Changes in the atherogenic risk factor profile according to degree of weight loss

T Reinehr, W Andler

Background: The atherogenic risk factor profile in obese subjects is characterised by hypertension, reduced high density lipoprotein (HDL) cholesterol, increased low density lipoprotein (LDL) cholesterol and triglycerides, and insulin resistance. Aims: To examine the amount of weight reduction required to improve the atherogenic profile. Methods: Changes of systolic and diastolic blood pressure, HDL and LDL cholesterol, triglycerides, and insulin resistance, based on the HOMA model over a one year period were studied in obese children who attended the intervention programme “Obeldicks”. The children were divided into four groups according to the change in body mass index standard deviation score (SDS-BMI): group I, increase in SDS-BMI; group II, decrease in SDS-BMI <0.25; group III, decrease in SDS-BMI ≥0.25<0.5; group IV, decrease in SDS-BMI ≥0.5. Results: A total of 130 children (mean age 10.7 years, range 4–15; mean SDS-BMI 2.5, range 2.0–4.0) were studied. The four groups did not differ in age, gender, or degree of overweight (SDS-BMI). An increasing SDS-BMI (group I: n = 20) was followed by a significant increase in insulin resistance (HOMA). Systolic and diastolic blood pressure, LDL cholesterol, triglycerides, and insulin resistance (HOMA) decreased significantly while HDL cholesterol increased significantly in group IV (n = 37). LDL cholesterol also decreased significantly in group III (n = 40); there was no significant change of the other parameters in groups I, II, and III. Conclusion: Over a time period of one year increasing weight in obese children leads to an increase in insulin resistance. Weight loss is associated with an improvement in the atherogenic profile and in insulin resistance, but only if the SDS-BMI decreases by at least 0.5 over a one year period.

MATERIALS AND METHODS
We examined all children suffering from obesity, who attended the intervention programme “Obeldicks” for obese children between 1999 and 2002. The one year outpatient training “Obeldicks” is based on a programme of physical exercise, nutrition education (high carbohydrate, fat reduced diet), and behaviour therapy including individual psychological care of the child and its family. An interdisciplinary team of paediatricians, diet assistants, psychologists, and exercise physiologists is responsible for the training.

Abbreviations: BMI, body mass index; HDL, high density lipoprotein; HOMA, homeostasis model assessment; LDL, low density lipoprotein; SDS, standard deviation score
There was no improvement in the parameters studied in groups I, II, and III. In group IV, systolic blood pressure decreased by a mean of 21 (SD 11) mm Hg and diastolic blood pressure decreased by a mean of 11 (SD 14) mm Hg in children suffering from hypertension (n = 21). LDL cholesterol decreased by a mean of 28 (SD 36) mg/dl and triglycerides decreased by a mean of 82 (SD 36) mg/dl while HDL increased by a mean of 9 (SD 6) mg/dl in children in group IV suffering from dyslipidaemia (n = 15). Apart from a decrease in LDL cholesterol in group III (see table 4) there was no improvement in the parameters studied in groups I, II, and III.

**DISCUSSION**

This is the first study on children concerning the changes of the cardiovascular risk factor profile in obesity in relation to

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**Table 1** The atherogenic risk-factor profile of the 130 children at baseline

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension*</td>
<td>45%</td>
</tr>
<tr>
<td>Decreased HDL cholesterol†</td>
<td>5%</td>
</tr>
<tr>
<td>Increased LDL cholesterol†</td>
<td>13%</td>
</tr>
<tr>
<td>Hypertriglyceridaemia</td>
<td>32%</td>
</tr>
<tr>
<td>HOMA &gt;4</td>
<td>36%</td>
</tr>
</tbody>
</table>

*blood pressure > 95th centile.††HDL cholesterol: <35 mg/dl. †LDL cholesterol: >150 mg/dl.

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**Table 2** Group I (increasing SDS-BMI): SDS-BMI, BMI, systolic and diastolic blood pressure, LDL and HDL cholesterol, triglycerides, and insulin resistance (HOMA) at baseline, one year later, and the changes between these time points in 20 children

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline Mean (SD)</th>
<th>One year later Mean (SD)</th>
<th>Change Mean (SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDS-BMI</td>
<td>2.4 (0.5)</td>
<td>2.6 (0.5)</td>
<td>-0.2 (0.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>27.9 (5.4)</td>
<td>30.0 (6.4)</td>
<td>+2.1 (1.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>121 (16)</td>
<td>125 (18)</td>
<td>+4 (16)</td>
<td>0.191</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>63 (9)</td>
<td>65 (10)</td>
<td>+2 (10)</td>
<td>0.408</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl)</td>
<td>101 (30)</td>
<td>108 (32)</td>
<td>+7 (19)</td>
<td>0.324</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>47 (8)</td>
<td>50 (12)</td>
<td>+3 (11)</td>
<td>0.300</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>132 (81)</td>
<td>134 (132)</td>
<td>+2 (81)</td>
<td>0.681</td>
</tr>
<tr>
<td>HOMA</td>
<td>4.3 (3.1)</td>
<td>7.4 (7.6)</td>
<td>+3.1 (7.5)</td>
<td>0.021</td>
</tr>
</tbody>
</table>

Data presented as mean (SD).

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**Table 3** Group II (decreasing SDS-BMI < 0.25): SDS-BMI, BMI, systolic and diastolic blood pressure, LDL and HDL cholesterol, triglycerides, and insulin resistance (HOMA) at baseline, one year later, and the changes between these time points in 33 children

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline Mean (SD)</th>
<th>One year later Mean (SD)</th>
<th>Change Mean (SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDS-BMI</td>
<td>2.7 (0.5)</td>
<td>2.6 (0.5)</td>
<td>-0.1 (0.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>31.4 (7.5)</td>
<td>30.9 (6.6)</td>
<td>-0.5 (1.7)</td>
<td>0.437</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>131 (23)</td>
<td>125 (20)</td>
<td>-6 (17)</td>
<td>0.097</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>70 (13)</td>
<td>65 (12)</td>
<td>-5 (16)</td>
<td>0.060</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl)</td>
<td>119 (50)</td>
<td>114 (42)</td>
<td>-5 (28)</td>
<td>0.512</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>49 (11)</td>
<td>49 (13)</td>
<td>0 (11)</td>
<td>0.629</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>124 (68)</td>
<td>125 (73)</td>
<td>+1 (50)</td>
<td>0.945</td>
</tr>
<tr>
<td>HOMA</td>
<td>4.3 (3.0)</td>
<td>4.8 (3.4)</td>
<td>+0.5 (2.6)</td>
<td>0.241</td>
</tr>
</tbody>
</table>

Data presented as mean (SD).

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colorimetric test (Vitros Trig-Analyseplättchen). Insulin was measured by microparticle enzyme assay (Abboth). Blood glucose was determined by colorimetric test (Vitros GLU-Analyseplättchen). Intra-assay and interassay coefficients of variation were <4.0% in all methods. Homoeostasis model assessment (HOMA) was used to detect the degree of insulin resistance; the resistance can be assessed from the fasting glucose and insulin concentrations by the formula: resistance (HOMA) = insulin [mU/l] × glucose [mmol/l]/22.5. Insulin resistance was defined by HOMA > 4. The cut off point of 4 was chosen because: (1) the lower limit of the top quintile of variation were <4.0% in all methods. Homoeostasis model assessment (HOMA) was used to detect the degree of insulin resistance; the resistance can be assessed from the fasting glucose and insulin concentrations by the formula: resistance (HOMA) = insulin [mU/l] × glucose [mmol/l]/22.5. Insulin resistance was defined by HOMA > 4. The cut off point of 4 was chosen because: (1) the lower limit of the top quintile of HOMA distribution values is below 4 in normal weight subjects, and (2) prospective study has shown that subjects with HOMA < 4 are unlikely to develop non-insulin dependent diabetes. The children were divided into four groups according to their changes of SDS-BMI in the time period of one year:

- **Group I**: increase in SDS-BMI
- **Group II**: decrease in SDS-BMI < 0.25
- **Group III**: decrease in SDS-BMI ≥ 0.25 – < 0.5
- **Group IV**: decrease in BMI ≥ 0.5.

Statistical analysis was performed by Winstat for Excel. Statistically significant differences were tested by the non-parametric Wilcoxon test for paired observation. Values are expressed as mean and standard deviation (SD).

**RESULTS**

A total of 130 children (mean age 10.7 years, range 4–15 years; 53% girls; mean SDS-BMI 2.5, range 2.0–4.0) were included in the study. At baseline, 81 (62%) children had at least one unfavourable atherogenic risk factor (see table 1).

The four groups did not differ in terms of age, gender, degree of overweight (SDS-BMI), or cardiovascular risk factors.

The changes of the atherogenic risk-factor profile and insulin resistance are shown in tables 2–5. An increase in SDS-BMI (group I, see table 2) was associated with a significant increase in insulin resistance (HOMA), while systolic blood pressure, LDL cholesterol, and triglycerides showed a non-significant increase. A decrease in SDS-BMI of ≥ 0.5 (group IV, see table 5) was associated with a significant decrease in systolic and diastolic blood pressure, LDL serum cholesterol, triglycerides, and insulin resistance (HOMA) while HDL serum cholesterol increased significantly. In group IV, systolic blood pressure decreased by a mean of 21 (SD 11) mm Hg and diastolic blood pressure decreased by a mean of 9 (SD 14) mm Hg in children suffering from hypertension (n = 21). LDL cholesterol decreased by a mean of 28 (SD 36) mg/dl and triglycerides decreased by a mean of 82 (SD 36) mg/dl while HDL increased by a mean of 9 (SD 6) mg/dl in children in group IV suffering from dyslipidaemia (n = 15). Apart from a decrease in LDL cholesterol in group III (see table 4) there was no improvement in the parameters studied in groups I, II, and III.
the degree of weight reduction. In agreement with previous reports,7,8 our study showed that up to two thirds of our obese children already had one or more unfavourable cardiovascular risk factors.

In our sample, a significant improvement of cardiovascular risk factor profile associated with obesity (hypertension, increase in LDL cholesterol and triglycerides, decrease in HDL cholesterol) was shown due to a reduction of SDS-BMI of at least 0.5 over the time period of one year, while a reduction of SDS-BMI below showed no significant improvement except a lowering of LDL cholesterol in the group of children with a reduction of SDS-BMI of at least 0.25. A reduction of LDL cholesterol despite an improvement of other cardiovascular risk factors is probably caused by diet and not due to effective weight loss. Since hypertriglyceridaemia and decreased HDL cholesterol are stronger risk factors for atherogenesis than insulin resistance,82 the clinical significance of decreased LDL cholesterol but no change in blood pressure, LDL and HDL cholesterol, triglycerides, and insulin resistance (HOMA) is questionable.

A few studies on children based on short term weight loss over a few weeks showed an improvement of cardiovascular risk factor profile associated with obesity (reduction of hypertension, triglycerides, and LDL cholesterol).6,12,23,24 The only long term study to examine the cardiovascular risk profile, which comprised only a small number of patients (n = 20) showed no clinically important improvement five years after weight reduction with a significant increase in HDL cholesterol but no change in blood pressure, LDL cholesterol, and triglycerides.25 The mean reduction of relative weight was 12.8% in this study. This small amount of weight loss (the mean reduction of relative weight was 22% in group IV of our sample) and the small sample may explain why there was no improvement of cardiovascular risk factor profile in the long term follow up.

The mean reduction of LDL cholesterol, triglycerides, and the increase of HDL cholesterol due to weight loss in children suffering from dyslipidaemia of group IV is comparable to the effect of medical therapy such as simvastatin in children with familial hypercholesterolaemia.26,27 Prospective data of pharmacological therapy in dyslipidaemic obese children without familial hypercholesterolaemia are not available. The mean reduction of systolic and diastolic blood pressure due to weight loss in group IV was greater than the effects of medical therapies such as captopril in adults.28,29 There are no prospective data on the effect of medical therapy on blood pressure reduction in childhood obesity. In summary, the improvements in lipid profile and blood pressure seen in group IV are as clinically significant as might be achieved with pharmacological treatment, but without the concern about possible side effects.

The observed changes in the atherogenic risk factor profile in our sample represented the effects of a reduced fat intake and increased physical activity due to an ambulant training programme.15,30 Physical activity improves dyslipidaemia.31 A reduction of triglycerides and LDL cholesterol has been reported in obese adolescents and adults on fat reduced diets.6,32 HDL cholesterol concentrations decrease during the period of dieting but tend to rise some months after the weight has stabilised at a reduced level.33,34

The improvement of cardiovascular risk factor profile in reduction of overweight is attributed to improvement of insulin resistance.23,24 Insulin resistance is the main cause of hypertriglyceridaemia, decrease of HDL cholesterol, and increased blood pressure in obesity, and correlates to degree of overweight.23,35 The improvement of insulin resistance and the improvement of the cardiovascular risk factor profile could not be detected in our sample before a reduction of SDS-BMI of at least 0.5 over the time period of one year. In our sample, without weight reduction (group I) there was a significant increase in insulin resistance over the time period of one year, probably due to puberty progression36 besides the effect of increasing overweight.

Even following such a wide ranging, costly programme as our “Obeldicks” training, only 28% of the participants can
achieve effective weight reduction with an improvement of the cardiovascular risk factor profile. In further studies, we could show that motivation was a strong predictor to therapy success and the reduction in overweight was stable over at least two years, even if longer follow up is required.

In summary, the obese child’s failure to achieve weight loss lead to an increase in insulin resistance after the time period of one year. An improvement of cardiovascular risk factor profile and insulin resistance is to be suspected after a reduction of BMI of at least 0.5.

References


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