ABSTRACT. Objective. Hyperinsulinemia, hyperlipidemia, hypertension, and coronary artery disease comprise a quartet known as Syndrome X. This syndrome was first described in adults, but has recently been described in children and adolescents. The purpose of our study was to determine if diet or exercise is able to change the clinical profile of Syndrome X in children.

Study Design. We recruited 36 obese (% ideal body weight = 170.3 ± 31.1), children (9 to 12 yrs old) known to have high fasting cholesterol levels (177.5 ± 33.5 mg/dL). Each participated in a 6-week protocol in one of three groups: control (C), diet (D), or exercise (E). Twenty-five of the patients completed the study with full compliance. At the beginning and end of the study, we measured weight, height, blood pressure, serum insulin, and a lipid profile including: cholesterol, low density lipoprotein, high density lipoprotein (HDL), triglycerides, and apolipoprotein A (ApoA). All subject groups were similar before the study. The D group had the greatest attrition (40%) and all of the E group completed the study.

Results. After the 6-week study period, there was no significant weight loss or change in body mass index for any group. There was no significant change in blood pressure and there was no significant decline of fasting cholesterol or low density lipoprotein levels in any of the groups. HDL levels were low in all groups and did not significantly change with treatment. There was a significant decline in the triglyceride levels in both the diet and exercise groups after the study (preD = 150 ± 60; postD = 122 ± 50; preE = 165 ± 50; postE = 116 ± 39). Both the D and E groups also demonstrated a significant decrease in ApoA levels (preD = 174 ± 33; postE = 142 ± 24; preE = 200 ± 50; postE = 161 ± 23). Most impressively, fasting insulin levels significantly decreased with both diet and exercise, but did not change in controls during the 6 weeks (preC = 52 ± 19; postC = 53 ± 21; preD = 54 ± 23; postD = 15 ± 8; preE = 48 ± 21; postE = 9).

Conclusions. The findings of this study are consistent with previous studies describing the presence of Syndrome X in childhood. Both diet and exercise were effective in lowering triglyceride, ApoA levels, and insulin levels. However, due to the large rate of noncompliance in the diet group, exercise seems to be the best treatment for improvement in Syndrome X in children. Pediatrics 1997;100(2).
TABLE 1. Subject Characteristics

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Body Weight (kg)</th>
<th>Body Mass Index</th>
<th>Systolic Blood Pressure</th>
<th>Diastolic Blood Pressure</th>
<th>Fasting Insulin (mU/mL)</th>
<th>Fasting Cholesterol (mU/dl)</th>
<th>Fasting Glucose (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control n = 7</td>
<td>56.6 ± 15</td>
<td>27.2 ± 2.7</td>
<td>111 ± 12</td>
<td>61 ± 10</td>
<td>47 ± 23</td>
<td>150 ± 39</td>
<td>81 ± 70</td>
</tr>
<tr>
<td>Diet n = 9</td>
<td>60.9 ± 14</td>
<td>29.9 ± 2.4</td>
<td>106 ± 13</td>
<td>62 ± 13</td>
<td>54 ± 23</td>
<td>170 ± 40</td>
<td>81 ± 112</td>
</tr>
<tr>
<td>Exercise n = 9</td>
<td>61.1 ± 17</td>
<td>27.9 ± 3.2</td>
<td>109 ± 10</td>
<td>64 ± 10</td>
<td>47 ± 38</td>
<td>167 ± 29</td>
<td>88 ± 9</td>
</tr>
<tr>
<td>Subject mean m = 25</td>
<td>59.8 ± 15</td>
<td>28.3 ± 1.4</td>
<td>109 ± 12</td>
<td>63 ± 11</td>
<td>51 ± 15</td>
<td>162 ± 36</td>
<td>82 ± 90</td>
</tr>
</tbody>
</table>

The study. The final number of children in each subgroup included: C group, 3 boys, 4 girls; D group, 4 boys, 5 girls; E group, 5 boys, 4 girls. Results for each treatment group are reported from the final subject number. At baseline, there was no significant difference between the subgroups. There was a tendency for the C group to have a lower body weight (kilograms) than the other two groups, but this difference was not statistically significant. Additionally, there was no difference in the lipid profiles from the children with a positive family history of hyperlipidemia, and those children who did not know their family history.

The average pretreatment total cholesterol for all of the patients was 178 ± 34 mg/dL, which is considered moderately high for age. ApoA levels were high when compared with age-matched normal values. In all patients, the average pretreatment SBP and DBP measurements were at the 75th to 95th percentile for age. The mean pretreatment fasting insulin level for all subjects was 50.5 ± 15 (normal, <20 μU/mL). Clearly the pretreatment data suggest that the clinical findings of these children is consistent with Syndrome X.

In Vitro Methods

Serum insulin was measured by radioimmunoassay (Coat-A-Count, Diagnostic Products Corp, Los Angeles, CA). Cholesterol, low density lipoprotein, triglyceride, and high density lipoprotein were measured by a photometric technique (COBAS MIRA analyzer, Roche, Somerville, NJ) after daily calibration. Control serum samples were used to check for precision and accuracy. ApoA levels were measured by radioimmunodiffusion assay (Bind-a-RID, The Binding Site, London, UK).

Statistical Analysis

All results are reported as the mean ± standard deviation. Statistical significance was determined by analysis of variance at a P level less than .05.

RESULTS

Of the initial 36 patients, 25 subjects completed the study with full compliance. Although more children initially selected the D group, this group had the highest rate of noncompliance and the largest dropout rate (combined attrition of 40%). There was no significant difference between the subjects who completed the diet, those who were noncompliant, and those who dropped-out from the D group. All children who requested the E group completed the study. The most significant finding of the study, is the marked decrease in the fasting insulin levels of the D and E groups after 6 weeks of treatment. These findings are illustrated by Fig 1.
DISCUSSION

The findings of this study support previous reports that suggest that Syndrome X begins in childhood. Furthermore, our study suggests that the predominant feature of hyperinsulinism can be successfully treated by either diet or exercise. Although both diet and exercise were successful at lowering serum insulin levels, blood pressure did not change and only some components of the lipid profile changed. No subject group had significant weight loss, although all members of the D group lost weight.

The most significant limitation of our study is that we allowed the patients and/or their parents to select the treatment group. We accepted this limitation at the study’s outset because we realized that families desired a particular treatment and to choose for them might adversely affect participation. Initially there were less children who selected the C group. Two of these patients did not return for the final blood work, thus the C group is slightly smaller than the D or E groups. Children who selected the D group tended to be the heaviest and had the worst lipid profiles.

The results from the D group suggest that even a modest reduction of fat intake for a short amount of time can result in decreased triglyceride and ApoA levels, as well as a small amount of weight loss, in children. Although these results are encouraging, the large percentage of drop-outs and noncompliant patients in this group tempers our enthusiasm. Our diet plan was aimed at reducing fat intake to age-recommended normal intake and therefore was not very personalized. diet plan was aimed at reducing fat intake to age-recommended normal intake and therefore was not very personalized. Our diet plan was successful in part because we offered transportation, and in part, because the children who chose this treatment group were interested in exercise. Although the mean VO₂ max did not statistically improve for the group, all patients improved his/her VO₂ max during the 6 weeks of exercise. Both diet and exercise resulted in improved triglyceride and ApoA levels. High serum triglyceride levels are associated with coronary heart disease. High ApoA levels have been found in Type II diabetes and are also associated with CAD. Reduction in triglyceride and ApoA levels with only 6 weeks of treatment suggests that children can improve their risk for both diabetes and CAD with small changes in lifestyle.

High fasting insulin levels are associated with insulin resistance, a hallmark of type II diabetes. High-fasting serum insulin levels is believed to be the underlying cause of many of the clinical problems noted in Syndrome X; for example, hypertriglyceridemia and CAD. Our study demonstrates that both diet and exercise successfully decrease high insulin levels in children. Some researchers believe hyperinsulinism is a result of obesity, yet our treatment groups successfully lowered fasting insulin levels without reducing body weight or BMI. Perhaps lower insulin levels precede the weight loss that occurs with diet or exercise. Although our study does not evaluate future development of disease, it seems plausible that sustained reduction of fasting insulin levels would lower the future risk for development of both diabetes and coronary heart disease.

In summary, results of this study suggest that Syndrome X is an entity that begins in childhood and can be treated by either diet or exercise. However, given the large percentage of the D group who were noncompliant, exercise is probably a better treatment choice in children. Prolonged diet or exercise may be necessary to unmask the full effect of these treatments in childhood Syndrome X.
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