Leptin and insulin levels in prepubertal obese children before and after an intensive educational program: preliminary data

Arigo T, Gatto E, Ferrai V, Munaco F, Costa A, Chirico V, Salpietro C
Department of Pediatrics, Unit of Genetics and Pediatric Immunology, University of Messina, Italy

Abstract
The present study evaluated fasting levels of glucose, insulin and leptin in a group of prepubertal obese children before and after weight loss. We enrolled 64 prepubescent obese children and 20 normal-weight prepubescent children as controls. Fasting plasma concentration of glucose, insulin, Homeostasis Model assessment for insulin resistance (HOMA-IR), and leptin levels were measured at baseline and after a 6-month an intensive educational program (i.e. improved nutrition and increased physical activity). After diet weight loss, the prepubertal obese children showed higher leptin levels than control subjects. Weight loss significantly (p=0.001) diminished plasma leptin and insulin concentrations. Weight loss in prepubertal children is associated with a significant change in leptin and insulin levels. These results confirm the hypothesis that these hormones are closely associated with obesity in childhood and might take part in glucose, fat and energy metabolism.

Keywords: obesity, insulin, leptin

Introduction
The prevalence of childhood obesity is increasing in most industrialized countries and is associated with a major risk for co-morbidity and mortality during the adult life (1). It has been reported that in Italy 24% of school children were overweight and 12% were obese (2). One of the largest health problems in obese adolescents and young adults is the development of type 2 diabetes mellitus, preceded by insulin resistance during childhood usually associated with visceral fat accumulation. Waist circumference correlates with cardiovascular morbidity as well as the body mass index (BMI) or percent body fat. There have been several studies reporting the role of insulin and leptin on energy homeostasis through control of appetite and energy expenditure: both hormones increase in direct proportion to adipose mass (3, 4). It has been reported that leptin and insulin levels were lower in normal weight than in obese children (5).

The aims of the present study were to investigate: i) fasting levels of glucose, insulin, leptin and ii) the relationship between clinical and hormonal data in a group of prepubertal obese children at baseline and after weight loss.

Materials and Methods
We enrolled 64 consecutive prepubescent obese children, 35 of who completed the study (mean age 7.6 ± 0.9 years, 19 females) and 20 normal weight children. The study design was approved by the Hospital’s Ethical Committee and written consent was obtained from the parents of patients. Obesity was defined according to the International Task Force of Obesity using population specific data, i.e. BMI ≥ 2.0 SD for gender and age (6).

The patients underwent to intensive educational program for obese children, based on daily aerobic physical activity (one hour), nutrition education, balanced hypocoric diet, and individual behavior therapy. Follow-up visits were scheduled at 2, 4, and 6 months after the first visit. Based samples were taken only at baseline for control group, while at baseline and six months later in obese study group, from each subject for the measurement of circulating concentrations of glucose (G), insulin (I) and leptin, after an overnight fast. Samples were centrifuged immediately after withdrawal. Serum specimens for insulin and leptin were frozen at -80°C and then thawed by commercial kits; G determinations were performed directly.

Statistical analyses were performed using SPSS 11.0 for Window package. The data are expressed as mean and standard deviations (SD).

Results
The main auxological and metabolic data of the patients, at baseline and after six-month follow-up, are summarized in Table 1. The children who dropped out the study (n= 29, i.e. 45%) were excluded from the analysis. Thirty-five children concluded the six month study protocol. On the basis of the threshold BMI z score, 23 of the 35 obese patients (65.7%) were moderately obese and 12 (34.3 %) severely obese. All patients presented abdominal obesity and normal fasting plasma glucose levels (FG) were within normal range in all patients: 5.0±0.5mmol/l (range 3.8-5.5 mmol/l).

Fasting plasma insulin levels were 7.9±4.5 μU/ml (range 2.0- 15.0 μU/ml) and significantly higher with respect to control group (p<0.001) (Table 1). Concerning leptin levels, 3/35 showed fasting hyperinsulinemia (8.6%), without clinical signs (i.e. acanthosis, skin tags). HOMA-IR was 1.8±1.0 (range 0.3-3.6). Nine patients had impaired insulin sensitivity HOMA–IR (25.7%). Leptin levels were 44.8 ± 6.7 ng/ml (range 34.2 – 59.3 ng/ml) and they were significantly (p<0.001) higher with respect to control group (9.1±3.4 ng/ml; range 4.2 -15.3 ng/ml).

After diet weight, BMI, BMI z-score significantly decreased (p<0.05). HOMA-IR, insulin and leptin concentrations decreased significantly (p<0.001) (Table 1).

Discussion
Pediatric obesity is a worldwide growing public health problem. Obesity and abdominal adiposity may be related to serious complications. Insulin resistance or hyperinsulinemia, in obese subjects, are associated with an increased risk for type 2 diabetes and metabolic syndrome. It has been reported that obese children have a twofold risk to have diabetes than children with normal weight (7).

Leptin and insulin regulate energy homeostasis and body weight at the hypothalamic level. It has been reported that obese subjects generally show hyperleptinemia and hyperinsulinemia, and are often resistant to the effects of both hormones. Leptin reduction in obese children during weight loss is associated to improved insulin sensitivity (8). Our study included a population of prepubertal obese children who were compared with normal-weight children at baseline and after a weight reduction program. Attention was focused in prepubertal children to avoid the influence of puberty on insulin-resistance. This study design also provided the opportunity to evaluate the role played by a short-term (6 months) nutritional and physical activity intensive program on clinical characteristics and their association with fasting levels of glucose, insulin and leptin. At baseline obese group showed higher insulin and leptin levels than in the controls. Educational intervention, prescribed in the present study, led to a significant drop in the BMI-SDS, leptin, and insulin concentrations, confirming previous reports (9).

It has been reported that a group of obese adolescents showed higher basal concentrations of leptin compared to the lean controls; after a 3-month randomized controlled physical activity based lifestyle intervention leptin levels dropped (10).

In conclusion, the present study confirms the positive effects of a short-term educational program, related to dietary and physical activity recommendations, on metabolic and clinical parameters in prepubertal obese children, though there was a significant dropout rate. These preliminary results confirmed the hypothesis that insulin and leptin levels are closely associated with obesity in childhood. Further longitudinal studies are required to improve our understanding of other hormones on weight gain and loss in prepubertal children.

Table 1. Main auxological and metabolic data of control group and obese children

<table>
<thead>
<tr>
<th>Metric</th>
<th>Control group (n=20)</th>
<th>Obese group (n=35)</th>
<th>Obese group (n=35) after 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>7.6 ± 0.9</td>
<td>7.6 ± 0.9</td>
<td></td>
</tr>
<tr>
<td>BMI SDS</td>
<td>2.0 ± 0.0</td>
<td>5.0 ± 0.5</td>
<td></td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>24.5 ± 3.1</td>
<td>33.5 ± 4.5</td>
<td></td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.8 ± 1.0</td>
<td>1.8 ± 1.0</td>
<td></td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>44.8 ± 6.7</td>
<td>9.1 ± 3.4</td>
<td></td>
</tr>
</tbody>
</table>

References


