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Effects of a low-calorie diet on resting metabolic rate and serum tri-iodothyronine levels in obese children

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Abstract The purpose of the study was to examine the effects of weight loss on resting metabolic rate (RMR) and on serum T3 levels in obese children and to investigate whether RMR changes are related to T3 changes. Sixty-four healthy, overweight, children (age: 12.1 ± 1.1 years, body mass index 29.3 ± 4.3 kg/m^2) were studied during a 6-week weight reduction programme. RMR (by indirect calorimetry) total T3, total T4, TSH and fat-free mass (FFM) (by anthropometry) were measured at baseline and after 6 weeks of dietary treatment. Weight loss resulted in a 10.1% decline in RMR ($P < 0.01$) and a 23.4% decrease in serum T3 levels ($P < 0.001$). RMR was correlated with FFM before ($r = 0.78$, $P < 0.001$) and after weight loss ($r = 0.76$, $P < 0.001$). The changes in RMR were positively correlated with the changes in FFM ($r = 0.48$, $P < 0.05$) but also with the changes in serum T3 levels ($r = 0.47$, $P < 0.05$). The initial T3 levels predicted the subsequent fall in T3 that occurred after 6 weeks of dietary treatment ($r = -0.60$, $P < 0.001$).

Conclusions A significant decrease in serum T3 concentrations and resting metabolic rate occurred as a result of a 6-week weight reduction programme in an obese child population. The decline in T3 levels combined with fat-free mass loss could be responsible for the reduction in resting metabolic rate.

Key words Obesity · Resting metabolic rate · Tri-iodothyronine · Weight loss · Fat-free mass

Abbreviations *BMI* body mass index · *FFM* fat-free mass · *RMR* resting metabolic rate · *T3* triiodothyronine · *T4* thyroxine · *TSH* thyrotropine

Introduction

Resting metabolic rate (RMR) is the major component of total energy expenditure [16, 22]. It has been found that adults with low RMR adjusted for fat-free mass (FFM) have a greater risk to develop obesity [24].

The relationship between RMR and FFM under non-starvation conditions is the same in obese and non-obese children with non-obese adolescents and with obese and non-obese adults. The equation for these groups is: RMR (MJ/d) = 2.44 + 0.084 FFM. However the slope for the line relating RMR and FFM in obese adolescents is different from the above [19]. Data on obese adolescents demonstrate higher RMR when expressed as a function of FFM than do adults or prepubescent children. The RMR of obese adolescents is significantly higher (117% ± 14%) than that predicated by the normal line [19]. The reason for this is not known.

Numerous studies in adults have shown that an important decrease of RMR and serum T3 levels occurs during weight reduction programmes [1, 8, 12, 13, 15, 29, 30]. The reduction in RMR is in part explained by

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the decrease in FFM [5, 9, 11, 14, 15]. The fact that changes in RMR are correlated with the changes in serum T3 levels is controversial. Some studies have demonstrated this correlation [4, 13] whereas others disagree [1, 12, 30].

In children, weight loss due to caloric restriction is associated with a significant decrease in RMR [20, 31]. Very few data exist concerning the effects of weight loss on thyroid hormone concentrations in children. To our knowledge there is no study examining the possible correlation between RMR changes and T3 changes in children.

The specific objectives were to assess: (1) the effects of a balanced hypocaloric diet on RMR and serum T3 levels, and (2) the relationship between RMR changes and T3 changes in a population of obese children.

Materials and methods

Subjects

A total of 64 obese children with a relative body weight > 120%, 22 boys and 42 girls, aged 10–14 years, were studied for 6 weeks. All the subjects and their parents gave informed consent before their participation in the study. All children except for being obese had a normal physical examination and normal urinalysis. Subjects with endocrine or metabolic disorders were excluded from the study. Smokers and children taking any medication including oral contraceptives and medication that could affect RMR were also excluded. All participants reported no significant change in their body weight for at least 3 months prior to entry into the study.

No regular exercise was included in the treatment and the subjects were instructed to continue their previous physical activity.

Dietary treatment

The dietary energy prescription was 5030 kJ/day (1200 Kcal/day). The energy distribution in the food plans was calculated in such a way that 48% of the total energy intake was supplied as carbohydrates, 30% as fat and 22% as protein. Each week a medical visit took place, accompanied by at least one parent, to check body weight, arterial blood pressure and to discuss problems related to the prescribed diet. Furthermore, the 24 h recall method was used during 2 weekdays and 1 weekend day in order to assess the actual caloric intake during the study period.

Body composition

Body weight, height and skinfold thickness at four sites (biceps, triceps, subscapular and supra-iliac) were measured by the same physician before and after 6 weeks of treatment. Skinfolds were obtained with a Harpenden skinfold caliper (John Bull, British Indicators, St. Albans, Herts, UK) three times at each location on the right side of the body and the mean value was then calculated. Body weight was measured on a beam balance with an accuracy of ± 50 g and body height by a stadiometer. Relative weight was calculated from the child's weight divided by the expected weight for height and multiplied by 100. Body mass index (BMI) was calculated as body weight (kg) divided by height squared (m^2). Body fat, FFM were calculated by body weight and skinfold thickness using Lohman's formulas [18].

Resting metabolic rate

In 26 children RMR was measured by computerised indirect calorimetry (SensorMedics, Anaheim, Calif., USA). All measurements were performed early in the morning (between 08 00–09 00 hours) after at least 30 min rest. For the 12 h preceding each measurement, subjects were instructed not to exercise, not to eat or drink anything except water. The test was performed at a constant ambient temperature (23°C). Before each test the equipment was calibrated with a standard gas mixture. RMR was calculated from oxygen consumption and CO_2 production according to Weir [28].

Biochemical variables

Before and after dietary treatment, venous blood samples for hormonal analyses were taken after a 12 h overnight fast. Commercially available RIA kits were used to measure the serum concentration of T3 and T4 (Boehringer-Manheim, Manheim, Germany). TSH was measured with a sensitive immunoradiometric sensitive assay (RAI-gnost hTSH, Behring, Marburg, Germany).

Statistical analysis

Results are expressed as means ± SEM. To compare baseline with the 6-week values, the Student's paired *t*-test for variables with normal distribution was used. Otherwise the Wilcoxon rank sum test was used. The relationships between variables were studied using the Pearson product moment linear correlation coefficient.

Results

With the use of 24 h recall method, a high compliance with the prescribed diet was observed.

Subjects characteristics before and after the dietary treatment are shown in Table 1. After 6 weeks of a low-calorie diet, a significant weight reduction was achieved (6.4 ± 0.15 kg). Moreover a statistically significant decrease in BMI, fat and FFM occurred. The weight loss was mainly due to a decrease in fat mass (2/3 fat vs 1/3 FFM).

The RMR declined from 6906.8 ± 202.8 kJ/day (1648 ± 48.4 Kcal/day) to 6210.4 ± 196.6 kJ/d (1482.2 ± 46.9 Kcal/day) ($P < 0.01$) after 6 weeks of dietary intervention. Moreover, a slight reduction in RMR/FFM ratio occurred (from 151 ± 7 kJ/kg to 142 ± 6 kJ/kg). Serum T3 levels decreased from 162.3 ± 3.1 ng/dl to 124.3 ± 2.8 ng/dl ($P < 0.001$). The initial T3 levels predicted the subsequent fall in T3 (defined as final T3 minus the initial T3), that occurred after 6 weeks of dietary treatment ($r = -0.60$, $P < 0.001$). Those subjects with the lowest basal T3 levels had the smallest subsequent decrease in T3 values. The decrease of T3 was not correlated with the percentage of carbohydrates in the diet. Serum T4 and TSH concentrations did not change significantly.

Prior to dietary treatment, RMR was strongly correlated with FFM ($r = 0.78$, $P < 0.001$). The correlation was maintained after 6 weeks of low-calorie diet ($r = 0.76$, $P < 0.001$). Furthermore the observed

changes in RMR correlated with the changes in FFM ($r = 0.48$, $P < 0.05$). The changes of RMR were also correlated with the changes of the serum T3 levels ($r = 0.47$, $P < 0.05$).

Discussion

In the present study, the dietary treatment resulted in a significant decrease in body weight mainly due to a decrease in fat mass. This is in agreement with previous reports concerning adults [9, 14, 23, 25] and children [20].

In adults, hydrodensitometry with measurement of pulmonary residual volume is the preferred method to assess body composition. However, in children progressive maturation results in changes in FFM density and chemical maturity is reached at 15 to 18 years of age. Thus hydrodensitometry cannot be validly applied to children without measuring body water and skeletal density; skinfold measurements are preferred [18]. Furthermore, the variability of this method is quite low when it is performed by the same physician each time.

Indirect calorimetry, when performed under the same conditions (time of the day, temperature etc), is a very precise technique with low variability and the mean test-retest error for RMR is limited to 0.2% ± 1.4% [26].

The important decrease in RMR observed in this study, confirms previous reports in adults and children [1–4, 6, 8–15, 20, 23, 26, 29–31]. This implies that after weight loss, children should readjust their energy intake level downwards in order to maintain their new body weight.

Before and after 6 weeks of low-calorie diet, RMR was strongly correlated to FFM ($P < 0.001$) (Table 1). Moreover the observed changes in RMR during this weight reduction programme were positively correlated with the changes in FFM ($r = 0.48$, $P < 0.05$). These results are consistent with those from previous studies in adults and children [1, 9, 14, 20, 22, 26, 31]. The importance of the decrease in FFM on the decline in RMR is controversial. In some studies the changes in FFM would totally explain the decline in RMR [2, 8, 20, 23] but there are reports indicating that other factors may play an important role in the decrease in RMR [1, 6, 9, 11, 14, 15, 31]. In most of these studies the RMR/FFM ratio was used. The use of this ratio implies that FFM contributes to RMR consistently over the full range of FFM down to zero. However the association does not regress through the zero intercept [27]. This could be a possible explanation for the discrepancy of the results. Therefore, one has to consider the other reasons which may play a role in the decrease in RMR.

Numerous studies in adults have shown that an important decrease in serum T3 levels occurs during weight reduction programmes [1, 7, 8, 12, 13, 15, 21, 25, 29, 30]. This occurs because the typical conversion of T4 to T3 in the peripheral tissues decreases and T4 is converted to metabollically inactive rT3 instead [1, 7, 21, 25]. Serum T3 levels may decrease on a hypocaloric diet because of a reduction in enzymes responsible for de-iodinating T4 to T3 [1, 7, 21, 25]. Very few data exist concerning the effects of weight loss on thyroid hormone concentrations in children. In the present study a statistically significant decrease in T3 was observed after 6 weeks of hypocaloric diet. On the contrary, T4 and TSH concentrations did not change significantly confirming reports in adults [1, 13, 15]. The initial T3 levels predicted the subsequent fall in T3 which is in agreement with studies concerning adults [12, 17].

Children taking any medication or having a medical condition which can affect binding proteins were excluded from the study. Due to this fact the measurement of total T3 and total T4 concentrations is a good method to assess thyroid hormone status before and after weight loss.

In some studies it has been shown that carbohydrates play an important role in the regulation of serum T3 levels during weight loss [7, 9, 25]. In the present study no correlation was found between the decrease in T3 and the percentage of carbohydrates in the diet. However, the percentage of dietary carbohydrates did not vary greatly among our patients (43–53%). For this reason the effect of carbohydrates on serum T3 levels could be minimised. Moreover, it has been shown that when a normal amount of carbohydrates is precribed (200 g), the percentage of carbohydrates may have a minor role in the regulation of T3 levels [7]. In the present weight reduction programme the carbohydrate intake was quite important (almost 50% of energy intake in a 5030 kJ/day diet). Further studies on obese children are required to evaluate the exact role of dietary carbohydrates in the decrease of T3.

Table 1 Subjects' characteristics before and after weight loss (*BMI* body mass index, *FFM* fat-free mass, *RMR* resting metabolic rate, *T3* triiodothyronine *T4* thyroxine, *TSH* thyrotropine

	Pre-diet	After 6 weeks diet	*P*
Body weight (kg)	75.5 ± 2.1	69.1 ± 1.9	< 0.001
BMI (kg/m^2)	29.3 ± 0.54	26.7 ± 0.44	< 0.001
Fat mass (kg)	29.8 ± 0.82	25.4 ± 0.72	< 0.001
FFM (kg)	45.7 ± 0.92	43.7 ± 0.84	< 0.001
24h RMR (kJ/day)	6906.8 ± 202.8	6210.4 ± 196.6	< 0.01
RMR/FFM (kJ/kg)	151 ± 7	142 ± 6	N.S.
T3 (ng/dl)	162.3 ± 3.1	124.3 ± 2.8	< 0.001
T4 (μg/dl)	8.2 ± 0.15	7.9 ± 0.14	N.S.
TSH (mUI/ml)	2.5 ± 0.12	2.6 ± 0.12	N.S.

The decrease in T3, a major thermogenic hormone, might be an adaptive mechanism designed to conserve energy during caloric deprivation. This hypothesis has not been fully proven since in some of the studies concerning adults, a positive correlation was found between the changes in serum T3 levels and the RMR changes [4, 13], whereas in others, no statistical significant correlation was observed [1, 12, 15, 30]. The reason for this discrepancy is not apparent. A possible explanation could be the different dietary treatments used in these studies. It is interesting to notice that Hendler et al. [13] observed a statistical significant correlation of T3 and RMR changes with a 800 Kcal/day diet but when a 440 Kcal/day diet was used, no relationship was found [12]. To our knowledge no data exist in children. In the present study a statistically significant correlation between the decline in T3 and the decrease in RMR was found ($r = 0.47$, $P < 0.05$). These results indicate that in children, the changes in RMR may in part be explained by the decrease in serum T3 levels.

The clinical and scientific relevance of these findings is that, due to the decrease in RMR, children after weight loss should reduce their energy intake in order to maintain their new body weight. Furthermore, the changes in T3 and RMR and the significant correlation between these two parameters suggest that in obese children the decrease in T3 during energy restriction could be an adaptive mechanism for caloric conservation. Further research is needed to determine whether with a more restrictive diet similar results will be observed.

In obese children a significant decrease in RMR and serum T3 levels occurs after weight loss, achieved by a well-balanced low-calorie diet. The fall in RMR is mainly, but not completely, explained by the changes in FFM. The decline in T3 concentrations seems to play an important role in the decrease of RMR in children.

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ANNOUNCEMENTS

The 4th International Skeletal Dysplasia Meeting

July 29–August 1, 1999
Baden-Baden, Germany

The 1999 International Skeletal Dysplasia Meeting will be held in Baden-Baden, Germany, July 29 to August 1, 1999. Attendance will be limited. A key topic will be the mechanisms and errors of skeletal morphogenesis. The abstract deadline will be April 30, 1999 and the estimated comprehensive fee is US $ 600.
Baden-Baden is a renowned spa in the Black Forest and can be reached directly by train from the international airports of Frankfurt, Stuttgart, Strasbourg or Zurich.

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9th International conference of the International Society for Research in Human Milk and Lactation (ISRHML) on "Short and long term effects of breast feeding on child health"

October 2–6, 1999
Kloster Irsee Manstery, Kaufbeuren (near Munich), Germany

Scientific organizers:
Prof. B. Koletzko, Munich (Germany)
Prof. O. Hernell, Umea (Sweden)
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