Childhood obesity: The increasing vascular drama

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Obesity is one of the most important health problems in industrialized countries irrespective of socio-economic status, age, sex or ethnicity. The prevalence of childhood obesity in children has reached alarming levels, even in developing countries. It is estimated that about 1 billion people worldwide are overweight, with 22 millions being under the age of 5 years and 300 million people are obese. By 2010 it is estimated that 26 million children in E.U. countries will be overweight, including 6.4 million who will be obese.

The reasons for childhood obesity include environmental factors, lifestyle preferences, and also cultural background. However, in our affluent society an increase in caloric and fat intake is one of the major causes for developing overweight and obesity. On the other hand, there is rising evidence that a marked decline in physical activity also plays a major role in the dramatically increasing rates of obesity all around the world. Consequently, both over-consumption of calories and reduced physical activity are involved in childhood obesity.

Already in early childhood, overweight and obesity are associated with the classical risk factors for the development of cardiovascular diseases like diabetes or pre-diabetes, high blood pressure or high cholesterol levels. These diseases all together contribute to the so called "metabolic syndrome". Furthermore, the dramatic increase in weight also results in orthopaedic disorders, like erosions and arthrosis of waist or knee joint, making any physical activity impossible, even if the children were willing to do it.

Given the fact that up to 50% of obese children are suffering from metabolic syndrome, it is conceivable that these children are already characterized by vascular damages resulting in developing plaque formation, referred to as atherosclerosis. It is well known that a normal function of vessels depends on a balance between relaxing and contracting factors produced within the internal lining of arterial vessels, the endothelium. The major endothelium-derived relaxing factor is nitric oxide. The availability of nitric oxide is critically influenced by the above mentioned risk factors and diseases leading to a mismatch between relaxation and contraction of the vessels. The occurrence of endothelial dysfunction is considered to be the earliest stage of atherosclerosis and can be present years before an atherosclerotic lesion will be detectable. Moreover, recent studies suggest a prognostic impact of endothelial dysfunction. That means, if endothelial dysfunction is present, the likelihood of developing a cardiovascular disease or to die from it is considerably increased.

With our present, still ongoing study, we aim to investigate whether obesity in early childhood is associated with endothelial dysfunction or other damages of the vessels as an early stage of atherosclerosis. Furthermore we are interested in the relationship between markers of metabolic syndrome (high blood glucose, elevated blood pressure or cholesterol) and the degree of vessel injury.

We included 80 obese or overweight children at an average age of 12 years into this study and compared them with 60 age-matched lean control children. We took blood samples to determine cholesterol levels and performed a so called "oral glucose tolerance testing", a test investigating the individual blood glucose response to a defined amount of glucose intake. With this standardized test we are able to detect diabetes or pre-diabetic alterations like insulin resistance.

As measures of vessel injury we determined intima-media-thickness of

the carotid artery and endothelium-dependent relaxation of the forearm, both well-established markers of early vessel alteration which are easily and non-invasively assessable.

Since we know that vessel integrity is strongly associated with self-healing processes managed by the body's own bone-marrow-derived stem or precursor cells, we measured the number and function of specific stem cells in the blood that are known to contribute to vessel repair und formation of new blood vessels.

In our study, we were able to show that at an average of 12 years obese or overweight children suffer from pre-diabetes as indicated by much higher levels of insulin in oral glucose tolerance testing compared to lean healthy children. The concentration of "bad" LDL cholesterol was higher and that of "good" HDL cholesterol much less in obese children. In obese children 24 h-blood pressure monitoring indicates an about 8 to 10 mmHg higher systolic blood pressure over the day. Finally, nearly all components of metabolic syndrome are evident in our population of obese children.

The most result of our trial was that endothelium-dependent relaxation of forearm arteries is already impaired by the same in adults with chronic heart failure, and this in our 12-years old obese children! We found a clear relationship between the degree of obesity and the impairment of endothelial function: those with the highest body weight had the worst vessel function.

Also the extent of intima-media-thickness of carotid artery was increased, and this was again more pronounced in those with severe obesity.

These vascular alterations are accompanied by a significantly impaired release of stem and precursor cells from the bone marrow indicating that

self-healing capacity might be diminished.

Considering these disastrous alterations of arterial vessels and also the hampered repair mechanisms in obese children, it is not surprising that this vascular drama obligatory results in atherosclerosis followed by acute myocardial infarctions or strokes even in young adults.

Therefore, primary or secondary prevention strategies starting early in childhood should aim at reversing current increase in childhood obesity. A number of potential strategies can be implemented to target built environment, physical activity, and diet. These strategies can be initiated at home and in preschool institutions, schools or after-school care services as natural setting to influence diet and physical activity in the entire children population. However, further research needs to explore the most effective strategies to prevent and treat obesity.

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