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ORIGINAL ARTICLE

Relationships between changes in leptin and insulin resistance levels in obese individuals following weight loss

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Abstract Obesity can augment insulin resistance (IR), leading to increased risk of diabetes and heart disease. Leptin, ghrelin, and various fatty acids present in the cell membrane may modulate IR. In this study, we aimed to investigate the impact of weight loss on IR, serum leptin/ghrelin levels, and erythrocyte fatty acids, and studied the associations between changes in these variables. A total of 35 obese (body mass index $\geq$ 27) adults participated

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Weight control

in a weight loss program for 3 months. IR was assessed using homeostasis model assessment for insulin resistance (HOMA-IR). The obese participants had a mean weight loss of 5.6 ± 3.8 kg followed by a 16.7% and 23.3% reduction in HOMA-IR and leptin ($p < 0.001$) levels, and an 11.3% increase in ghrelin levels ($p = 0.005$). The level of erythrocyte saturates decreased by 2.8%, while the level of $n-3$ polyunsaturates increased by 16.8% (all $p < 0.05$). The changes in leptin levels (−5.63 vs. −1.57 ng/mL) were significantly different ($p = 0.004$) in those with improved IR (changes in HOMA-IR < 0) than those without improvement (changes in HOMA-IR ≥ 0), though there were no differences in the changes of ghrelin ($p = 0.120$) and erythrocyte fatty acids (all $p > 0.05$) levels. After adjusting for age, gender, changes in ghrelin, and body fat, we found a significant correlation between decreases in leptin and less risk of no improvement in HOMA-IR levels [odds ratio (OR) = 0.69, $p = 0.039$]. In conclusion, a moderate weight reduction in obese participants over a short period significantly improved IR. This weight reduction concomitantly decreased serum leptin, increased ghrelin, and elevated some erythrocyte unsaturates. Only leptin correlated independently with IR improvement upon multivariable logistic regression analysis, which indicates that leptin may play a role in the modulation of IR following weight loss.

Introduction

Obesity and its associated metabolic pathologies affect 30—50% of the adult population worldwide, depending on the area studied [1,2]. Increased consumption of energy-dense food induces obesity, which increases the risk of insulin resistance (IR), type 2 diabetes, coronary heart diseases, and cancer [3]. Results of various studies suggest that 5—10% weight loss can improve IR and other metabolic risk factors in both adults [4—6] and children [7].

Levels of leptin, an adipokine produced by the adipose tissue, are higher in obese adults than in lean ones [8], and this state is commonly referred to as leptin resistance. Leptin resistance occurs during the early stages of obesity and greatly influences the metabolism of muscle fatty acids and insulin sensitivity [9]. In contrast, circulating ghrelin level, a hormone produced by the stomach, is lower in obese individuals [10]. Altering the circulating levels of leptin and ghrelin influences appetite and energy balance in obese people, and they are involved in the development of IR and vascular damage [10—12].

The fatty acid compositions in the membrane phospholipids of insulin-targeted tissues play important roles in modulating insulin sensitivity [13,14]. Human and animal studies have reported positive correlations between long-chain polyunsaturates and insulin sensitivity [13—16]. However, obese adults and adolescents have decreased blood levels of longer-chain polyunsaturates (C20—C22), especially the $n-3$ series, but increased levels of saturates [15,16]. Diet supplementation with $n-3$ polyunsaturates is reported to improve several metabolic factors, including IR, in obese individuals [17].

Based on these findings, both circulating leptin and ghrelin as well as certain fatty acids may contribute to the development of IR [9,10]. To date, very few studies have investigated the effects of weight loss on changes in IR along with changes in blood leptin/ghrelin levels and fatty acid composition in obese individuals. This study investigated these relationships in obese individuals participating in a dietitian-led weight loss program, and further explored whether there might be an association between changes in leptin/ghrelin levels and the composition of erythrocyte fatty acids and improvement in IR following weight loss. Erythrocyte fatty acids, which were used as makers for dietary exposure, have also been considered as a valid proxy for fatty acid composition in the liver [15] and adipose tissues [16] in human and most animal tissues [18].

Materials and methods

Study population

Nondiabetic obese adults between 18 and 60 years of age with a body mass index (BMI) ≥ 27 ($n = 35$) were recruited from the community to participate in a dietitian-led weight-reduction program, in which the participants were counseled on how to reduce caloric intake following a low-fat diet. All individuals with diabetes or taking antidiabetic drugs or who had a history of cardiovascular or renal diseases, pregnancy, or lactation were excluded. This study was approved by the Human Ethics Committee of Kaohsiung Medical University. All participants provided informed consent.

Weight loss program

Obese participants were enrolled in a 12-week weight loss program. Counseling and group classes were provided by registered dietitians from a teaching hospital in southern Taiwan. All participants were generally in good health as evidenced by physical examination by physicians and biochemical indicators. During the 12-week period, participants met with dietitians every 1 or 2 weeks to receive group nutrition and weight-control counseling. The main dietary goal was to reduce calories and fat intake. The enrollees were introduced to the topics of obesity and health, the six major food groups, serving sizes, recognition of foods high in nutrient density, calculation of fat content, tips for light cooking, eating out, modifying holiday eating habits, and understanding food labels. The participants