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Association of Changes in Body Composition with Changes in Systemic Oxidative Stress Following Weight Loss Program in Obese Adults Attending Obesity Clinic, Hospital Universiti Sains Malaysia

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Abstract: The main objective of the present study was to evaluate the association of changes in body composition with changes in systemic oxidative stress markers among obese adults participating in a weight loss program. Thirty four obese adults were recruited from the Obesity Clinic, Hospital Universiti Sains Malaysia (USM) to voluntarily participate in a weight loss program comprising of physical exercise and dietary modification. Levels/activities of oxidative stress markers were measured before and after the program. Mean body weight, body mass index (BMI), waist circumference (WC), hip circumference (HC) and percentage of body fat mass decreased significantly while mean body lean mass and body water increased significantly after the weight loss program. Plasma glutathione peroxidase (GPx) activity and 4-hydroxynonenal (4-HNE) concentration increased significantly while other enzymatic antioxidant activities such as catalase (CAT) and superoxide dismutase (SOD) were not significantly increased. The ratio of reduced glutathione (GSH) to oxidized glutathione (GSSG) was significantly decreased. There was no significant association between changes in body composition and changes in systemic oxidative stress markers among obese adults. In conclusion, changes in body composition were not associated with changes in systemic oxidative stress markers among obese adults.

Keywords: Body composition, dietary, exercise, obesity, oxidative stress, weight loss program.

INTRODUCTION

Obesity has been associated with inadequate tissue antioxidants such as superoxide dismutase (SOD) and glutathione peroxidase (GPx) [1-2], increased inflammatory cytokines such as interleukin 1 (IL-1), IL-6, tumour necrosis factor α (TNF-α) and C-reactive protein (CRP) [3-6], elevated plasma cholesterol and triglycerides [7], excessive renin-angiotensin system hormones [8], and insulin insensitivity [9]. The combination of these systemic changes associated with obesity, together with inadequate exercise and/or poor dietary antioxidant intake over a period of years, are likely to exacerbate oxidative stress and hasten the clinical manifestation of obesity-related diseases such as cardiovascular disease, diabetes mellitus, hypertension and arthritis [10-13].

Lifestyle factors which have a major impact on the whole organism oxidative stress response include impaired nutrition, reduced physical activity, alcohol consumption, and cigarette smoking. If the lifestyle factors persist for a lengthy duration of the individual's life, they may become major contributors to the failure of systemic homeostasis. Physical activity and diet, in particular, have been suggested to seriously influence the oxidative stress response in humans, tipping the balance of oxidative burden/antioxidant response to one side or the other [14].

The effects of exercise on oxidative stress may be beneficial or detrimental to physiological function depending on several factors. The potential detrimental effects of reactive oxygen and nitrogen free radicals (RONS) include impairing exercise performance by altering contractile function and/or accelerating muscle damage/fatigue secondary to oxidation of contractile fibers and/or mitochondrial enzymes [15-17]. The low grade oxidative stress appears necessary for various physiological adaptations [18-20]. An earlier study reported that eight weeks of moderate intensity exercise program did not increase the oxidative stress in older adults [21]. Such repeated exposure of the body system to increased RONS production from chronic exercise training leads to an upregulation in the body's antioxidant defense system [22] and an associated shift in redox balance in favor of a more reducing level, thus providing adaptive protection from RONS during subsequent training sessions, as well as when exposed to non-exercise related conditions such as disease state.

Epidemiological studies suggest that diet can influence oxidative damage positively and negatively [23]. Hence, changes in dietary composition could be a useful strategy in

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the prevention of obesity-related diseases. Evidence shows that dietary composition can influence oxidative stress *in vivo*; this effect is clear for monounsaturated fatty acids (MUFA) [24-27], fruits and vegetables [24, 28], which improve oxidative stress; and for saturated fatty acids (SFA) [24-27] and alcoholic beverages [29-30], which worsen oxidative status.

We have earlier reported that plasma GPx activity and 4-hydroxynonenal (4-HNE) level increased significantly, while the ratio of reduced glutathione to oxidized glutathione (GSH:GSSG) decreased significantly following a 12-week weight loss program. Other enzymatic antioxidant activities such as catalase (CAT) and SOD were not significantly changed. Changes in plasma GPx activity were negatively correlated with changes in serum triglyceride (TG) and VLDL-cholesterol concentrations [31]. Therefore, we hypothesized that changes in body composition among obese adults are associated with changes in systemic oxidative stress levels/activities and the present study aimed to evaluate this association.

MATERIALS AND METHODOLOGY

Study Subjects

A total of 34 Malay subjects aged between 18-62 years old (4 males) were recruited from the Obesity Clinic, Hospital Universiti Sains Malaysia (USM) to voluntarily participate in a weight loss program comprising of physical exercise and dietary modification. Subjects were obese with a body mass index (BMI) of more than 30 kg/m^2. Potential subjects were excluded if they were pregnant or had intention to get pregnant during the intervention period, had enrolled within the past three months in a formal weight reduction program or clinical trial, or had uncontrolled hypertension, diabetes, or other serious illnesses during the previous six months. The research protocol was approved by the Research and Ethics Committee of USM.

Weight Loss Program

The potential risks and benefits of the program were explained to every subject before obtaining written consent. A complete medical history was taken and physical examination was performed to determine the health status and physical fitness of each subject. The subject was then instructed to record his/her daily food intake and physical exercise in a diary throughout the study period.

The weight loss program involved weekly physical exercise and dietary modification under supervision for 12 weeks. The subjects were instructed to attend a weekly exercise program consisting of brisk walking for 2-4 km (approximately 1 hour), 30 minutes aerobic exercise and 30 minutes dumbbell (4 kg) resistance exercise. They were also instructed to perform daily moderate intensity physical exercise such as brisk walking at home. At home, the duration and frequency of their physical exercise were gradually increased from 10 to 60 minutes each session and from 3 to 5 days per week respectively.

Weekly dietary assessments included discussion on nutrition education module and food diary with a nutritionist. The subjects were advised to modify their type and/or amount of usual food intake when their dietary intake was either insufficient or exceeded the normal energy requirement. If the subject's weekly target weight loss was unachieved, they were instructed to discuss the strategies to achieve the weight loss target for the next visit in a small group discussion.

Measurement of Body Composition

Body weight and height were measured using Seca 767/220 (SECA, Hamburg, Deutcshland). BMI was calculated as body weight in kilograms divided by height in meters squared. Body fat, water and impedens were measured using Bodystat 1500 (Bodystat, Isle of Man, British Isles). Measurements were taken in the fasted state.

Determination of Systemic Oxidative Stress Markers

Blood specimen was collected after an overnight fast before and after the weight loss program. Blood was processed to serum and plasma according to standard procedures. Blood samples were stored frozen at -80 ℃ until assayed. Plasma CAT, plasma GPx and serum SOD activities, blood GSH:GSSG (Calbiochem, EMD Biosciences, Inc), and plasma 4-HNE (OxiSelect, Cell Biolabs, Inc) concentrations were determined using commercially available ELISA kits according to the manufacturer’s instruction. Total protein was determined using a commercially available protein assay (Bio-Rad Laboratories, Inc.).

Statistical Analysis

The results were analyzed using PASW Statistics version 18 software. Paired *t* test was used to compare the mean difference in body composition values and blood oxidative stress levels/activities before and after the weight loss program. The Pearson correlation analysis was utilized to examine the association between changes in body composition and changes in blood oxidative stress levels/activities. A $P < 0.05$ was considered statistically significant.

RESULTS

The body weight, BMI, waist circumference (WC), hip circumference (HC) and percentage of body fat mass decreased significantly after the weight loss program while the mean body lean mass and body water were significantly increased as shown in Table **1**.

Plasma GPx activity and 4-HNE concentration were significantly increased after the weight loss program. Blood GSH/GSSG ratio was significantly reduced but other antioxidant enzymes were not significantly increased as shown in Fig. (**1**). There was no significant correlation between changes in body composition and changes in systemic oxidative stress levels/activities.

Table 1. Measurement of body composition.

Variables	Before	After	%Δ
Weight (kg)#	86.65 ± 22.38	80.75 ± 23.05*	-7.32
BMI (kg/m^2)#	34.90 ± 5.15	32.80 ± 3.69*	-7.18
Body fat mass (%)	43.17 ± 6.81	40.51 ± 6.89*	-6.16
WC (cm)	102.56 ± 13.38	95.88 ± 11.88*	-6.50
HC (cm)	116.00 ± 10.85	109.96 ± 9.37*	-5.21
Body lean mass (%)	56.83 ± 6.81	59.49 ± 6.89*	4.68
Body water (%) #	42.65 ± 6.23	44.25 ± 6.47*	4.49

Values are expressed as mean ± SD, #median ± interquartile range
***P** < 0.05, significant differences before and after weight loss program

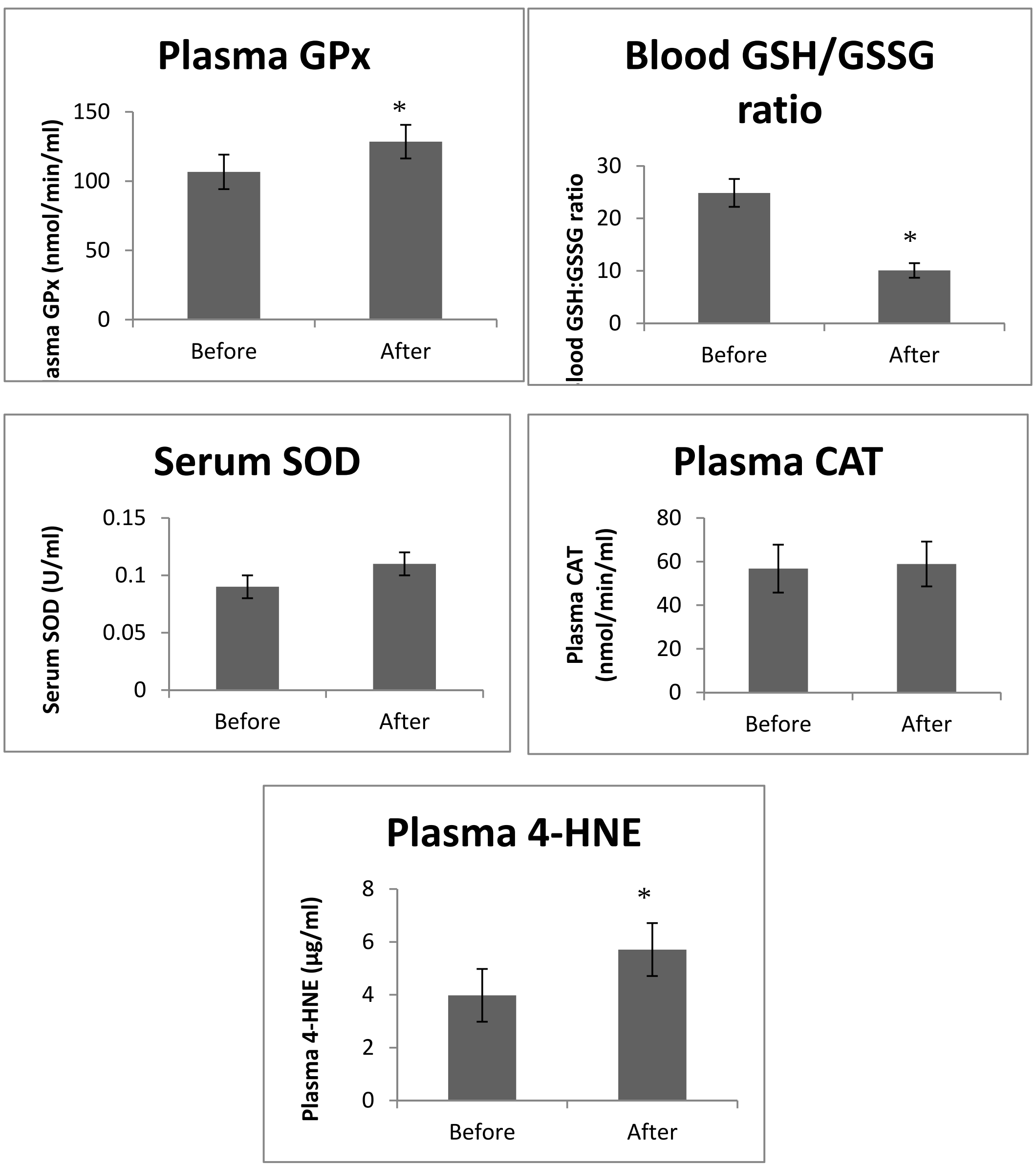

Fig. (1). Level/activity of blood oxidative stress markers before and after weight loss program.

***P** < 0.05, significant difference before and after weight loss program.

DISCUSSION

In humans, redox balance is generally evaluated by measuring markers of antioxidant defense and/or oxidative stress. However, most of the previous studies examined the effect of weight loss program on the oxidative damage such as malondialdehyde (MDA), oxidized low density lipoprotein (ox-LDL), thiobarbituric reactive acid substances (TBARS), protein carbonyl, 8-hydroxy-2'-deoxyguanosine (8-OhDG) and 8-epi-prostaglandin $F_{2\alpha}$ (8-epi-$PGF_{2\alpha}$) levels [32-35]. Only a few studies measured levels/activities of antioxidant enzymes such as SOD, GPx and CAT or 4-HNE and F_2-isoprostanes for lipid oxidative damage marker.

The present study demonstrated that GPx levels were increased significantly following a weight loss program in obese adults but not other antioxidant enzymes. However, it was not clear whether physical exercise or dietary modification or both had contributed to the increased antioxidant defense and further studies are required to confirm this finding. GPx levels were also shown to increase following intervention in different groups of subjects [36-39]. In contrast, Daud *et al.* [40] demonstrated reduced GPx levels following different exercise intensity and no favorable changes in the levels of SOD, CAT and total anti-oxidative capacity were recorded following a 16-week internet-delivered lifestyle physical activity intervention in overweight adults [41].

The GSH:GSSG assay was utilized to determine the oxidative stress status among subjects following the interventions. The GSH:GSSG ratio was reduced and reflected an increase in oxidative stress following the weight loss program. The result was further confirmed by increased oxidative damage to lipid as shown by increased plasma 4-HNE levels after intervention. Increased oxidative stress in the present study possibly serves as an essential "signal" for upregulating antioxidant defenses, thus providing protection against subsequent exposure to free radical environments in obese adults. The increased oxidative stress could be induced by the obese state [42], physical exercise [43-44] or dietary modification or any combinations of these. Further studies should consider separating physical exercise, dietary modification and a combination of both into different groups and using objective physical exercise and dietary assessments.

Previous studies demonstrated that BMI, total body fat, and WC positively correlated with urinary F2-isoprostane level and inversely correlated with paraoxonase 1 (PON 1) activity [45-47] in adults. F2-isoprostane level has been shown to predict total adiposity loss over time. A strong significant inverse association between urinary F2-isoprostanes and weight gain was demonstrated by both the Insulin Resistance Atherosclerosis Study (299 participants) [48] and the Health, Aging, and Body Composition Study (726 participants) [49] during a five-year follow-up period. This inverse association has been interpreted as a positive physiological response to address excess adiposity and/or a catabolic response to inflammation. In other studies, diet-induced obesity increases cerebrocortical oxidative stress [50] and high fat diet-induced obesity also correlates with mitochondrial dysfunction and increases oxidative stress in skeletal muscle and liver of mice [51]. A recent study found SOD to be significantly and positively associated with BMI with the Pearson rank correlation: $r = 0.3$ ($P = 0.04$) and $r = 0.15$ ($P = 0.036$) respectively for boys and girls [52]. Despite the strong association between obesity and oxidative stress, none of the changes in body composition significantly correlated with the changes in systemic oxidative stress levels/activities in the present study. This could again be explained by the small sample size and further studies with a larger sample size are needed to confirm these findings.

In conclusion, our weight loss program successfully improved abnormal body composition and increased antioxidant levels. However, there was no significant association between the changes in body composition and the changes in systemic oxidative stress markers.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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