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STUDY OF OXIDATIVE STRESS AND OVER WEIGHT IN POST MENOPAUSAL WOMEN OF INDIA

Biochemistry

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ABSTRACT

It has been suggested that several medical complications can develop after menopause. Over weight and oxidative stress are the clinical conditions associated with post menopause. Hormonal changes in women are likely to cause some physiological changes which can eventually lead to above clinical state in most of the post menopausal women. The objective of this study is to evaluate the oxidative stress and BMI in post menopausal women of India. We performed a study in post menopausal women aged 60-70 years. (n=45).

Oxidative stress was evaluated by measuring the lipid peroxidation product MDA and plasma enzymes involved in antioxidant activity i.e. SOD and catalase in the experimental subjects. We also measured the BMI of subjects for categorizing overweight.

Thus post menopause is a physiological state accompanied by increased oxidative stress and weight gain. Marker of oxidative stress MDA increases significantly and also decreased antioxidant enzymes due to their greater utilization is observed. BMI in the range of 22-25 was calculated which is a determinant of overweight. Antioxidant supplementation can prove to be a good adjuvant therapy in controlling oxidative stress.

KEYWORDS

oxidative stress, BMI, Postmenopause.

INTRODUCTION

Post menopause is a term applied for women who have not experienced a menstrual cycle for about a year, assuming that they do still have a uterus, and are not pregnant or lactating. The menopause is associated with changes in body composition: a decline in bone mineral content, a decrease in collagen synthesis, a loss of lean body mass and an increase in total and abdominal fat mass. Estrogen deficiency seems to play a role in the menopause-related changes, but life styles (diet, exercise, smoking habits, alcohol consumption) are also involved.

Majority of adults are becoming increasingly overweight and one of the subpopulations in which this prevalence is growing most rapidly is postmenopausal women. 8.3 million Population is forecasted to be obese in age of 50 years or older. (1)

Postmenopausal women have an increased tendency for gaining weight. It is still not very clear that how the menopausal transition leads to weight gain. It is known that the physiological withdrawal of estrogen brings about changes in fat distribution together with physical inactivity, and this can be the probable cause for weight gain.(2)

The prevalence of obesity among the post-menopausal women was 36% (21/59) with a further 41% (24/59) in the overweight range. In U. K. half of the postmenopausal women (48.27%, 14/29) were observed as overweight/obese. Kawaljit Kaur et al 2010 have reported prevalence of obesity in Indian postmenopausal women was 75.09% (3, 4, and 5)

17-beta-estradiol is the main estrogen in women's body. Estrogens travel to adipose tissue and liver cells by endocrine way. They are also produced in these cells from androgens. In adipose tissues, 17-beta-estradiol can be stored as esters with long-chain fatty acids. Estrogens receptors are found in adipose & liver cells but their density is lower than in gonads. Within the cells, estrogens regulate mRNA synthesis for proteins involved in lipid metabolism. In adipose tissue 17-beta-estradiol has a direct effect on lipoprotein lipase (LPL) and hormone-sensitive lipase (HSL). In the case of the first enzyme its synthesis is faster, while the synthesis of the latter is slower. On the other hand, indirect action of estrogens on adipose tissue is connected with the stimulation of the releasing of other hormones which increase HSL activity.

The lack of estrogens in women after menopause may cause coronary heart disease. Estrogen plays a major role in the delayed expression of coronary heart disease (CHD) in women, and recent data indicate that postmenopausal estrogen therapy reduces the incidence of CHD by >40% (6). The mechanisms through which estrogen exerts this benefit are unknown, although effects on blood pressure, carbohydrate and lipid metabolism, and coagulation have been suggested. We hypothesized that at least part of the effect of estrogen in reducing the incidence of CHD is due to an effect on endothelial cell function.(7) Studies of hormone replacement therapy in postmenopausal women show around a 50% reduction in risk of a coronary event in women using unopposed oral estrogen.(8).

Estrogen withdrawal during menopause has a damaging effect on metabolism which changes body fat distribution from a gynoid to an android pattern, reduced glucose tolerance, abnormal plasma lipids, hypertension, endothelial dysfunction and vascular inflammation. As a result postmenopausal obesity leads to compounds the situation leading to increased rates of physiological disorders. (9, 10).

Oxidative stress represents an imbalance between the production of reactive oxygen species and a biological system's ability to readily detoxify the reactive intermediates or to repair the resulting damage. Postmenopausal women are at risk of cardiovascular disease (CVD) as a result of unfavorable blood lipid profiles and increased oxidative stress. (11). Several workers have reported an increase in body mass index of post menopausal women. (12, 13). Blew RM et al have suggested a direct correlation between % fat and BMI among the post menopausal women. (14) Menopause is associated with a progressive gain in body weight and an increased tendency for central adiposity with advancing age.(15)

As we do not have such comparative statistics in Indian studies, so in the present study an attempt has been made to assess the prevalence of being overweight and the degree of oxidative stress among postmenopausal women of India.

MATERIAL & METHODS

The study was carried out at the Bioscience department, SCM institute of professional studies, Indore (M.P.), India between October 2011 and January 2012. The study was conducted on 45 healthy volunteer females, out of which 17 were of pre-menopausal age, (mean=33.64±8.22 years) and 28 were of post-menopausal age (mean=62.58±4.75 years). All subjects were confirmed free of disease on the basis of clinical history, physical examination and routine laboratory tests, and all participants were not on any medical treatment including supplementation of antioxidants or alcohols. A written consent was taken from all the subjects.

About 3-4 ml. venous blood from different participants was obtained using vein puncture. The blood was centrifuged at 2000rpm for 10 minutes at RT and the serum was collected.

The serum was evaluated for lipid peroxidation product MDA & antioxidant enzymes SOD and catalase levels.

Lipid peroxidation in erythrocytes was determined in terms of Malondialdehyde as a measure of oxidation of polyunsaturated lipids.

This method is based on the formation of a red chromophore, which absorbs at 532 nm. (16).

Serum SOD level was determined by Marklund & Marklund method 1974 modified by Nandi et al (1988) (17). This method utilizes the inhibition of auto-oxidation of pyrogallol by SOD. One unit of SOD activity being defined as amount of enzymes required to cause 50 % inhibition of pyrogallol auto-oxidation per 3 ml of assay mixture.

The activity of serum catalase was determined by method of L Goth (1991) Catalase present in serum reacts with its substrate H2O2 (one mol of H2O2/ ml decomposed by 1 unit of catalase per min.). The enzymatic reaction was stopped with ammonium molybdate and the yellow complex of molybdate and H2O2 is measured at 405 nm.(18).

BMI of all the subjects was calculated by Metric BMI formula to assess the degree of obesity in post menopausal women compared with pre menopausal women.

BMI = (Weight in Kilograms / (Height in Meters x Height in Meters)

Statistical analysis: The results obtained were statistically analyzed with the help of Statistical package for social sciences SPSS software, version 15.0 and mean values for each parameter was expressed as +/- SD. Students 't' test and the level of significance (p value) was calculated to compare between cases and the controls. The significance of p value is tested at 5% and 1% level of significance with n-2 degree of freedom.

RESULTS

Table: 1 Mean SD of oxidant & antioxidant status in Pre menopausal and Post menopausal women.

Groups	*MDA n mol/ ml*	SOD U/ml	CAT KU/l
Pre menopausal women N=17	1.190.33	4.900.48	54.504.96
Post menopausal women N= 28	4.060.55**	2.030.41**	42.303.62**

** P<0.001 highly significant when compared with Pre menopausal control group

In the present study a significant rise in MDA level was observed in study groups when compared with pre menopausal control. Significantly high levels were observed for MDA in **(Table 1).** The antioxidant enzymes SOD and CAT activity found to be decreased in post menopausal women when compared with control group. The mean MDA level is high post menopausal women (4.06 n mol/ ml) as compared with pre menopausal control (1.19 n mol/ ml). Antioxidant enzyme SOD levels were decreased in post menopausal women (2.03 U/ml) as compared with control SOD level (4.90 U/ml). Antioxidant enzyme catalase also found to be decreased in post menopausal women (42.30 KU/l) when compared with control group (54.50 KU/l)

Graphical representation of MDA levels, SOD and Catalase activity are shown in Fig. 2,3 and 4 respectively).

BMI of post menopausal women was calculated to be >25 kg/m(2) with an average value of 27 ± 2.16 suggesting overweight which can lead to obesity.

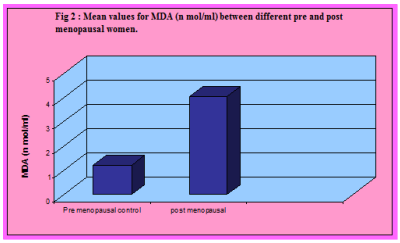

Fig 2 : Mean values for MDA (n mol/ml) between different pre and post menopausal women.

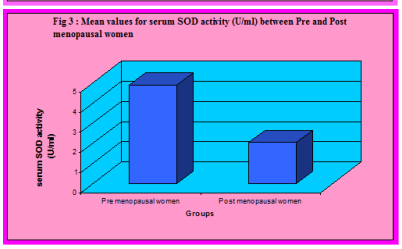

Fig 3 : Mean values for serum SOD activity (U/ml) between Pre and Post menopausal women

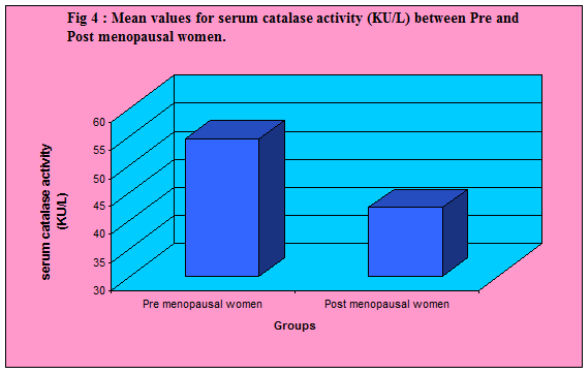

Fig 4 : Mean values for serum catalase activity (KU/L) between Pre and Post menopausal women.

DISCUSSION

Free radicals have a tendency to cause lipid peroxidation. Markers of lipid peroxidation (MDA) are increased during Post menopausal age. A significant rise in the lipid peroxidation product MDA was observed in post menopausal women when compared with the control pre menopausal women.

Menopause is known to be associated with a wide variety of physical and psychological symptoms.(19)

Free radical reactions are involved in processes connected with aging. Estradiol acts as an antioxidant and free radical scavenger, but the mechanism of this action remains unknown. (20). The deficiency of estrogen in post-menopausal women is believed to be a factor in the development of oxidative stress, and the release of free radicals or reactive oxygen species (ROS) which becomes the cause of various pathologies. This may explain in part, the significantly higher serum MDA levels in the post menopausal group in the present study.

The formation of excessive amounts of reactive oxygen species (ROS), including peroxide (H2O2) and superoxide anions (O2-) is toxic to cells, hence, metabolizing and scavenging systems to remove them are functionally critical and tightly controlled in the cells. Glutathione peroxidase (GPx) in concert with catalase and superoxide dismutase (SOD) function to protect the cell from damage due to ROS. Glutathione peroxidase detoxifies peroxides with glutathione acting as electron donor in the reduction reaction, producing oxidized glutathione (GSSG) as an end product.(21)

Omar et al reported increased levels of serum MDA 1.32±0.05 µmol/L in postmenopausal women. (22). The highly significant reduction in SOD and Catalase observed in the post-menopausal-group in this study could be due to the increase in its free radical scavenging property and increased consumption to counteract the elevated levels of oxidative stress and to inhibit membrane lipid peroxidation.

The hormonal changes associated with menopause e.g. low plasma levels of estrogen and high levels of Leutenizing and follicle stimulating hormones exerts a significant role on metabolism.(23) Berg et al also reported abnormal levels of estrogen, LH and FSH with increase in their BMI. (24) Estrone is a major endogenous estrogen in postmenopausal women It is formed by peripheral aromatization of plasma androstenedione secreted from ovaries and or adrenal glands. Adipose tissue is one of the loci of this conversion, and the transfer constant of conversion of plasma androstenedione to estrone is positively related to body weight. This peripheral mechanism is also active in premenopausal women with normal ovulatory cycles. Although the affinity of estrone for the receptor is one-half to one-third that of estradiol, plasma estrone may supplement the effects of estradiol, which starts to decrease in the mid-thirties. Therefore, we think that increased peripheral production of estrone in obese women may contribute patho-physiologically to the delay in age at menopause resulting from obesity. (25)

CONCLUSION

The association of this increase in serum MDA with reduced antioxidant defense system may lead to the speculation that they could be considered an index or a marker of oxidative stress in the post-menopausal women.

The present study depicts a statistically significant increase in MDA and a fall in antioxidant enzymes reflecting increased oxidative stress

in post menopause. BMI of all the post menopausal women was also found to be increased which is a suggestive of post menopausal obesity. So care should be taken during this period to minimize the pathogenesis caused by free radical damage and obesity. Balanced nutritional diet along with antioxidants and regular exercise can prevent further clinical manifestations.

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