OXIDATIVE STRESS AND BLOOD LIPID PROFILE IN CAMEROONIAN OBESE SUBJECTS

JULIUS E. OBEN
University of Yaounde I
Faculty of Science, Department of Biochemistry
P.O.Box 812 , Yaounde, Cameroon
juliusoben@hotmail.com

DAMARIS M. ENYEGUE
JUDITH L. NGONDI
GILLES I. D. FOMEKONG
GABRIEL A. AGBOR
University of Yaoundé I, Cameroon

ABSTRACT

The relationship between obesity, blood lipids and oxidative stress was investigated in 200 participants. The Body Mass Index of the subjects were positively correlated with the percentage body fat, the systolic and diastolic blood pressure, the fasting blood glucose level, the oxidation of proteins and lipids as well as the concentrations of total and LDL cholesterol. On the other hand, the Body Mass Index was negatively correlated to sulhydryl and protein levels. Obese subjects also had significantly higher body fat ($p<.001$), waist circumference ($p<.001$), fasting blood glucose ($p<.01$) as well as systolic blood pressure ($p<.05$). Obesity, therefore, can be said to increase the oxidation of plasma proteins and lipids while reducing the antioxidant status as observed by the inverse relation between plasma sulfhydryl groups and the percentage body fat. This increase in oxidative stress can predispose obese people to illnesses such as cardiovascular diseases and diabetes mellitus.

Key Words: obesity, oxidative stress, anthropometric parameters, lipid profile, Cameroon.

INTRODUCTION

Obesity is a state characterized by a relatively absolute excess fat stored in the adipose tissue. Fatty tissues are normally present in the organism in reasonable quantity that is proportional to the height of an individual. The exact measurement of these fatty tissues is difficult. As such, one can only be termed obese when overweight. Since it is difficult to determine the ideal weight of an individual, the body mass index (BMI) is being used to give an idea of what the ideal weight could be. The BMI is also referred to as the Quetelet index that is defined as weight/height^2. Risk of obesity begins when the BMI is greater than 25 kg/m^2.

Obesity is a risk factor for adult coronary heart disease and is in increasing order among young people and adults (McGill *et al.,* 2002), and it is a principal causative factor of metabolic syndrome (Montague & O'Rahilly, 2000; Matsuzawa, Shimomura, Nakamura, Keno, Kotani, & Tokunaga, 1999; Spiegelman & Flier, 2001; Kahn & Flier, 2000;

Furukawa *et al*., 2004). The coexistence of these metabolic syndromes - hyperglycemia, dyslipidemia, and hypertension in the same individual is a growing medical problem in industrialized countries (Furukwa *et al.,* 2004; Ford, Giles, & Dietz, 2002; Isoma, Almgren, & Tuomi, 2001; Grundy, Brewer, Cleeman, Smith, & Lenfant, 2004). It has been reported that obesity may induce systemic oxidative stress and that increased oxidative stress in accumulated fat is associated with dysregulation of adipocytokines and development of metabolic syndrome (Furukawa *et al.,* 2004).

The present study addresses the relationship between obesity, oxidative stress and dislipidemia.

MATERIAL AND METHODS

Study Population

Two hundred healthy individuals of both sex with confirmed consent, aged between 19 and 55 years, resident in Yaoundé, Cameroon and with a BMI between 18.5 and 35.5 kg/m^2 were recruited for the study and divided into two groups as follows: BMI $\geq$ 30 (30 individuals), BMI < 30 (170 individuals).

Anthropometric Measurements

The subject height was determined with aid of an anthropometer (± 0.1 cm). The weight and body fat percentage were assessed using a clinical balance (TANITA, USA) (± 0.05 kg) and the BMI calculated ($kg.m^{-2}$). Groups were formed according to the classification of WHO (1998).

Physiological Measurements

Arterial pressure (diastolic, systolic and cardiac frequency) were measured in a resting position using a wrist blood pressure monitor (BDM-1, AFK Germany).

Plasma Analysis

Plasma was prepared from blood samples collected from subjects in the morning after an overnight fast of 12 hours. Plasma glucose was determined using glucose test strips (Johnson and Johnson). Total cholesterol (CHOL), high-density lipoprotein-cholesterol (HDL-C), and triglycerides (TG) were measured enzymatically using standard enzymatic kits (Sigma diagnostics). Low-density lipoprotein-cholesterol (LDL-C) was estimated using the Friedwald, Levy and Fredrickson (1972) formula while total protein was estimated by applying the method of Gornall, Bardwill and David (1949). Oxidative stress markers such as thiol groups (Habeeb, 1972), carbonyl group (Levine, Garland, & Oliver, 1990), and malonaldehyde (Yagi, 1976) were also measured.

Oxidative stress markers were evaluated for 195 subjects because plasma level was not enough for their assay.

Statistical Analysis

The results are presented as a mean ± standard deviation. Differences between the groups were analysed using Student's t-test. The Pearson product moment correlations were used to determine the relationships between variables. All calculations were done with SPSS 10.1 (SSPS Inc., Chicago, IL, USA) statistical package. Statistical significance was defined at $p<.05$.

RESULTS

Anthropometric and physiological parameters of obese and overweight subjects compared to normal subjects are presented in Table 1.

Table 1. Anthropometric and Physiological Parameters of Obese and Overweight Subjects Compared to Normal Subjects

Parameters	**Normal Subjects (100)**	**Overweight Subjects (65)**	**Obese subjects N = (30)**
BMI (Kg/m^2	22-25	26-30	> 30
Body Fat (%)	23.27 ± 1.01	26.91 ± 0.91[a]	41.7 ± 1.10[a]
Waist circumference (cm)	77.27 ± 1.77	79.30 ± 1.41	97.27 ± 2.76[a]
Systolic pressure (mmHg)	123.69 ± 1.22	124.72± 0.99	129.13 ± 1.74[a]
Diastolic pressure (mmHg)	86.82 ± 1.26	87.13 ±11.64	88.27 ± 2.44
Pulse rate (min^{-1})	76.40 ± 1.47	74.64 ± 1.03	77.03 ± 2.21

[a] significant $p<.0001$

The percentage fat and waist circumference of the overweight and obese subjects were significantly higher ($p<.0001$) than those of the normal subjects. This high fat deposit is the cause for overweight and obesity. However, the physiological parameters such as diastolic and pulse rate were not statistically different between the three categories and the systolic pressure of the obese subjects was significantly higher ($p<.0001$) than that of the normal subjects.

Table 2 compares the blood glucose and lipid parameter of the overweight and obese subjects with the normal subjects.

Table 2. Blood Glucose and Lipid Parameters of Overweight and Obese Subjects Compared to Normal Subjects

Parameters	Normal Subjects (n=100)	Overweight Subjects (n=65)	Obese Subjects (n=30)
Blood glucose (mg/dl)	78.46 ± 1.79	79.10 ± 1.40	91.75 ± 4.51[a]
Total Cholesterol (mg/dl)	112.73 ± 6.49	118.55 ± 4.94	138.27 ± 13.47
LDL Cholesterol (mg/dl)	65.86 ± 6.58	72.91 ± 5.05	92.79 ± 14.29
HDL Cholesterol (mg/dl)	32.70 ± 3.44	30.29 ± 2.13	25.66 ± 2.15
Triglycerides (mg/dl)	89.41 ± 6.86	94.89 ± 5.38	93.79 ± 7.46

[a] significant p<.001

It was observed that only the blood glucose was significantly higher in the obese subjects than in the normal subjects though the glucose concentration was still within the normal range. No significant alternation was noticed in the lipid parameters.

The oxidative stress markers of overweight and obese subjects compared to normal subjects are presented in Table 3.

Table 3. Oxidative Stress Markers of Overweight and Obese Subjects Compared to Normal Subjects

Parameters	Normal Subjects (n=100)	Overweight Subjects (n=65)	Obese Subjects (n=30)
Sulfhydryl (µmol/g protein)	0.64 ± 0.04	0.58 ± 0.033[a]	0.43 ± 0.047[a]
Carbonyl (µmol/g protein)	1.37 ± 0.63	1.59 ± 0.06[b]	2.22 ± 0.10[b]
Malonaldehyde (µmol/l)	0.08 ± 0.008	0.13 ± 0.014[c]	0.25 ± 0.037[c]
Proteins (g/l)	59.11 ± 2.25	60.01 ± 1.90	51.34 ± 7.77

[a] significant p<.05, [b] significant p<.0001, [c] significant p<.002

Significant decrease in sulfhydryl groups (p<.0001), significant increase in carbonyl groups and malonaldehyde were observed in both the overweight and obese. This confirms the presence of oxidative stress in both the overweight and obese subjects.

DISCUSSION

The incidence of obesity in adults as well as children is on an increase globally. Once considered a problem of developed countries, this global epidemic also affects developing countries. Coupled with this epidemic are obesity-related complications such as cardiovascular disease, stroke, depression and Type-2 diabetes, which are spreading rapidly across poor and middle-income countries, where infectious diseases and malnutrition have previously overshadowed such illnesses (McGill *et al*., 2002). HDL-cholesterol corroborates earlier work that showed an inverse relation between BMI and HDL-cholesterol, the latter imparting possible health benefits in over-weight and obese people (Pietrobelli, Lee, Capristo, Deckelbaum, & Heymsfield, 1999; Knuiman, West, & Burema, 1982). The increase in the concentration of HDL-cholesterol and a decrease in the concentration of LDL-cholesterol could lead to a lowering of the atherogenicity and therefore a significant reduction in the potential incidence of coronary heart disease (Griffin, 1999) (54% reduction of risk for a 0.6 mmol/L reduction of serum cholesterol) (WHO, 1998). A reduction of fasting blood glucose levels as well as MDA levels have been previously reported to accompany weight loss in obese subjects (Yesilbursa, Serdar, Serdar, Sarac, & Jale, 2005). The above observation could be linked to an increase in circulating creatinine and serotonin over the 8-week trial period. Serotonin is known to have a positive effect on mood and to reduce binge eating, which is common in obese people. Several previous studies (Nelson, Day, Glickman-Weiss, Hegstad, & Sampson, 1997; Rockwell, Rankin, & Toderico, 2001) have shown a direct link between serotonin levels and weight loss. On the other hand, an increase in creatinine concentrations parallels an increase in lean muscle mass and a probable reduction in body fat.

Obesity may induce systemic oxidative stress, and increased oxidative stress in accumulated fat is one of the underlying causes of dysregulation of adipocytokines and development of metabolic syndrome (Furukawa *et al*., 2004). Oxidative stress plays critical roles in the pathogenesis of various diseases (Brownlee, 2001). In order to investigate if oxidative stress was increased in the obese participants, we measured lipid peroxidation which represent the plasma Thiobarbituric acid reactive substances (TBARS) and the carbonyl compounds as markers of oxidative injury, which correlates with the BMI. The high plasma concentration of TBARS and carbonyl compounds was an indication of oxidative stress in the obese and overweight participants.

In the diabetic condition, oxidative stress impairs glucose uptake in muscle and adipose tissue (Maddux, 2001; Rudich, 1998) and decreases insulin secretion from pancreatic ß cells (Matsuoka, 1997). Increased oxidative stress also underlies the pathophysiology of hypertension (Nakazono, 1991) and atherosclerosis (Ohara, Peterson, & Harrison, 1993) by directly affecting vascular cell walls.

In the present study, we suggest that obesity per se may induce systemic oxidative stress and that increased oxidative stress in adipose tissue is, at least in part, the underlying cause of dysregulation of adipocytokines and development of metabolic syndrome. As an early indicator of obesity associated metabolic syndrome, increased oxidative stress in adipose tissue should be an important target for the development of new therapies.

REFERENCES

Brownlee, M. (2001). Biochemistry and molecular cell biology of diabetic complications. *Nature, 414*, 813–820.

Ford, E.F., Giles, W. H., *&* Dietz, W. H. (2002). Prevalence of the metabolic syndrome among US adults. *Journal of the American Medical Association, 287*, 356–359.

Friedwald, W. T., Levy, R. I., & Fredrickson, D. S. (1972). Estimation of concentration of low density lipoprotein cholesterol in plasma without use of the ultracentrifuge. *Clinical Chemistry, 18*, 449–502.

Furukawa, S., Fujita, T., Shimabukuro, M., Iwaki, M., Yamada, Y., Nakajima, Y., Nakayama, O., Makishima, M., Matsuda, M., & Shimomura, I. (2004). Increased oxidative stress in obesity and its impact on metabolic syndrome. *Journal of Clinical Investigation, 114*(12), 1752–1761.

Gornall, A. G., Bardwill, C. J., & David, M. M. (1949). Determination of serum proteins by means of the biuret reaction. *Journal of Biological chemistry, 177*, 752–766.

Griffin, B. A. (1999). *Lipoprotein and atherogenicity: An overview of current mechanisms. Proceedings of the Nutrition Society, 58*, 163–169.

Grundy, S.M., Brewer, H.B, Cleeman, J.I., Smith, S.C., & Lenfant, C. (2004). *Definition of Metabolic Syndrome. Circulation, 109*, 433–438.

Habeeb, A.F.S.A. (1972). Reaction of protein sulfhydryl groups with Ellman's reagent. *Methods in Enzymology, 25*, 457–464.

Isoma, B., Almgren, P., & Tuomi, T. (2001). Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes care, 24,* 683–689.

Kahn, B.B., & Flier, J.S. (2000). Obesity and insulin resistance. *Clinical Investigation,* 106: 473–481. Knuiman, J. T., West, C. E., & Burema, J. (1982). Serum total and high density lipoprotein cholesterol concentrations and body mass index in adult men in 13 countries. *American Journal of Epidemiology, 116,* 631–642.

Knuiman, J. T., West, C. E., & Burema, J. (1982). Serum total and high density lipoprotein cholesterol concentrations and body mass index in adult men in 13 countries. *American Journal of Epidemiology,* 116:631–642.

Levine*,* R. l., Garland, D., & oliver, C.N. (1990). Determination of carbony*l* content in oxidatively modified proteins. *Methods Enzymology*, *186,* 464–478.

Maddux, B.A. (2001). Protection against oxidative stress-induced insulin resistance in rat L6 muscle cells by micromolar concentrations of α-lipoic acid. *Diabetes, 50,* 404–410.

Matsuoka, T. (1997). Glycation-dependent, reactive oxygen species-mediated suppression of the insulin gene promoter activity in HIT cells. *Journal of Clinical Investigation, 99,* 144–150.

Matsuzawa, Y., Shimomura, I., Nakamura, T., Keno, Y., Kotani, K., & Tokunaga, K. (1999). Pathophysiology and pathogenesis of visceral fat obesity. *Annals of the New York Academy of Sciences, 892* (1), 146–154.

McGill, H. C. J., McMahan, C. A., Herderick, E. E., Zieske, A. W., Malcom, G. T., Tracy, R. E., & Strong, J. P. (2002). Obesity Accelerates the Progression of Coronary Atherosclerosis in Young Men. *Circulation, 105,* 2712–2718.

Montague, C.T., *&* O'Rahilly, S. (2000). The perils of portliness: causes and conséquences of viscéral adiposity. *Diabètes, 49,* 883–888.

Nakazono, K. (1991). Does superoxide underlie the pathogenesis of hypertension? *Proceedings of the National Academy of Sciences (US), 88,* 10045–10048.

Nelson, A., Day, R., Glickman-Weiss, E., Hegstad, M., & Sampson, B. (1997). Creatine supplementation raises anaerobic threshold. *FASEB Journal*, *11,* A589.

Ohara, Y., Peterson, T. E. & Harrison, D. G. (1993). Hypercholesterolemia increases endothelial superoxide anion production. *Journal Clinical Investigation, 91,* 2546–2551.

Pietrobelli, A., Lee, R. C., Capristo, E., Deckelbaum, R. J., & Heymsfield, S. B. (1999). An independent,inverse association of high-density-lipoprotein-cholesterol concentration with nonadipose body mass. *.American Journal Clinical Nutition, 69,* 614–620.

Rockwell, J. A., Rankin, J. W., & Toderico, B. (2001). Creatine supplementation affects muscle creatine during energy restriction. *Medicine & Science in Sports & Exercise, 33*(1), 61–68.

Rudich, A. (1998). Prolonged oxidative stress impairs insulin-induced GLUT4 translocation in 3T3-L1 adipocytes. *Diabetes, 47,* 1562–1569.

Spiegelman, B.M., & Flier, J.S. (2001). Obesity and the regulation of energy balance. *Cell*, *104,* 531–543.

World Health Organization (WHO) (1998). Obesity Preventing and Managing the Global Epidemic, *Report of WHO Consultation,* Geneva.

Yagi, K. (1976). A simple fluorometric assay for lipoperoxide in blood plasma. *Biochemistry Research*, *15,* 212–216.

Yesilbursa, D., Serdar, Z., Serdar, A., Sarac, M., & Jale, C. (2005). Lipid peroxides in obese patients and effects of weight loss with orlistat on lipid peroxides levels. *International Journal of Obesity, 29,* 142–145.