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An intensive lifestyle intervention reduces circulating oxidised low-density lipoprotein and increases human paraoxonase activity in obese subjects

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Summary
Objective: Obesity has a great impact on cardiovascular morbidity and mortality, the treatment of this pathological state is important given the significant health consequences. Lifestyle and behaviour changes play a significant role in weight management. The purpose of this study was to investigate the impact of an intensive multidisciplinary lifestyle intervention on well-known atherogenic factors in a group of overweight and obese subjects.
Methods: A total of 44 people with overweight/obesity underwent a lifestyle intervention based on nutritional education, psychological support and a 3-month exercise training program with a frequency of twice a week. Several anthropometric and biochemical parameters were measured before and after the lifestyle intervention.

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Results: Lifestyle intervention led to a significant reduction in metabolic profile including body mass index (BMI), waist circumference, systolic and diastolic blood pressure, plasma glucose, and plasma triglycerides. These reductions were also accompanied by a significant increase in maximal oxygen consumption and muscle strength. Furthermore, paraoxonase and lactonase activities and the concentration of Apoliproteins A1 (APO A1) were significantly increased and the serum levels of oxLDL reduced without any changes in the circulating levels of LDL and HDL.
Conclusion: In conclusion, our study suggests that an intensive lifestyle intervention in obese subjects promotes a series of beneficial antiatherogenic changes which included increased enzyme activites of paraoxonase and lactonase, concentration of Apoliproteins A1 and decreased circulating levels of oxLDL.

Introduction

Obesity is now a global epidemic and a major risk factor for chronic diseases that can accelerate morbidity and mortality. Scientific guidelines recommend lifestyle change and regular physical activity as primary therapeutic tools for people with obesity [1]. Regular physical exercise in population with obesity is associated not just with weight loss, but also significant improvement in the cardiovascular risk factors [1]. Some recent cross-sectional and longitudinal studies have demonstrated a significant positive association between circulating levels of oxidised low-density lipoprotein (oxLDL) and the body mass index (BMI), waist circumference, obesity, weight loss, and physical fitness [2].

Obesity is a multifactorial disease that appears to be influenced by both genetic and environmental factors [3]. In recent years, evidence has emerged showing that oxidative damage of lipoproteins may be linked with obesity [4,5]. Altered oxidant/antioxidant status and higher susceptibility LDL to lipid peroxidation have been reported in obese patients [4—7]. Increased adipose tissue volume promotes the development of glucose metabolism disturbances and insulin resistance, the factors known to strongly correlate with the accelerated progression of atherosclerosis [8].

The paraoxonase (PON) enzyme family consists of 3 members, namely PON1, PON2 and PON3 that share common chromosome location, structural and calcium-dependent ester hydrolase activities tightly associated with apoA-1 in HDL [9—11]. Although, the exact physiological role of PON is still unclear, they have the potential to prevent and reverse LDL oxidation [9—11]. It is thought that the presence of PON on HDLs protects LDL from lipid peroxidation [12]. Mice lacking PON1 activity appear to be highly susceptible to atherosclerosis [13,14]. ApoA-I is the major apo in HDL particles and initiates the 'reverse cholesterol transport'. ApoA-I can 'pick up' excess cholesterol from peripheral cells and transfer it back to the liver in the HDL particles. ApoA-I also manifests anti-inflammatory and antioxidant effects [15].

The aim of this study was to investigate the impact of a multidisciplinary lifestyle intervention on a series of parameters that increase cardiovascular risk including BMI, waist circumference, blood pressure, plasma glucose, total cholesterol, LDL, HDL, APO A1 and plasma triglycerides, Our working hypothesis was that in obese subjects, lifestyle intervention potentially increases PON activity which in turn influences the circulating levels of oxLDL.

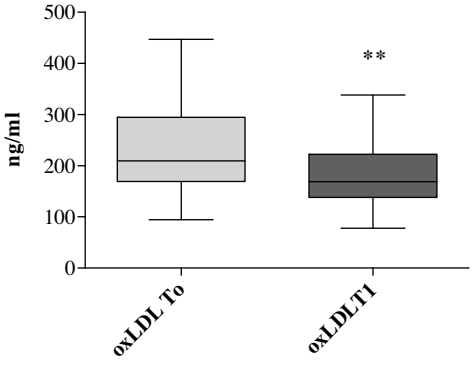

Fig. 1 Levels of oxLDL in obese subject. The serum levels of oxLDL were measured using a competitive sandwich ELISA; the assay was performed in triplicate, data represent the values are median (lower quartile-upper quartile). Statistical analysis was performed using Student's t test. Asterisks indicate statistical significance $P < 0.05$.

Subjects

The participants were a subgroup of a multidisciplinary lifestyle intervention program at the Lifestyle Institute of the University of Perugia (CURIAMO). The CURIAMO trial (registered in the Australian New Zealand Clinical Trials Registry, ACTRN12611000255987) has been approved by the local Ethics Committee (CEAS Umbria Region, HREC number 1/10/1633). Between January 2012 and June 2014, 24 males and 20 females with a mean age of 54 ± 2 years (mean $\pm$ SE), affected by overweight (n = 13, BMI 28.4 ± 0.3) or obesity (n = 31, BMI 41.5 ± 4.2) were enrolled. Overweight and obesity were defined using the national BMI reference tables for age and sex. Among the

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