THE EFFECT OF WEIGHT LOSS ON PLASMA MDA, LIPIDS PROFILE AND APOA AND APOB IN OBESE WOMAN

Fatemeh Ramezani[(1)], Ali Keshavarz[(2)], Mahmud Jalali[(3)], Mohamadreza Eshraghian[(4)], Maryam Chameri [(5)]

Abstract

INTRODUCTION: Obesity increased reactive oxygen species generation that it result in oxidative injury on lipids profile and lipoproteins that all of which insert atherosclerotic effect. Nutritional intervention by means of a hypocaloric diet could produce protective effects against the redox unbalance. In this context, the aim of this intervention trial was to estimate the ability of weight loss to improve oxidative stress biomarkers related to lipids peroxidation and lipid profile and apoproteins concentrations of serum in obese women.

METHODS: Thirties eight obese women, 15-45 years old, with body mass index (BMI <30 kg/m^2 were recruited. The obese women were assigned to energy-restricted dietary treatments for 12 week. Before and after nutritional intervention and 10% weight reduction, anthropometric measurements were taken and fasting blood was drawn. Plasma levels of (MDA) determined with TBAR and triglyceride, total cholesterol and HDL cholesterol.

Keywords: MDA, lipid profile, obese woman, Weight loss.

***ARYA Atherosclerosis Journal* 2008, 4(2): 77-81**

Date of submission: 29 Feb Sep 2008, ***Date of acceptance:*** 2 Apr 2008

Introduction

Obesity has developed globally, with more than 1 billion adults overweight that at least 300 million of them clinically obese.[1] Obese individual has the life expectancy shorter than that of a normal weight individual about 7 years.[2] In women, the risk of nonfatal and fatal myocardial infarction is increased by 42% with body mass index (BMI) > 25.[3] Obesity is linked with an increase in a number of health risks including coronary heart disease, diabetes, hypertension, gall bladder disease and certain types of cancer.[4] Previous studies have shown that circulating MDA levels are higher in obese subjects than in non-obese healthy controls.[5] This is likely be related to a number of metabolic impairments and accompanied by oxidative stress disturbances.[6-8] Increased reactive oxygen species generation in the obese woman may result in oxidative injury on cell lipids and proteins.[9,10] Native low-density lipoprotein (LDL) cholesterol is damaged by oxidative species originated by monocytes/macrophages at the endothelium.[11] Thus, reactive oxygen species accelerate lipid peroxidation, leading to cardiovascular disease by oxidative stress stimulation.[7]

Hypocaloric diet in a nutritional intervention could produce protective effects against the redox unbalance.[12]

This protective effect against cardiovascular disease could be related to a decrease in susceptibility of LDL oxidation[13,14] or stimulation of other antioxidative processes.[15]

In this context, the aim of this intervention trial was to estimate the ability of weight loss to improve oxidative stress biomarkers related to lipid peroxidation and lipid profile and apoA and apoB concentrations in healthy obese women.

Materials and Methods

Subjects

38 obese women, more than 15 years old, with body mass index (BMI) > 30 kg/m^2 who referred to the diet therapy clinic between 2005-2007 was recruited.

1) MSc. Department of Nutrition and Biochemistry, School of Health, Tehran University of Medical Sciences, Tehran, Iran.
E-mail: ramezani_71@yahoo.com
2) PhD. Professor of Nutrition, Department of Nutrition and Biochemistry, School of Health, Tehran University of Medical Sciences, Tehran, Iran
3) PhD. Professor of Biochemistry, Department of Nutrition and Biochemistry, School of Health, Tehran University of Medical Sciences, Tehran, Iran.
4) PhD. Associate Professor. Department of Biostatistic, School of Health, Tehran University of Medical Sciences, Tehran, Iran
5) MSc. Department of Nutrition and Biochemistry, School of Health, Tehran University of Medical Sciences, Tehran, Iran

Corresponding author: *Fatemeh Ramezani*

All the participants were in apparent good health as determined by medical history, physical examination, and routine biochemical and hematological laboratory tests. Women who were pregnant, lactating or who wished to become pregnant were also excluded. The enrolled women fulfilled the following inclusion criteria: 1. they were premenopausal; 2. they had no history of diabetes mellitus, high blood pressure, or dyslipidemia; 3. they did not smoke; 4. they had not been alcoholic; and 5. they had not taken supplemental vitamin or minerals and regular prescription of medications in the last 3 month.

Study design

The trial was a nutritional intervention controlled by trained dietitians. The obese women were assigned to energy-restricted dietary treatments for 12 week. The hypo caloric diets were designed to produce an energy restriction of 500 - 1000 kcal/d from the individual requirement energy. Compliance to energy and nutrient intakes were assessed by 3-d food records and calculating nutrient composition with the Medisystem nutritional database (Food Procosser ÍÍ). Before and after nutritional intervention, anthropometric measurements were taken and fasting blood was drawn. Body weight and triceps skin fold thickness (TSF) of each subject was measured in the morning on the first and ninetieth of study under overnight-fasting conditions

Blood sampling and laboratory analyses

Blood samples were obtained by veni-puncture after an 8–14 h overnight fast. Blood samples were drawn on the morning of those days that subjects had their body weight and body composition measured. Plasma levels of triglyceride, total cholesterol were colorimetrically and enzymatically and high-density lipoprotein (HDL) cholesterol and LDL cholesterol was assayed enzymatically by specific commercial assays. malondialdehyde (MDA) was colorimetrically determined with TBAR.[16]

Statistical analysis

Data are expressed as means ± standard deviation. Student's paired t-test was applied to determine the significance of the changes within treatment .Pearson's correlation analysis was applied to determine the significance of correlation between two variables. A probability level of 0.05 was designated as the level of statistical significance.Statistical analysis was performed with SPSS-11.5.

Results

Thirties eight obese women with a mean age of 33.1 ± 8.3 year and a mean body mass index of 36.5 ± 4.8 kg/m² were recruited. Changes in body weight, BMI, TSF, and total cholesterol, LDL-C, HDL-C, and total TG, apoA, and apoB concentrations as a result of weight reduction are summarized in table 1.

Table 1. Effects of a calorie-restricted nutritional treatment on anthropometric and metabolic variables.

Biological parameters	Day 0	Day 90	*P Value*
Body weight (kg)	91.7 ± 2.1	82.7 ± 2	< 0.001
Body mass index (kg/m^2)	36.49 ± .78	32.89 ± 0.73	< 0.001
TSF (mm)	4.36 ± 0.12	3.72 ± 0.16	< 0.001
Total cholesterol (mg/dl)	185.47 ± 7.55	186.27 ± 5.98	0.937
Triglyceride (mg/dl)	156.28 ± 10.75	115.86 ± 5.91	< 0.001
ApoA (mg/dl)	136.94 ± 5.71	124.42± 2.96	0.022
AopB (mg/dl)	98.71 ± 3.77	89.28 ± 2.55	0.002

All volunteers lost body weight, as induced by the energy restriction, which was accompanied by marked decreases ($P < 0.001$) in body mass index and TSF (Table 1).

The mean weight loss was 9 ± 2.6 Kg. During weight reduction, the concentration of total cholesterol did not change. But, triglyceride (156.28 ± 10.75 vs. 115.86 ± 0.5.91 mg/dl; $P < 0.001$) apoA (136.94 ± 5.71 vs. 89.28 ± 2.55; P = 0.022) apoB (98.71 ± 3.77 vs. 89.28 ± 2.55; P =0.002) concentrations significantly decreased at the endpoint in relation to baseline.

Weight reduction induced by nutritional intervention was associated with a decrease in MDA circulating levels, which reach statistical significance (5.42 ± 0.29 vs. 2.82 ± 0.37; P < 0.001) (Table 2).

Table 2. Oxidative state and LDL cholesterol response to calorie-restricted intervention by hypocaloric diets

Oxidative biomarkers	Day 0	Day 90	P Value
MDA (nmol/l)	5.42 ± 0.29	2.82 ± 0.37	< 0.001
LDL cholesterol (mg/dl)	106.87 ± 8.67	138.45 ± 5.9	0.348
HDL cholesterol (mg/dl)	40.64 ± 2.76	47.34 ± 2.87	< 0.001

Circulating levels of LDL cholesterol did not change (P = 0.008) but HDL-C level significantly increased (P < 0.001) during weight reduction (Table 2).

Discussion

Obesity and associated morbidities such as cardiovascular diseases have been related to low-grade inflammation, which could benefit from weight reduction and ant oxidative control.[6] Lipid per oxidation appears to be involved in oxidative modifications of LDL that yield the formation of atherosclerotic injury.[17,18] In this study, this was designed to evaluate whether weight reduction could specifically contribute to the MDA decrease as an indicator of oxidative changes and changes in lipid profile. In this study MDA concentration significantly decreased during weight reduction. Malondialdehyde (MDA) has been proposed as an indicator of lipid per oxidation because this molecule is one of the end products of this oxidative process.[19] Malondialdehyde (MDA), the main component of plasms TBARS, originates from several sources: 1. peroxidation of plasma lipids, 2. blood platelets, 3. peroxidation of lipid endotlial and other cells.[20] Therefore the mechanism of increased TBARS in obesity may multifactorial. LDL oxidation is associated with atherogenesis.[18] Previous studies have shown that circulating MDA levels are decreased in obese subjects than in non-obese healthy controls.[10] Moreover, a decrease in this lipid per oxidation marker has been related to weight loss.[21]

High calories diet may stimulate mitochondrial oxidative metabolism and increase leakage of electrons from mitochondrial respiratory chain.[22] Apolipoprotein (apo)A-IV is an anti atherogenic apolipoprotein, which may be involved in the regulation of food intake. Plasma apoA-IV is elevated in human obesity and apoA-IV polymorphisms have been associated with the extent of obesity Plasma apoA-IV decreases markedly in overweight adolescents undergoing weight reduction.[23] ApoB is the predominant apolipoprotein in LDL and is required for the secretion of VLDL. Both of these lipoproteins have been associated with increased risk for heart disease.[24] In this study, restricted energy diet result of decrease of apoA, apoB concentration statistically. The reduction in apoB and apoA concentrations observed in obese postmenopausal women in the present study could be related to decreased production of apoB during weight loss progresses. Most studies that have shown a relationship between modest weight loss and improvement in lipid parameters.[25,26] Studies indicate that changes in cholesterol turnover after weight loss were negatively predicted by changes in visceral adipose tissue in hyperlipidemic overweight and obese women. Weight loss resulted in favorable changes in plasma cholesterol concentrations suggesting an amelioration of CVD risk.[26] But in this study, there was statistically no change in total cholesterol and LDL-C in women whose mean total cholesterol concentration were (P = 0.348).Also there was decrease of TG and increase of HDL-C concentrations in this study during weight reduction t. The outcome of this nutritional trial shows that restricted diet, as well as weight reduction is seemed to be effective in decreasing oxidative stress, production of apoA and apoB and TG. These may increase cardiovascular risk factors related to obesity.

References

1. Allison DB, Zannolli R, Faith MS, Heo M, Pietrobelli A, VanItallie TB, et al. Weight loss increases and fat loss decreases all-cause mortality rate: results from two independent cohort studies. Int J Obes Relat Metab Disord 1999; 23(6): 603-11.
2. Peeters A, Barendregt JJ, Willekens F, Mackenbach JP, Al Mamun A, Bonneux L. Obesity in adulthood and its consequences for life expectancy: a life-table analysis. Ann Intern Med 2003; 138(1): 24-32.
3. Willett WC, Manson JE, Stampfer MJ, Colditz GA, Rosner B, Speizer FE, et al. Weight, weight change, and coronary heart disease in women. Risk within the 'normal' weight range. JAMA 1995; 273(6): 461-5.
4. Aljada A, Mohanty P, Ghanim H, Abdo T, Tripathy D, Chaudhuri A, et al. Increase in intranuclear nuclear factor kappaB and decrease in inhibitor kappaB in mononuclear cells after a mixed meal: evidence for a proinflammatory effect. Am J Clin Nutr 2004; 79(4): 682-90.
5. Prazny M, Skrha J, Hilgertova J. Plasma malondialdehyde and obesity: is there a relationship? Clin Chem Lab Med 1999; 37(11-12): 1129-30.
6. Moreno-Aliaga MJ, Campión J, Milagro FI, Berjón A, Martínez JA. Adiposity and Proinflammatory state the chicken or the egg. Adipocytes 2005; 1: 1–16.
7. Higdon JV, Frei B. Obesity and oxidative stress: a direct link to CVD? Arterioscler Thromb Vasc Biol 2003; 23(3): 365-7.
8. Auer J, Weber T, Berent R, Lassnig E, Maurer E, Lamm G, et al. Obesity, body fat and coronary atherosclerosis. Int J Cardiol 2005; 98(2): 227-35.
9. Furukawa S, Fujita T, Shimabukuro M, Iwaki M, Yamada Y, Nakajima Y, et al. Increased oxidative stress in obesity and its impact on metabolic syndrome. J Clin Invest 2004; 114(12): 1752-61.
10. Dandona P, Mohanty P, Ghanim H, Aljada A, Browne R, Hamouda W, et al. The suppressive effect of dietary restriction and weight loss in the obese on the generation of reactive oxygen species by leukocytes, lipid peroxidation, and protein carbonylation. J Clin Endocrinol Metab 2001; 86(1): 355-62.
11. Fan J, Watanabe T. Inflammatory reactions in the pathogenesis of atherosclerosis. J Atheroscler Thromb 2003; 10(2): 63-71.

12. Parra MD, Martinez de Morentin BE, Martinez JA. Postprandial insulin response and mitochondrial oxidation in obese men nutritionally treated to lose weight. Eur J Clin Nutr 2005; 59(3): 334-40.

13. Stocker R, Keaney JF, Jr. Role of oxidative modifications in atherosclerosis. Physiol Rev 2004; 84(4): 1381-478.

14. Yeomans VC, Linseisen J, Wolfram G. Interactive effects of polyphenols, tocopherol and ascorbic acid on the Cu2+-mediated oxidative modification of human low density lipoproteins. Eur J Nutr 2005; 44(7): 422-8.

15. Tapiero H, Townsend DM, Tew KD. The role of carotenoids in the prevention of human pathologies. Biomed Pharmacother 2004; 58(2): 100-10.

16. Ohkawa H, Ohishi N, Yagi K. Reaction of linoleic acid hydroperoxide with thiobarbituric acid. J Lipid Res 1978; 19(8): 1053-7.

17. Witztum JL. The oxidation hypothesis of atherosclerosis. Lancet 1994; 344(8925): 793-5.

18. Steinberg D. Lewis A. Conner Memorial Lecture. Oxidative modification of LDL and atherogenesis. Circulation 1997; 95(4): 1062-71.

19. Nielsen F, Mikkelsen BB, Nielsen JB, Andersen HR, Grandjean P. Plasma malondialdehyde as biomarker for oxidative stress: reference interval and effects of life-style factors. Clin Chem 1997; 43(7): 1209-14.

20. Frankel EN, Neff WE. Formation of malonaldehyde from lipid oxidation products [Lipid oxidation, malonaldehyde synthesis, thiobarbituric acid]. Elsevier Biomedical Press 1983; 754 (3): 264-70.

21. Yesilbursa D, Serdar Z, Serdar A, Sarac M, Coskun S, Jale C. Lipid peroxides in obese patients and effects of weight loss with orlistat on lipid peroxides levels. Int J Obes (Lond) 2005;29(1): 142-5.

22. Bakker SJ, IJzerman RG, Teerlink T, Westerhoff HV, Gans RO, Heine RJ. Cytosolic triglycerides and oxidative stress in central obesity: the missing link between excessive atherosclerosis, endothelial dysfunction, and beta-cell failure? Atherosclerosis 2000; 148(1): 17-21.

23. Lingenhel A, Eder C, Zwiauer K, Stangl H, Kronenberg F, Patsch W, et al. Decrease of plasma apolipoprotein A-IV during weight reduction in obese adolescents on a low fat diet. Int J Obes Relat Metab Disord 2004; 28(11): 1509-13.

24. Vega GL, Denke MA, Grundy SM. Metabolic basis of primary hypercholesterolemia. Circulation 1991; 84(1): 118-28.

25. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972; 18(6): 499-502.

26. Santosa S, Demonty I, Lichtenstein AH, Jones PJ. Cholesterol metabolism and body composition in women: the effects of moderate weight loss. Int J Obes (Lond) 2007; 31(6): 933-41.

27. Ditschuneit HH, Frier HI, Flechtner-Mors M. Lipoprotein responses to weight loss and weight maintenance in high-risk obese subjects. Eur J Clin Nutr 2002; 56(3): 264-70.

28. Erciyas F, Taneli F, Arslan B, Uslu Y. Glycemic control, oxidative stress, and lipid profile in children with type 1 diabetes mellitus. Arch Med Res 2004; 35(2): 134-40.

29. Kondo A, Muranaka Y, Ohta I, Notsu K, Manabe M, Kotani K, et al. Relationship between triglyceride concentrations and LDL size evaluated by malondialdehyde-modified LDL. Clin Chem 2001; 47(5): 893-900.

30. Tsai AC, Sandretto A, Chung YC. Dieting is more effective in reducing weight but exercise is more effective in reducing fat during the early phase of a weight-reducing program in healthy humans. J Nutr Biochem 2003; 14(9): 541-9.

31. Olshansky SJ, Passaro DJ, Hershow RC, Layden J, Carnes BA, Brody J, et al. A potential decline in life expectancy in the United States in the 21st century. N Engl J Med 2005; 352(11): 1138-45.

32. Pi-Sunyer FX. The epidemiology of central fat distribution in relation to disease. Nutr Rev 2004; 62(7 Pt 2): S120-S126.

33. Wing RR, Jeffery RW. Effect of modest weight loss on changes in cardiovascular risk factors: are there differences between men and women or between weight loss and maintenance? Int J Obes Relat Metab Disord 1995; 19(1): 67-73.

34. Collins JK, Arjmandi BH, Claypool PL, Perkins-Veazie P, Baker RA, Clevidence BA. Lycopene from two food sources does not affect antioxidant or cholesterol status of middle-aged adults. Nutr J 2004; 3: 15.