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COMPREHENSIVE APPROACH TO TREATMENT OF EXOGENOUS-CONSTITUTIONAL OBESITY IN CHILDREN

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ABSTRACT-- *In this paper, we presented a new tactic for managing children with exogenous-constitutional obesity against the background of leptin resistance. Body weight in children with and without leptin resistance did not differ statistically, but the degree of reduction in the 1 to 3 course of therapy was more expressed in children in the comparison group, without leptin resistance. So in the comparison group after the 1st course, the weight decreased by 2.27±0.78 kg, and in the main group - by 1.63±0.56 kg (p<0.001); after the second course of therapy, these values (weight reduction) were 4.40±1.43 kg and 3.28±1.10 kg (p<0.001); and finally after the last 3 courses - 6.60±2.14 and 4.91±1.64 (p<0.001).Signs of leptin resistance in children against the background of TMS became less noticeable and most children after 2 months noted a decrease or even absence of the majority, in contrast to children whose parents did not want to try to correct the child's condition with TMS. Therefore, it is very important that a year after therapy in children who passed 3 courses of TMS, the trend remained: 95% of children continued to lose weight and only two people (4.8%) increased their weight. And in children receiving standard therapy, the vast majority (97.5%) returned to their original weight level or even increased slightly. This scheme of complex therapy will improve the quality of life of children in this category significantly.*

Keyword-- *exogenous-constitutional obesity, children, leptin resistance.*

I. INTRODUCTION

Worldwide, more than 15 million children are obese. The prevalence of the disease has increased from 4% recorded in 1975 to 18% now. WHO estimates that the number of obese children will exceed 70 million by 2025. [3,6,9,11].

One of the mechanisms of accumulation of excess body weight and, as a consequence, the development of exogenous- constitutional obesity is in increasing the volume of adipocytes without increasing their number, which is formed in childhood (up to 20 years). After 20 years, about 10% of fat cells are updated annually in the body of any person, but this process does not affect the total number of grown adipocytes that produce the "saturation hormone" - leptin [5,7,12].

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Children who are overweight produce a huge amount of leptin, which should completely block the child's desire to eat, but this does not happen. A huge amount of leptin does not affect the hypothalamus in any way. The cause is leptin resistance. Obese patients continue to "overeat" despite their elevated leptin levels, which indicates that they have a violation of the feedback mechanism in the "leptin-receptor" system [10,13].

Treatment of obesity with standard methods in such children, without taking into account the cause in the form of leptin resistance, leads to a rapid return of the original body weight at the slightest interruption of treatment [1,8,14,15,16].**Purpose.** To determine the optimal management strategy for children with exogenous-constitutional obesity against the background of leptin resistance without medicamentous support.

II. MATERIALS AND METHODS

Our study included 160 children with exogenous-constitutional obesity from 7 to 17 years old, divided into two groups: the main group (82 people) - children with leptin resistance and the comparison group (78 people) - children without leptin resistance. Two subgroups were formed in each group, depending on the planned treatment algorithm.Children from the main group and the comparison group of subgroups I received standard therapy for weight loss (diet therapy and exercise therapy) and transcranial magnetic therapy, while children from subgroups II followed only the principles of diet therapy and performed daily physical activity.

III. RESEARCH RESULTS AND DISCUSSION

We conducted a survey of parents and children to identify clinical signs of leptin resistance. The combination of signs in the amount of more than 5 allowed us to assume the presence of this pathology in almost 52% of children. These children later formed the main group of the study.

Statistical analysis shows that subgroups I and II in the main group (p= 0.818) and the comparison group (p=0.822) were comparable by gender.

For laboratory confirmation of leptin resistance, an immunoassay analysis was performed for all children to determine the level of leptin in the blood serum. In both the main group and the comparison group, leptin levels were significantly higher than the age and sex norm. In the subgroups, the leptin concentration did not change initially statistically (in the main group, p=0.284; in the comparison group, p=0.313) (table 1).

Table 1: Leptin concentrations in children

	The main group I subgroup, n=42 Me (quartiles)	Main group II subgroup, n=40 Me (quartiles)	p
Leptin level in the blood , ng/ml before treatment	41,15 (28,48–53,58)	47,65 (28,65–78,48)	0,284

	Comparison group I subgroup Me (quartiles) n=39	Comparison group II subgroup Me (quartiles) n=39	p
	42,40 (29,10–79,00)	53,40 (36,94–75,40)	0,313

The program of complex therapy developed by us for elimination of exogenous-constitutional obesity in children with leptin resistance included: diet therapy, moderate daily physical activity (exercise therapy) and transcranial magnetic therapy. All children followed the following principles of the dietary approach:

- Breakfast with a focus on protein-containing food, eat no later than 30-60 minutes after waking up;
- forget about snacks;
- Go to 3 meals a day;
- Don't eat at night! Dinner no later than 3 hours before bedtime;
- Low-carb nutrition (no more than 25 g of fructose/day) (exclude: sweet, sweet fruit, potatoes, flour, rice)
- saturate the body with insoluble and soluble plant fiber (at least 400 gr of vegetables/day);
- Food must include saturated and monounsaturated fats: butter, cheese, sour cream, avocado, nuts, coconut oil, olive oil, fish oil)
- Give up all trans fats
- Strict ban on all industrial food products (soy, sausages, pates, curds, etc.).

Also, the necessary criteria for therapy were: adherence to a healthy full-fledged sleep, mandatory daily physical activity (preferably after 5 pm) and, if necessary, the possibility of consulting a psychologist.

The monitoring of compliance was carried out by means of diaries, which all patients filled out daily.

Transcranial magnetic therapy was performed on the device "AMO-ATOS-E" with the prefix "Headband". 1 course was 10 sessions. The procedure was performed in the sitting position of children. Fixation of the radiator terminals was performed in the temporal regions of the head. The running magnetic field mode was selected - ∪∩ (variable magnetic field), the frequency increased from 1 to 10 Hz from session to session. The duration of the session also increased gradually from 8 to 15 minutes [2].

The children were given 3 courses of transcranial magnetic therapy with an interval of 1 month. Monthly bioelectrical impedance analysis was held, anthropometric data was measured and signs of leptin resistance were recorded [4].

For the analysis, we used multidimensional approaches, in particular, we used covariance analysis (ANCOVA), where the method of weight correction or the presence of leptin resistance acted as a fixed factor, and age was used as a controlling feature. The use of this control variable made it possible to level out the age-related variations in body weight. The compliance with the conditions for ANCOVA was checked beforehand: the presence of normality and homogeneity of variances (according to the Liven criterion).

A month after therapy, the weight of children with exogenous constitutional obesity and leptin resistance who underwent transcranial magnetic therapy decreased by 3 %, after the 2nd course by 6%, and at the end of the 3rd

course by 9%. In children with leptin resistance who did not receive transcranial magnetic therapy, the weight decreased by 1% after 1 month, by 2% after 2 months, and by 2.8% after 3 courses.

That is, in both subgroups, regardless of the therapy received, there was a highly significant weight loss compared to the initial one ($p<0.001$). However, children receiving magnetic therapy starting from the 1st course had lower body weight values ($p=0.014$ on the first visit and $p<0.001$ on the next). The degree of weight loss — that is, the difference with the initial value - in the studied subgroups also turned out to be different. So I subgroup with TMS after 3 courses marked decrease in body weight in of 7.10±3.90 kg (9% of baseline), while in group II it decreased only at 1.54±0.85 kg (2.8% of baseline) ($p<0.001$) (figure 1).

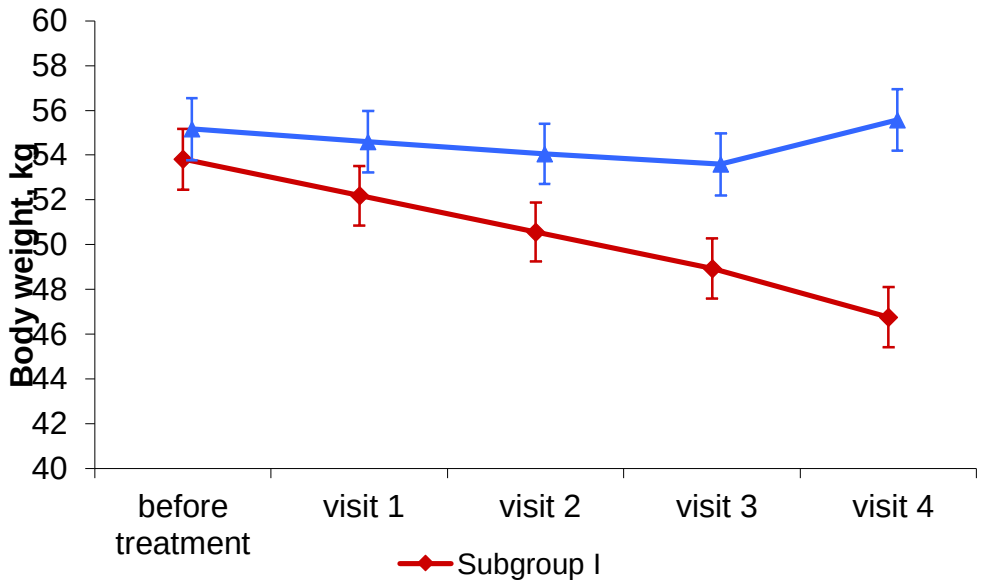

Figure 1: Body weight change in different treatment regimens in children with leptin resistance

Signs of leptin resistance in children on the background of TMS became less noticeable and most children after 2 months noted a decrease or even absence of the majority, in contrast to children whose parents did not want to try to correct the child's condition with the help of TMS.

Therefore, it is very important that a year after therapy in children who have passed 3 courses of TMS, the trend remained: 95% of children continued to decrease in weight and only two people (4.8%) increased in weight. And in children receiving standard therapy, the vast majority (97.5%) returned to their original weight level or even increased slightly.

Thus, after the termination of TMS courses, while remaining on maintenance standard therapy, after a year, the weight of children in the I subgroup decreased by 2.19±2.70 kg and reached 47.42±15.18 kg, and in the II subgroup the weight increased by 1.99±1.73 kg and reached a value of 54.88±18.77 kg ($p<0.001$).

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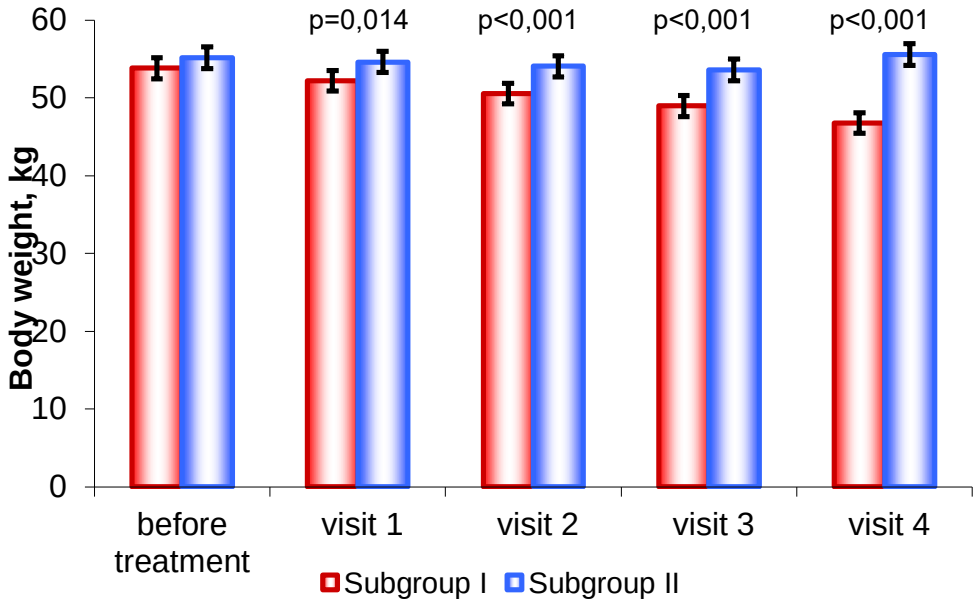

Figure 2: Body weight

In the comparison group, all children with exogenous-constitutional obesity without signs of leptin resistance did not statistically differ in baseline weight between subgroups I and II. After the start of complex therapy, there was a downward trend regardless of the treatment regimen.

In children without leptin resistance, who underwent transcranial magnetic therapy weight after 1 month (after 1 course) decreased by 4.1 %, after 2 courses by 8%, and after 3 courses by 12%. In a group of children without leptin resistance who did not undergo transcranial magnetic therapy, the intensity of weight loss was actually reduced by two times: after 1 month (after 1 course), body weight decreased by 3 %, after 2 courses by 6%, and after 3 courses by 9%.

Both approaches to correcting body weight in children with exogenous-constitutional obesity without leptin resistance showed a decrease in body weight compared to the baseline level ($p<0.001$), although the degree of reduction was greater in subgroup I where the complex therapy included magnetic therapy. Thus, the weight loss in subgroups I and II, respectively, after the first course was: 2.27±0.78 kg and 1.77±0.54 kg ($p<0.001$); after 2 courses for 4.40±1.43 kg and 3.52±1.08 kg ($p<0.001$), after 3 courses for 6.60±2.14 kg and 5.28±1.61 kg (p=0, <0.001), a year after the first treatment for 8.48±4.17 kg and 6.29±3.09 kg (p=0, <0.001).

Thus, during the year, the weight of children with exogenous-constitutional obesity without signs of leptin resistance and receiving TMS decreased by 15.4%, and in children with a similar medical history, but without passing TMS - by 10.7% of the original body weight. Numerical values of body weight a year after the start of treatment are 46.46±14.11 in subgroup I and 52.29±15.81 in subgroup II (p=0.002). Interestingly, the body weight itself in children with and without leptin resistance did not differ statistically, but the degree of reduction in the 1 to 3 course of therapy was more expressed in children in the comparison group, without leptin resistance. So in the comparison group after the 1st course, the weight decreased by 2.27± 0.78 kg, and in the main group - by 1.63± 0.56 kg ($p< 0.001$); after the second course of therapy, these values (weight reduction) were 4.40±1.43 kg and 3.28±1.10 kg ($p<0.001$); and finally after the last 3 courses — 6.60±2.14 and 4.91±1.64 ($p<0.001$).

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Table 1: Precentage of readuction from the original

Percentage of reduction from the original	Comparison group I subgroup	Comparison group II subgroup
Body weight, kg 1 visit	4,1%	3,0%
Body weight, kg 2 visit	8,0%	6,0%
Body weight, kg 3 visit	12,0%	9,0%
Body weight, kg 4 visit	15,4%	10,7%
Percentages of decrease from the previous level		
Body weight, kg 1 visit	4,1%	3,0%
Body weight, kg 2 visit	4,0%	3,1%
Body weight, kg 3 visit	4,3%	3,2%
Body weight, kg 4 visit	3,9%	1,9%

Using a mathematical evaluation of the data obtained, we were able to determine the effectiveness of the proposed complex therapy.

Table 2: Effectiveness of complex therapy in children with leptin resistance

	treatment effect			
	Good result – weight decreased from 3 to 4	Bad result – weight increased from 3 to 4	total	
Basic (new method)	40	2	42	
Conventional method	1	39	40	
	41	41	82	
	Value		RI low	RI up
Frequency of the outcome (good) in the cured groups	95,2%		84,21%	98,68%
Frequency of outcome (good) in the control group	2,5%		0,44%	12,88%
The rise in the relative use	3709,5%		448,1%	#######
The increase in absolute use	92,7%		77,6%	96,8%
Number of patients who need to be treated	1,08		1	1
Relative risk	38,10		5,48	264,79

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Odds ratio	780,00		67,94	8955,10
x2 (corrected by Yates)	66,82			
p	0,000			

* Note: In this case, FOT is the number of children whose weight decreased from 3 to 4 visit in the treatment group. And FOC - in the control group.

Table 3: Effectiveness of complex therapy in children without leptin resistance

	Treatment effect			
	Good result	Bad result	total	
Basic (new method)	38	1	39	
Conventional method	34	5	39	
	72	6	78	
	Value		RI low	RI up
Frequency of the outcome (good) in the cured groups	97,4%		86,82%	99,55%
Frequency of outcome (good) in the control group	87,2%		73,29%	94,40%
The rise in the relative use	11,8%		-1,9%	27,4%
The increase in absolute use	10,3%		-2,6%	24,3%
Number of patients who need to be treated	9,75		4	-39
Relative risk	1,12		0,98	1,27
Odds ratio	5,59		0,62	50,25
x2 (corrected by Yates)	1,63			
p	0,202			

* Note: In this case, FOT is the number of children whose weight decreased from 3 to 4 visit in the treatment group. And FOC - in the control group.

IV. CONCLUSIONS

Complex therapy of exogenous-constitutional obesity in children using TMS makes the correction of body weight in children with leptin resistance and without it almost identical. This confirms the high effectiveness of TMS in children with leptin resistance. In the comparison group, after 1 course, the weight decreased by 2.27± 0.78 kg, and in the main group-by 1.63± 0.56 kg($p< 0.001$); after the second course of therapy, these values were 4.40±1.43 kg and 3.28±1.10 kg ($p<0.001$); and finally after the last 3 courses— 6.60±2.14 and 4.91±1.64 ($p<0.001$).

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