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Mild weight loss reduces inflammatory cytokines, leukocyte count, and oxidative stress in overweight and moderately obese participants treated for 3 years with dietary modification

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ABSTRACT

Obesity-induced oxidative stress and inflammation are involved in the pathogenesis of cardiovascular disease. We investigated whether diet-induced, long-term, mild weight loss improved proinflammatory cytokine levels, leukocyte count, and oxidative stress. Overweight/obese participants (25 ≤ body mass index < 34 kg/m^2, N = 122, 30-59 years) joined a 3-year-long clinical intervention involving daily 100-kcal calorie deficits. *Successful weight loss* was defined as a reduction in initial body weight equal to 2 kg after the clinical intervention period. Body weight in the successful mild weight loss group (SWL, n = 50) changed 5.4% (–4.16 ± 0.31 kg) compared to 0.05 ± 0.14 kg in the unsuccessful weight loss group (n = 49). After 3 years, SWL participants exhibited significantly reduced insulin, triglycerides, total and low-density lipoprotein cholesterol, free fatty acids, and leukocyte count ($P = .030$). Furthermore, in the SWL group, serum interleukin (IL)-1β, IL-6, and urinary 8-epi-prostaglandin (PG)F$_{2\alpha}$ were significantly reduced (45%, 30%, and 14%, respectively). In contrast, the unsuccessful weight loss group exhibited significant increases in percentage of body fat, waist circumference, oxidized low-density lipoprotein, and tumor necrosis factor–α, as well as a significant decrease in high-density lipoprotein cholesterol. After adjusting for baseline values, the 2 groups demonstrated significantly different percentage of body fat, waist circumference, leukocyte count ($P = .018$), insulin, IL-6 ($P = .031$), IL-1β ($P < .001$), and tumor necrosis factor–α ($P < .001$), as well as urinary 8-epi-PGF$_{2\alpha}$ ($P = .036$). A positive correlation existed between IL-1β and urinary 8-epi-PGF$_{2\alpha}$ ($r = 0.435$, $P < .001$) and between changes in IL-6 and urinary 8-epi-PGF$_{2\alpha}$ ($r = 0.393$, $P < .001$). Long-term mild weight loss reduces inflammatory cytokine levels, leukocyte counts, and oxidative stress and may

Abbreviations: BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; FFA, free fatty acids; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; hs-CRP, high-sensitivity C-reactive protein; IL, interleukin; LDL, low-density lipoprotein; ox, oxidized; PG, prostaglandin; SE, standard error; SWL, successful mild weight loss; TNF, tumor necrosis factor; UWL, unsuccessful weight loss; WBC, white blood cell.

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reverse the elevated oxidative stress induced by inflammatory mediators in the overweight and obese.

1. Introduction

The prevalence of overweight and obese individuals has escalated dramatically over recent decades. Several lines of evidence indicate that obesity constitutes a low-grade inflammatory state [1] and leads to oxidative stress [2]. Oxidative stress and inflammation develop progressively as body mass index (BMI) and abdominal fat increase. In addition, it is well known that obesity-induced oxidative stress and inflammation are involved in the pathogenesis of cardiovascular disease (CVD) [2,3].

Dietary treatment has always been considered integral to weight reduction therapy. Numerous studies have reported that lifestyle modifications involving a calorie reduction diet can lead to weight loss and concomitant improvement in many of the metabolic complications often associated with obesity, including insulin resistance [4-6]. A very low calorie diet, less than 800 kcal/d, is an effective way to lose weight quickly. However, the dropout rates from such interventions are often very high [7]. When taking into consideration the safety and effectiveness of weight loss, a low-calorie diet could be sustainable for dietary interventions. Several studies have reported that a short-term low-calorie diet intervention improved the metabolic syndrome profile but not the vascular dysfunction associated with obesity in healthy overweight or obese adults [8,9]. However, data are scarce with respect to the effects of long-term mild weight loss on proinflammatory cytokines, oxidative stress, and leukocyte count, which is an inexpensive and reliable marker of inflammation, in overweight and obese participants treated with dietary modification.

To investigate whether diet-induced, long-term, mild weight loss improves the inexpensive and reliable marker of inflammation in overweight and obese participants, we tested the hypothesis that a 3-year period of clinical intervention involving dietary modifications with an individualized calorie-restricted diet (approximately 100-kcal/d negative calorie balance) decreases circulating levels of inflammatory cytokines, leukocyte count, and oxidative stress associated with cardiovascular events in overweight and obese participants. We also tested the relationship between changes in these variables before and after dietary modification.

2. Methods and materials

2.1. Study participants

One hundred twenty-two overweight or obese participants (25 $\leq$ BMI < 34 kg/m^2) aged 30 to 59 years were recruited at the health promotion center of the National Health Insurance Corporation Ilsan Hospital in Korea between August 2006 and August 2007. Participants were sedentary and had not participated in weight reduction programs within the previous 3 years. Participants also completed a personal health and medical history questionnaire, which served as a screening tool. Exclusion criteria were type 2 diabetes, CVD, psychiatric problems, and/or use of any medications (antihypertensive, lipid lowering, antiplatelets, antidiabetic, etc). The participants were enrolled by recommendation or volunteered to participate in this study. The paper-based informed consent forms, stored in a document system after obtaining the necessary signatures, were used to record the intent and identify the will to join in the research. The Institutional Review Board of the National Health Insurance Corporation Ilsan Hospital approved the study protocol, which was conducted in accordance with the Helsinki Declaration.

2.2. Weight reduction protocol and calorie intake

The study duration was 3 years, and the program goal was to achieve a weight loss of approximately 5% of initial body weight. During the study period, the diets of the participants were mildly calorie restricted, with an approximate 100-kcal/d calorie deficit. The typical baseline dietary intake of each participant was assessed using a semiquantitative food frequency questionnaire and 24-hour recall method. Based on the reported intake of each participant, individualized and nutritionally balanced diets were planned. There were 4 trained dietitians who instructed about 30 participants each. The instructions included changes in food choice, cooking methods, reduction in frequency of snack consumption, exchange of high-calorie foods with low-calorie ones, low-fat foods, and limitation of simple sugar consumption. The contents of the instructions were slightly different depending on dietitians and each participant; but the fundamental policy was identical, and so there was no statistical difference in outcomes between dietitians. To evaluate and reinforce compliance during the intervention period, the dietitians interviewed participants bimonthly via telephone; and participants were asked to report 3-day food records (2 weekdays and 1 weekend day) at each visit. Dietary energy values and nutrient contents from the 3-day food records were calculated using the Computer Aided Nutritional Analysis Program (CAN-pro 2.0; Korean Nutrition Society, Seoul, Korea). Total energy expenditure (in kilocalories per day) was calculated from activity patterns of each participant by the paper-based questionnaires (basal metabolic rate, 24-hour physical activity, and specific dynamic action of food). Successful weight loss was defined as a reduction in initial body weight of at least 2 kg at the end of the 3-year clinical intervention period.

2.3. Anthropometric parameters, blood pressure, and blood collection

Body weights and heights of participants who were unclothed and without shoes were measured in the morning. BMI (kilograms per square meter) was calculated from body height and weight. Percentage of body fat was analyzed by a TBF-105