively). After 6 months, BMI and TSH average in the intervention group compare to the control group had significant decrease ($p = 0.02$ and $p<0.001$, respectively), and average of FT4 and FT3 was significantly increased ($p <0.001$ and $p=0.025$, respectively).

Conclusion: Educational intervention was effective in reducing BMI and improving thyroid tests; hence, is highly recommended for the modification of BMI and the improvement of thyroid tests in obese children and adolescents.

Key Words: Adolescents, BMI, Children, Educational intervention, Obesity.

*Please cite this article as: Neda Ebrahimi, Fatemeh Taheri, Mitra Moodi, Mahmoud Zardast. The Effect of Educational Intervention on Body Mass Index and Thyroid Function Tests in Children and Adolescents with Obesity and Overweight. Int J Pediatr 2018; 6(8): 8101-10. DOI: **10.22038/ijp.2017.27747.2403**

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Received date: Dec.10, 2017; Accepted date: Feb.22, 2018

1- INTRODUCTION

Obesity has been identified as one of the 21st century most important threats to human health, and has been predicted to lead to serious health problems in children all around the world (1). Child obesity has increased in many developing countries, such as Iran, due to changes in life style, nutrition transition, and lack of physical activity (2-4). Obesity and overweight which can affect children's life quality, can be controlled by a change of life style, including increased physical activity and proper dieting both at school and home (5). Obesity is associated with thyroid activates. In fact, earlier investigations have shown that thyroid disorders can cause obesity. However, recent studies propound that obesity is what causes thyroid abnormalities; these studies state that the structural and functional changes of thyroid are common in obese children. There has been shown to be a connection between body mass index (BMI), and thyroid hormone levels, and an increase in body fats could lead to the changes in thyroid tissues. Studies demonstrate that the thyroid activity and Thyroid-Stimulating Hormone (TSH) return to the normal condition after weight loss, refers to the fact that the increase of TSH in serum does not require treatment (6).

Long-term changes in thyroid hormones due to weight loss have not been deeply investigated. Some studies among adult patients with thyroid obesity showed that the high body fat is associated with increasing in TSH (7-9), free Triiodothyronine (FT3) or total Triiodothyronine (T3)(7-9); and a slight decrease in free Thyroxine (FT4) (9). Nevertheless, the data is limited and contradictory, and the relationship between obesity and measured fat and TSH (10, 11), T3 (10), and FT4 (7, 8, 11), has not been investigated. There are even fewer studies done on the pediatrics, which had relatively small sample sizes (5, 12, 13); and contrary many studies in adults, in the majority of the pediatric studies have not found any connection between FT4 and BMI (12-16). Anyway, most of the studies have reported an association between TSH and BMI (12, 13, 15, 16), as well as T3 and BMI (12, 13, 15, 16). Considering such important issue and the limited available data on weight loss, educational intervention can have beneficial effects on thyroid hormones function. Therefore, this study aimed to investigate the effect of education intervention on BMI and thyroid function in children and adolescents with overweight or obesity, in Birjand city, Iran.

2- MATERIALS AND METHODS

2-1. Study design and population

The current randomized clinical trial research (IRCT2017081935772N1) which included 126 overweight or obese children and adolescents (BMI higher than 85 or BMI above 85% percentile) (17) with an age range of 7 to 18 years old was conducted in Birjand, South Khorasan located in Eastern Iran.

2-2. Procedure

The samples were selected from the students of the research project named "Metabolic Syndrome of Students" (18). The above-mentioned research project was a cross-sectional descriptive study which was conducted on 4,340 students, including 1,621 primary school, 1,457 middle school, and 1,262 high school students between 2011 and 2012 in Birjand, Iran. In this study, the areas in Birjand were initially arranged based on school distribution, later, the elementary levels, middle schools, and high schools in each area were classified and divided into clusters; then, the random samples of each cluster were systematically selected from obese children and adolescents who had health records in Atherosclerosis and Coronary Artery Research Center. The students were randomly divided into two groups of 63 (the intervention and the control groups). Unlike the control group, the intervention group was examined under lifestyle educational intervention and healthy diet for 6 months between 2015 and 2016. Weight, height, and Body mass index (BMI) were measured once every month by pediatrician assistant followed by training. The training was lectured with PowerPoint for parents, children, and adolescents in six sessions (60 minutes) which included the following subjects: obesity definition and its disadvantage in childhood and adulthood; the importance and benefits of weight control; recommendations and necessary actions for control weight, lifestyle modification, healthy diet, physical activity, and parental attitudes towards children.

2-3. Measuring

A comprehensive physical examination was done on the samples by a pediatrician. Weighing was done with light clothes and no shoes using the design glass scale Beurer Summer Sky (Beurer GmbH, Germany) with accuracy of 100 grams. The height of participants was measured with an accuracy of 0.5 cm, while feet flat together and heels, buttocks, and shoulders were contacted with the wall, facing directly ahead, and arms by the sides. BMI was calculated as the ratio of weight in kilogram to the square of height in square meter for each student.

2-4. Laboratory tests

Blood samples (each sample was 5 ml) were taken from the Cubital vein left hand in Vali-e-Asr hospital in the early morning to measure TSH, FT3, and FT4. Based on the laboratory kits, reference range for the thyroid function tests were as follows: for TSH the range of 0.4- 6.2 mIU/ml, FT4 0.9 to1.7 ng/dl, and FT3 3.00 to 5.07pg/ml. The data obtained from out of these ranges were considered as an abnormal thyroid function or thyroid disorders (19). After the blood clotting, the serum of the samples was separated, and they were immediately centrifuged at 25 ° C to prevent the hormones degradation and remain their levels constant. TSH, FT4 and FT3 of the serums were quantified using Electro Chemiluminescence or Electrogenerated Chemiluminescence (ECL) method (Cobas E411 analyzer, Roche Diagnostics, Germany). After 6 months of educational intervention TSH, FT3, FT4 and BMI were again quantified for both interventional and control group to investigate the effect of educational intervention on BMI and thyroid function. Educational intervention was carried out based on valid and reliable sources (20-23).

2-5. Ethical consideration

Ethical considerations in this study correspond with the Declaration of Helsinki, 1964, and in this regard, the following steps were performed:

- Obtain permission from the Ethics Committee of the Birjand University of Medical Sciences (Ethical code: Ir.BUMS.1394.298), and registration of study in the clinical trials system;
- Eligible children for the study, after explaining the purpose of the study to parents and informed consent were enrolled;
- No cost to the families of the studied children for experiments;
- If children have thyroid disorders, were referred to a specialist for follow-up.

2-6. Inclusion and exclusion criteria

The criteria for the selection of students include:

- The children and adolescents with overweight and obesity (BMI above 85% percentile),

- Non-syndromic children and adolescents with an age range of 7 to 18 years, and
- The parental informed consent.

The criteria for the exclusion of students include:

- The children who had a medical history using radioactive iodine (radioiodine), thyroid hormones, and anti-thyroid drugs or any medication that may affect thyroid,
- The children with a known type of endocrine or metabolic abnormalities, and
- Students with lack of the parental consent.

2-7. Data Analyses

The data were analyzed using SPSS software version 19.0 and the Kolmogorov–Smirnov test (K–S test) was used to determine the data normality. Comparison of the variables was done through the Chi-square test and t-test (independent and paired) and Pearson correlation coefficient was applied to assess the relationship between BMI, TSH, FT4, and FT3 in the two groups. $P \leq 0.05$ was considered as the significant level.

3-RESULTS

In this randomized clinical trial study, 63 obese and overweight students with an average age of 13.41 ±2.9 years as the control group (**Table.1**), including 30 boys (47.62%) with an average age of 13.1± 2.94 years and 33 girls (52.38%) with an average age of 13.7 ± 2.88 years; and also 63 students as the intervention group (**Table.1**) with an average age of 12.71 ± 3.26 years, including 27 boys (42.86%) with average age of 12.18 ± 3.29 years and 36 girls (57.14%) with average age of 13.11 ± 3.22 years, were investigated.

Table.2, illustrate the average BMI, TSH, FT3, and FT4 in the control and intervention groups (separately), before and after 6 months of educational intervention, using paired sample t-test. As shown in **Table.2**, compared to the first time testing, the average BMI and TSH significantly increased in the control group after 6 months of the study ($p < 0.001$); while the average FT4 and FT3 after 6 months, significantly decreased ($p=0.001$ and $p=0.009$, respectively).

The average TSH significantly decreased ($p = 0.003$) in the intervention group (**Table.2**) after 6 months of educational intervention. However, the average BMI is not of significant value ($p = 0.144$). Both FT4 and FT3 increased after the educational intervention, nevertheless, only the average FT4 significantly increased ($p<0.001$).

The analyzed results by the independent t-test listed in **Table.3**, showed that the average BMI and TSH of the intervention group significantly decreased compare to the control group ($p=0.02$ and $p<0.001$, respectively), also the average FT4 and FT3 in the intervention group significantly increased after the 6 months of intervention ($p<0.001$ and $p=0.025$, respectively) which confirms that the 6 months educational intervention was successful.

As depicted in **Table.4**, using the Pearson test, there are no significant correlation between BMI, TSH, FT4 and FT3 in the control and intervention groups before and after 6 months except for the BMI and FT4 in the intervention group before the 6-month educational intervention ($p= 0.016$ and $r= -0.30$).

Table-1: Statistical information of subjects (number, age, gender, and BMI) in the control and interventional groups before 6 months (at the first test)

Subjects in the control group	Number of Participants	Percent	Average age with standard deviation (Year)	Average BMI with standard deviation (Kg/m^2)
	63	100	13.41 ± 2.9	24.85 ± 2.81
Boys	30	47.62	13.1 ± 2.94	2.96 ± 24.61
Girls	33	52.38	13.7 ± 2.88	25.07 ± 2.70
Subjects in the interventional group	**Number of Participants**	**Percent**	**Average age with standard deviation (Year)**	**Average BMI with standard deviation (Kg/m2)**
	63	100	± 3.26 12.71	24.30 ± 3.09
Boys	27	42.86	12.18 ± 3.29	23.92 ± 3.17
Girls	36	57.14	13.11 ± 3.22	24.59 ± 3.05

BMI: Body mass index.

Table-2: Comparison of the average BMI, TSH, FT3, and FT4 in the control and interventional groups at the first time testing and testing after 6 months

Variables	Control Group	Average Value	Standard Deviation	Paired t-test P-value
BMI (Kg/m^2)	first time	24.8492	2.80718	<0.001
	after 6 months	24.9790	2.84523	
TSH (mIU/ml)	first time	4.3211	0.64102	<0.001
	after 6 months	4.3868	0.65487	
FT4 (ng/dl)	first time	1.3014	0.15468	0.001
	after 6 months	1.2771	0.14837	
FT3 (pg/ml)	first time	3.9010	0.44954	0.009
	after 6 months	3.8571	0.45923	
Variable	**Interventional Group**	**Average Value**	**Standard Deviation**	**Paired t-test P-value**
BMI (Kg/m^2)	Before intervention	24.3032	3.09390	0.144
	after intervention	23.6779	3.31337	
TSH (mIU/ml)	Before intervention	4.1992	0.75413	0.003
	after intervention	3.8265	0.75448	
FT4 (ng/dl)	Before intervention	1.2995	0.14265	<0.001
	after intervention	1.4162	0.14876	
FT3 (pg/ml)	Before intervention	4.0321	0.53892	0.672
	after intervention	4.0606	0.54677	

BMI: Body Mass Index; TSH: Thyroid stimulating hormone; FT3: Free triiodothyronine; FT4: Free thyroxine.

Table-3: Comparison of the average BMI, TSH, FT3 and FT4 in the interventional and control groups after educational intervention

Variable	Groups after 6 months	Average Value	Standard Deviation	Paired t-test P-value
BMI (Kg/m^2)	Control	24.9790	2.84523	0.02
	interventional	23.6779	3.31337	
TSH (mIU/ml)	Control	4.3868	0.65487	<0.001
	interventional	3.8265	0.75448	
FT4 (ng/dl)	Control	1.2771	0.14837	<0.001
	interventional	1.4162	0.14876	
FT3 (pg/ml)	Control	3.8571	0.45923	0.025
	interventional	4.0606	0.54677	

BMI: Body Mass Index; TSH: Thyroid stimulating hormone; FT3: Free triiodothyronine; FT4: Free thyroxine.

Table-4: The matrix of significant correlation between BMI, TSH, FT4, and FT3 in the control and interventional groups at the first time and after 6 months of intervention

Variables in the control group at the first time	BMI (Kg/m^2)	TSH (mIU/ml)	FT4 (ng/dl)	FT3 (pg/ml)
BMI (Kg/m^2)	-	p= 0.66 r= 0.06	p= 0.21 r= -0.16	p= 0.12 r= -0.20
TSH (mIU/ml)	p= 0.66 r= 0.06	-	p= 0.56 r= 0.07	p= 0.25 r= -0.15
FT4 (ng/dl)	p= 0.21 r= -0.16	p= 0.56 r= 0.07	-	p= 0.44 r= 0.10
FT3 (pg/ml)	p= 0.12 r= -0.20	p= 0.25 r= -0.15	p= 0.44 r= 0.10	-
Variables in the interventional group before intervention	**BMI (Kg/m^2)**	**TSH (mIU/ml)**	**FT4 (ng/dl)**	**FT3 (pg/ml)**
BMI (Kg/m^2)	-	p= 0.45 r= 0.10	p= 0.016* r= -0.30	p= 0.62 r= -0.06
TSH (mIU/ml)	p= 0.45 r= 0.10	-	p= 0.18 r= -0.17	p= 0.93 r= -0.01
FT4 (ng/dl)	p= 0.016* r= -0.30	p= 0.18 r= -0.17	-	p= 0.20 r= 0.16
FT3 (pg/ml)	p= 0.62 r= -0.06	p= 0.93 r= -0.01	p= 0.20 r= 0.16	-
Variables in the control group after 6 months	**BMI (Kg/m^2)**	**TSH (mIU/ml)**	**FT4 (ng/dl)**	**FT3 (pg/ml)**
BMI (Kg/m^2)	-	p= 0.55 r= 0.08	p= 0.22 r= -0.16	p= 0.09 r= -0.21
TSH (mIU/ml)	p= 0.55 r= 0.08	-	p= 0.80 r= 0.03	p= 0.28 r= -0.14
FT4 (ng/dl)	p= 0.22 r= -0.16	p= 0.80 r= 0.03	-	p= 0.48 r= 0.09
FT3 (pg/ml)	p= 0.09 r= -0.21	p= 0.28 r= -0.14	p= 0.48 r= 0.09	-
Variables in the interventional group after intervention	**BMI (Kg/m^2)**	**TSH (mIU/ml)**	**FT4 (ng/dl)**	**FT3 (pg/ml)**
BMI (Kg/m^2)	-	p= 0.60 r= 0.07	p= 0.07 r= -0.23	p= 0.86 r= -0.02
TSH (mIU/ml)	p= 0.60 r= 0.07	-	p= 0.22 r= -0.16	p= 0.53 r= -0.08
FT4 (ng/dl)	p= 0.07 r= -0.23	p= 0.22 r= -0.16	-	p= 0.69 r= 0.05
FT3 (pg/ml)	p= 0.86 r= -0.02	p= 0.53 r= -0.08	p= 0.69 r= 0.05	-

BMI: Body Mass Index; TSH: Thyroid stimulating hormone; FT3: Free triiodothyronine; FT4: Free thyroxine.

4- DISCUSSION

After the educational intervention in the intervention group, with the slight decrease in BMI, remarkable changes in thyroid hormones was observed (TSH and FT4), which indicates that the changes are not only due to the decrease in BMI, but the educational interventions (physical activity, healthy diet, etc.) could also directly affect thyroid functioning. Unlike the results in the intervention group, after a 6-month period, the control group showed an increase in BMI and TSH, while FT4 and FT3 decreased significantly than before, which confirms the effects of educational intervention. Therefore, inattention to weight control can lead to a higher increased level of TSH in obese children. It should be mentioned, at the end of the study, the control group was also trained under the educational intervention. Since a concurrency exists between leptin and TSH (24), in this study, the successful 6-month intervention in the intervention group can also be related to leptin which is regulated by body fat. Previous studies have not indicated any relationship between TSH and leptin (25), although recently, Reinehr et al. have reported that TSH is associated with both BMI and leptin in patients with obesity and anorexia (13). However, the regulating mechanism of TSH is more complicated than a simple linear correlation between TSH and leptin levels because the TSH production is controlled by several different hormones and transmitters (such as neuropeptide Y [NPY], alpha-melanocyte-stimulating hormone (a-MSH), and leptin) which regulate body weight and satiety (26).

The recent study in animal models showed that the leptin usage can reduces the activity of deiodinase type II (D2) in pituitary tissue; thereby it can lead to the modification effect of T3 on TSH secretion (27). At least, some observed thyroid disorders in severe obesity are reversible with weight loss (28); thus the possibility of irregular signaling by obesity related to the hormonal factors is propounded. Potential causes of the observed thyroid dysregulation in obesity include: obesity due to excessive secretion of thyrotropin-releasing hormone, and resistance or adaptation of TSH that increases energy consumption (29, 30). Adipose tissue-derived leptin regulates energy balance through the hypothalamic-pituitary-thyroid axis using up regulating hypothalamic thyrotropin-releasing hormone gene expression and can also stimulate conversion of T4 to T3 via activation of thyroid deiodinases (29). It has been revealed that leptin is inversely correlated with FT4 (10). Probably higher fat mass in obese adolescents lead to greater physiological effects that are easily visible. Maybe subclinical autoimmune thyroiditis is more common in adolescents and exacerbated. Carlson et al., in a research showed that decreasing sedentary behavior and consuming beverages sweetened with sugar have followed decreasing of body fat levels, but has been ineffective on BMI (23). Kelishadi et al., was performed a non-pharmacological clinical trial study on 4-18 year-old children attending outpatient clinics of Isfahan Endocrine and Metabolism Research Center (Iran). Their study showed that although one session of interventional education had no significant effects on children's anthropometric measurements, it could change their lipid profile. Moreover, the intervention was more effective on improving lipid profile in children over 10 years of age. Therefore, effective interventional strategies must be invented and implemented on children based on their age group (20).

Also, a randomized, controlled trial was conducted to determine whether a 6-week low calorie diet and aerobic exercise intervention could alter metabolic syndrome (MetS) risk factors in pre-pubescent obese Chinese children by Luo et al. Their results revealed that an intensive, 6-week diet and exercise intervention had favorable effects in altering MetS risk factors in obese Chinese children aged 11 to 13 year-old (22). Based on the results of the study that conducted by Matusik et al., in obese adolescents with isolated subclinical hypothyroidism, intervention through diet and behavioral management has helped to reduce BMI. Their results indicated that relatively high TSH level is due to overweight (31). Reinehr and Andler investigated thyroid hormones before and after weight loss in obese children, and revealed that decreasing of overweight was associated with a significant reduce in T3 and T4, but there was no significant difference in TSH (16). According to the study results of the Klakk et al., the intervention effect of adding four times exercise per week in school on obesity of school children was significant (32). Compare the relative frequency of thyroid function disorders in obese children with non-obese children was conducted by Ebrahimi et al., and revealed that obesity in children can be effect on increase of TSH and decrease of FT4 and FT3 (33). In a study that were done by Grandone et al., was given to the children with hyperthyrotropinemia a 6-month weight loss program. BMI and free T3 (FT3) in the patients with increased TSH than those who had normal TSH were higher. In subjects with intervention significantly with weight loss was simultaneously decreased TSH and FT3.

The results revealed that the increase of the mean concentration of TSH, often seen in the obese children, and hyperthyrotropinemia is reversible after weight loss (15). The present study indicated that only the relationship between BMI and FT4 in intervention group, before the 6-month intervention, is significant. In this regard, a study by Krause et al. was performed which examined the association between obesity with indicators of thyroid function in children. According to their results, relationship of TSH with BMI and fat mass was positive; while there was negative relationship between FT4 with BMI and fat mass. They stated that obesity of children is associated with higher TSH and lower FT4 concentrations and with a higher prevalence of abnormally high TSH. They also expressed the possible effects of leptin on the secretion of TSH (34). In the some studies have suggested that subclinical hypothyroidism leads to the deterioration of metabolism profile, blood lipid abnormalities or dysfunction of the heart (35). Therefore based on the results of present study, since overweight and obesity is associated with increased TSH and decreased FT4 and FT3; so in order to lose weight and improve thyroid function tests in obese children, lifestyle modification includes proper nutrition, encouraging more physical activity, appropriate manner dealing of parents with the children and their continuous follow up are recommended. Moreover according to the contradictory results of the various studies about relationships between thyroid hormone levels and obesity, long-term studies with greater sample size and more specific interventional studies are suggested to evaluate the individual effects of lifestyle modification on the relationship between thyroid hormones level and obesity. However, the low sample size due to the lack of participation of all samples calculated in this plan is one of the limitations of the present study. Nevertheless, since lifestyle interventions, unlike drug therapy, have no complications and are a precautionary and low-cost measure, these interventions are one of the strengths of the present study.

5- CONCLUSION

Since in this study, educational intervention was effective in reducing BMI and improving thyroid tests; hence, the educational intervention is highly recommended for the modification of BMI and the improvement of thyroid tests in children and adolescents with obesity and overweight. Also, it is suggested that in future studies, the percentage of body fat and leptin should also be considered as a result for more accurate evaluation of the relationship between thyroid function tests and obesity and overweight in children and adolescents.

6- CONFLICT OF INTEREST

The authors had not any financial or personal relationships with other people or organizations during the study. So there was no conflict of interests in this article.

7- ACKNOWLEDGMENT

This paper was extracted from the pediatric dissertation (thesis code of 884, the ethical code of Ir.BUMS.1394.298 and IRCT ID is IRCT2017081935772N1) and supported by the Research Vice-Chancellery of Birjand University of Medical Sciences. The authors are grateful to the students and their parents who participated in this research.

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