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RESEARCH ARTICLE

Comparison of oxidative stress between premenopausal and postmenopausal women

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ABSTRACT

Background: Menopause is a natural biological phenomenon during which irreversible changes in the hormonal and reproductive functions of the ovaries lead to physical, social, and psychological changes in women. The progressive loss of estrogen and its protective effects predisposes to the development of oxidative stress and related diseases in postmenopausal women which, in turn, can impair their quality of life. **Aims and Objectives:** This study aims to study and compare the levels of serum malondialdehyde (MDA) and superoxide dismutase (SOD) in premenopausal and postmenopausal females. **Materials and Methods:** A cross-sectional comparative study was conducted in 100 healthy women, of which 50 were postmenopausal in the age group of 50–60 years and 50 were premenopausal in the age group of 30–40 years. The data were analyzed using Statistical Package for the Social Sciences version 18. **Results:** Oxidative stress was increased in postmenopausal women as evidenced by significantly elevated MDA and reduced SOD. **Conclusion:** Menopause is associated with oxidative stress which predisposes to the development of cardiovascular diseases, vasomotor disturbances, osteoporosis, depression, diabetes, and hypertension. Dietary management, antioxidant supplementation, and moderate physical activity would help them to prevent diseases related to menopause.

KEY WORDS: Menopause; Oxidative Stress; Osteoporosis; Cardiovascular Diseases

INTRODUCTION

Menopause is a natural age-related transition that occurs in women with ovarian senescence causing a decline in production of estrogen.[1] It is defined as permanent cessation of menstruation for 1 year and occurs around 45–55 years of age.[2] Menopause is a natural biological process during which women experience physical, social, and psychological changes which can influence their quality of life.[3] With better nutrition and advancements in medicine, average life expectancy has increased and is about 80 years in developed countries. Hence, at present, 95% of females experience menopause and most of the women live at least one-third of their lives in menopause.[1]

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Pacifi attributed the adverse effects of menopause to be due to the deficiency of estrogen.[4] Estrogens prevent osteoporosis by inhibiting the stimulatory effects of interleukin (IL)-1, IL-6, and tumor necrosis factor-α on osteoclasts.[5] Estrogen deficiency after menopause leads to a significant increase in osteoclastic activity. As a result, bone resorption is accelerated and is not balanced by compensatory bone formation.[1] Estrogen has a positive effect on mood and provides a sense of well-being. Hence, estrogen deprivation after menopause results in depression, anxiety, irritability, and mood swings.

Estrogen is a powerful antioxidant which prevents lipid peroxidation and its deficiency after menopause leads to

increased oxidative stress.[6] Oxidative stress is an imbalance between the production of reactive oxygen species (ROS) (free radicals) and antioxidant defenses.[7] Both oxidant and antioxidant substances are required by the human body for normal metabolism, regulation of cellular functions, and signal transduction. Thus, each cell maintains a state of homeostasis between the oxidant and antioxidant species. The term antioxidant refers to any molecule which is capable of either stabilizing or deactivating free radicals before they cause damage to cells and play an important role in maintaining optimal cellular functions and thus systemic health and well-being of an individual.[8] Oxidative stress can cause damage to almost all the major cellular components such as proteins, DNA, and membrane lipids, which may result in cell death.[9]

Ansar *et al*. reported that there is enhanced oxidative stress and decreased antioxidant defense in postmenopausal females which increases the risk of hypertension, diabetes mellitus, cardiovascular diseases, and osteoporosis.[10] Lipid peroxidation and consequent degradation products such as malondialdehyde (MDA) are produced which are seen in biological fluids. Hence, serum MDA can be used to assess the levels of oxidative stress. Serum superoxide dismutase (SOD) enzyme is the principal enzymatic antioxidant and it catalyzes the conversion of superoxide anions to dioxygen and hydrogen peroxide. Since superoxide is the primary ROS produced from several sources, its dismutation by SOD is of primary importance for each cell and serum SOD enzyme can be used to assess the level of antioxidant status.

The present study has been designed to compare oxidant-antioxidant status between premenopausal and postmenopausal females. Since menopause associated decline in circulating estrogen has been linked with an elevated risk for cardiovascular diseases, hypertension, vasomotor disturbances, depression, diabetes, and osteoporosis, it is important to know whether enhanced oxidative stress could lead to the development of such diseases in postmenopausal women. This study emphasizes the importance of screening of all postmenopausal women for oxidative stress so that appropriate lifestyle modifications could prevent diseases related to menopause. A better understanding of such factors could contribute to prevention strategies that help postmenopausal women to maintain their independence and quality of life.

MATERIALS AND METHODS

It was a cross-sectional comparative study done in Government Medical College, Kozhikode, after obtaining necessary clearance from the Institutional Ethics Committee. The study was conducted for a period of 1 year.

Study Population

A total of 100 healthy female subjects were selected for the study, of which 50 were in the postmenopausal and 50 in the premenopausal age group. The subjects were selected from among the hospital staff and bystanders of patients admitted in the wards at Government Medical College, Kozhikode. To ensure their voluntary participation, subjects were briefed about the objectives and methods of study and an informed written consent was taken before the study. Detailed history was taken as per the pro forma. Relevant clinical examination was done. Blood samples were collected for blood investigations.

Inclusion Criteria

A total of 100 healthy women participated in the study were divided into two groups.

- Group 1 – 50 postmenopausal women in the age group of 50–60 years with cessation of menstruation for more than 1 year
- Group 2 – 50 premenopausal women in the age group of 30–40 years with regular menstrual cycles.

Exclusion Criteria

- Females with a history of intake of oral contraceptive pills or hormone replacement therapy were excluded from the study
- Subjects with a history of hypertension, diabetes mellitus, renal disease, heart disease, stroke, and neurodegenerative diseases were also excluded from the study.

Estimation of Serum MDA

MDA is one of the most frequently used indicators of lipid peroxidation. MDA was measured in serum using the thiobarbituric acid test based on Pasha and Sadasivadu's procedure for the estimation of MDA.[11] The thiobarbituric acid test is one of the oldest and most frequently used tests for measuring lipid peroxidation of fatty acids in membrane as well as in food products.

Principle

MDA reacts with thiobarbituric acid to generate a colored product that absorbs light at 530 nm. The results were often expressed in terms of MDA produced in a given time in nmol/dL.

Estimation of SOD Activity

SOD is an enzymatic antioxidant which neutralizes superoxide anion, one of the most potent ROS. SOD activity was measured by the method suggested by Marklund, 1974 (modified by Nandi *et al*., 1988).[12]

Principle

This method utilizes the inhibition of auto-oxidation of pyrogallol by SOD.

Statistical Analysis

The present study was designed as a cross-sectional comparative study. Statistical analysis was done to determine the differences between the two groups. The data were analyzed using Statistical Package for the Social Sciences (SPSS) version 18. The results were expressed as mean ± SD. The mean value of each parameter was obtained by summing up all the individual values in the groups and dividing it by the number of subjects in the groups. The mean differences between the groups were analyzed using independent sample "*t*"-test. For all statistical tests, $P \leq 0.05$ was taken as the level of significance.

RESULTS

The present study was conducted to compare the oxidant-antioxidant status (MDA and SOD) between premenopausal and postmenopausal women. A total of 100 healthy subjects were selected and they were grouped into two groups, 50 premenopausal women in the age group of 30–40 years and 50 postmenopausal women in the age group of 50–60 years. The data were analyzed using the SPSS version 18. The results were expressed as mean ± SD.

There was a significant increase in serum MDA levels in postmenopausal females compared to premenopausal females and *P* value was significant ($P = 0.000$) [Figure 1].

There was a significant decrease in serum SOD levels in postmenopausal females compared to premenopausal females and *P* value was significant ($P = 0.000$) [Figure 2].

DISCUSSION

The present study was conducted to compare the oxidant-antioxidant status (serum MDA and SOD) between premenopausal and postmenopausal females. The study showed significantly elevated levels of serum MDA in postmenopausal compared to premenopausal females and serum SOD was significantly reduced in postmenopausal females. Among the subjects, the mean MDA was 163.92 ± 16.08 nmol/dL in postmenopausal and 93.10 ± 11.29 nmol/dL in premenopausal females [Figure 1]. The difference was statistically significant ($P = 0.000$). The mean levels of serum SOD were found to be reduced in postmenopausal (1.33 ± 0.68) compared to premenopausal females (3.12 ± 0.37) [Figure 2] and the difference was statistically significant ($P = 0.000$).

Many studies in the literature have similar results. In studies done by Vaishali *et al*.[6] and Rasheed *et al*.,[13] serum MDA was significantly elevated in postmenopausal compared to premenopausal group. Hence, they concluded that low levels of estrogen in menopause are associated with an increase in oxidative stress which is indicated by increase in lipid

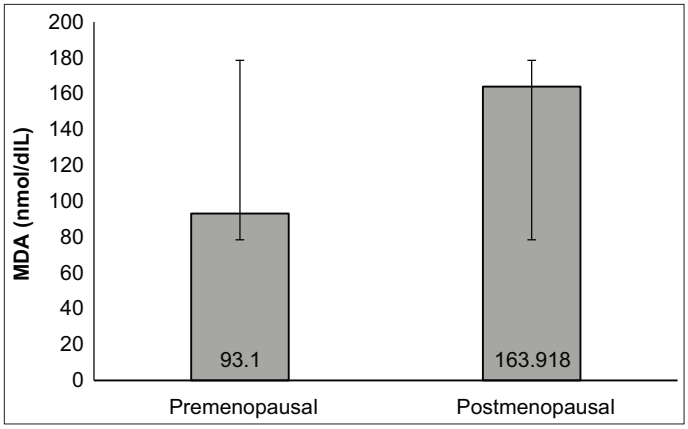

Figure 1: Comparison of serum malondialdehyde levels in premenopausal and postmenopausal females

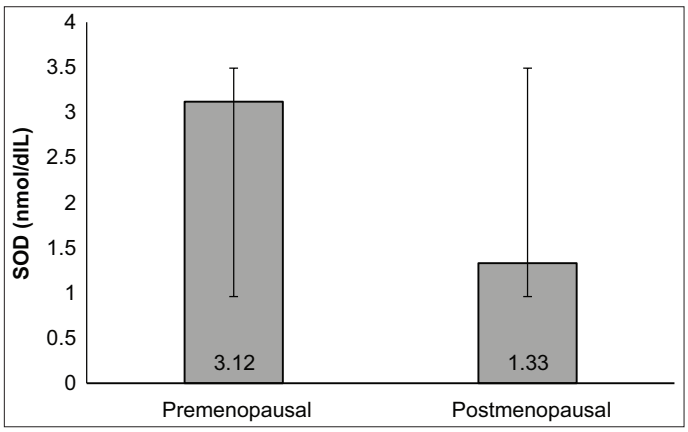

Figure 2: Comparison of serum superoxide dismutase levels in premenopausal and postmenopausal women

peroxidation product, MDA. Sanchez-Rodriguez *et al*. also reported that the levels of plasma lipoperoxides were higher in postmenopausal compared to premenopausal women.[14] The significantly reduced levels of serum SOD in postmenopausal females obtained in the current study were in agreement with the studies done by Ansar *et al*.[10] and Omran.[15]

Menopause is a natural and an inevitable stage in a woman's life, marking the permanent cessation of menstruation. It encompasses not only the biological changes but also physical, psychological, and cultural changes associated with the aging process. Menopause is the result of irreversible changes in the hormonal and reproductive functions of the ovaries. It affects all women and constitutes a significant health burden for middle-aged women all over the world. In 1990, there were around 467 million postmenopausal women in the world and this figure is expected to rise to 1200 million by 2030, of which 76% will be living in the developing countries.[16] Hence, the health of this large population group is of great importance to public health.

Menopausal women develop oxidative stress because of estrogen deficiency and this has been implicated in the pathogenesis of a number of diseases such as cardiovascular

disease, osteoporosis, diabetes, and hypertension. This shows the protective role of estrogen in our body.

Oxidative stress occurs when the antioxidant system is not able to effectively deal with the ROS and free radicals produced in living organisms. Estrogens have free radical scavenging capacity and thus it can function as antioxidant to inhibit the generation of ROS or neutralize excess ROS.[14] Thus, estrogen deficiency after menopause leads to increased formation of ROS and free radicals, which cause oxidative damage to biomolecules such as lipids, proteins, and DNA, which, in turn, leads to dysregulation of normal metabolism and physiology. ROS is difficult to measure directly because of their transient and unstable nature. Hence, their tendency to cause lipid peroxidation has been used as an indirect measure. MDA is the final product of lipid peroxidation.

Depletion of antioxidants is an indirect marker of oxidative stress during menopause. SOD is the principal antioxidant enzyme. It scavenges superoxide anions by catalyzing the conversion of highly reactive superoxide radicals to less toxic hydrogen peroxide and decreases cell damage.[10] The decrease in the level of SOD in postmenopausal females may be due to its increased consumption to counteract the increased oxidative stress. Hence, increased oxidative stress and decreased antioxidant levels after menopause play an important role in the development of many disorders such as cardiovascular disease, hypertension, diabetes, osteoporosis and depression.[4]

In the present study, only serum MDA and SOD were measured to compare the oxidant-antioxidant status. The results of the study would have been more conclusive if other markers of oxidative stress were also assessed. A larger sample size would ensure more accurate results.

CONCLUSION

The present study was conducted to compare the oxidant-antioxidant status (serum MDA and SOD) between premenopausal and postmenopausal females.

Serum MDA level was significantly increased and serum SOD was significantly reduced in postmenopausal compared to the premenopausal women. The above observations indicate that there is an enhanced oxidative stress and decreased antioxidant defense after menopause as a result of estrogen deprivation. This can cause potential oxidative injury in the cells, leading to the development of various disorders such as cardiovascular disease, hypertension, diabetes, vasomotor disturbances, osteoporosis, and depression. All the above findings suggest the need of a comprehensive health program for postmenopausal women. They should be screened for oxidative stress. Antioxidant supplementation has shown to decrease the effects of oxidative damage produced by free radicals. As a part of lifestyle modification, postmenopausal women should be encouraged to consume a diet which is rich in antioxidants. Moderate physical activity is also beneficial to maintain a good physical and mental health.

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