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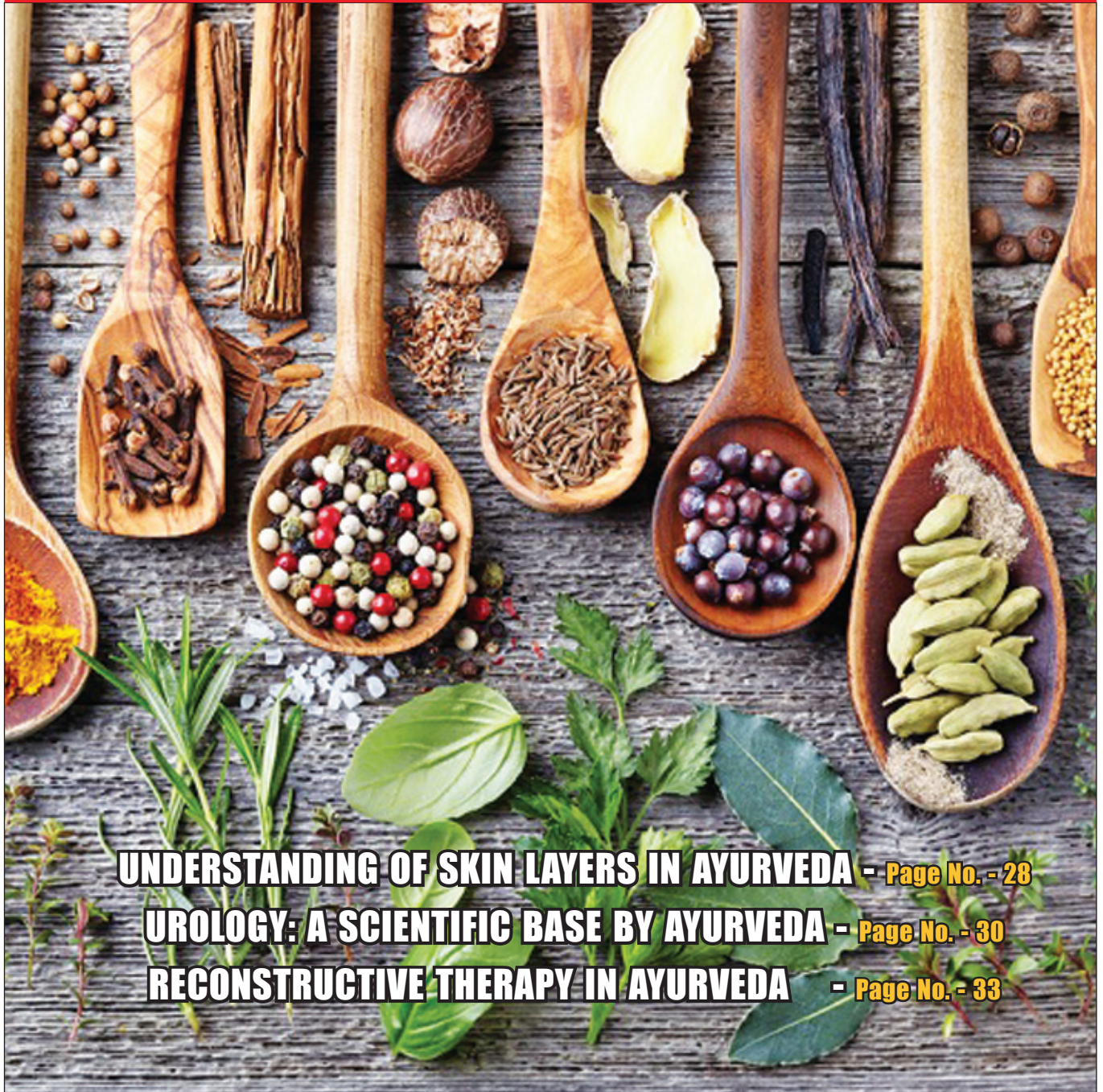
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Antioxidants and Menopause

SANJAY AGRAWAL

Introduction

Menopause, a form of reproductive aging, is defined as the permanent cessation of ovarian follicular activity and eventually, the menstrual cycle. Normally, menopause is a natural process of the body; however, it can be the result of other causes such as surgery, chemotherapy, or iatrogenic insult. Additionally, two hormones (progesterone and estrogen) integral to reproductive aging are no longer produced during menopause. Specifically, the decline and eventual cessation of estrogen production has been shown to cause a variety of symptoms during menopause, affecting each woman differently. These include hot flashes, night sweats, breast tenderness, vaginal dryness, irregular menses, mood changes, vaginal atrophy, osteoporosis, heart disease, and sometimes premature ovarian failure. Many therapies have targeted this hormonal decline in estrogen and have also expanded to include lifestyle modifications, such as diet and exercise. Additionally, foods rich in antioxidants have been shown to be of great benefit in women experiencing menopausal symptoms because they help to eliminate oxidative stress within the body. Overall, this paper will discuss in great detail the stress of free radicals and antioxidant deficiencies, both of which play a role in the pathogenesis of menopause.¹⁻⁴

Oxidative stress & Menopause

Oxidative stress plays an integral part of the aging process and results from the overproduction of free radicals such as reactive oxygen species (ROS), which overwhelm the body's antioxidant defense mechanisms. Normally, antioxidants neutralize ROS and thus help to prevent over exposure from oxidative stress. However, as the body ages, antioxidant levels decline, leaving the human body susceptible to a variety of age-related pathologies, such as non-alcoholic liver cirrhosis and atherosclerotic heart disease. This decline combined with a gradual loss of estrogen in the female reproductive system is highly associated with the various sequelae of menopause such as heart disease, vasomotor disturbances, and osteoporosis. The marked reduction in estrogen has been shown to increase levels of oxidative stress in the body, depending on the concentration and chemical structure of this hormone. Specifically, at high concentrations, estrogen tends to have a beneficial antioxidant effect by inhibiting the 8-hydroxylation of guanine DNA bases. However, at low concentrations, this hormone has pro-oxidant like effects, especially when its chemical structure contains a catechol. These effects include breaks in genetic material, formation of DNA adducts, and oxidation of bases. Additionally, serum concentrations of inflammatory cytokines and pro-oxidant biomarkers such as glutathione, 4-hydroxynenal, and malonaldehyde were found to be higher in postmenopausal women than in premenopausal women. The elevation of cytokines and

pro-oxidant makers suggests that there is a high degree of oxidative stress in the postmenopausal state.⁵⁻⁸

Consumption of foods rich in antioxidants may be helpful in enhancing the beneficial effects of pharmacotherapy for postmenopausal patients. Specifically, women who cannot tolerate the adverse side effects of MHT or are prone to develop estrogen-dependent breast cancer may find it advantageous to use dietary antioxidants to control the symptoms of menopause. Supplementation with antioxidants will not only improve the quality of life of menopausal women exposed to high amounts of oxidative stress, but also from other lifestyle-related factors such as smoking, stress, excessive alcohol consumption, and unhealthy eating habits. The following antioxidants were found to be beneficial to women in the perimenopausal and postmenopausal phases: Vitamin C, Vitamin E, phytoestrogens, melatonin, Acanthopanaxsenticosus, kamin, Curcuma longa, grape polyphenols, and lycopene.

Cardiovascular effects of menopause

Estrogen has been shown to play a physiologic role in the cardiovascular system by protecting against heart disease. This is facilitated via its atheroprotective effect on plaque stabilization and collateral vessel formation. This hormone also has favorable effects on insulin, glucose, and lipoprotein levels in the serum. However, because the antioxidant effect of estrogen is lost once women reach menopause, the incidence of

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atherosclerosis increases. This is due to a variety of factors, one of which is a higher level of oxidized LDL in the blood.

Vasomotor disturbances

Oxidative stress is also involved in the pathogenesis of menopausal symptoms, such as vasomotor disturbances. These disturbances include hot flashes or night sweats. Hot flashes are defined as a sudden feeling of warmth usually over the face, neck, and chest. During a hot flush, the metabolic rate temporarily increases, which often results in sweating, panic, and irritability.

Osteoporosis

is defined as a reduction in bone mineral density, which occurs when there is an imbalance between the creation of new bone and removal of old bone. A decline in estrogen has been shown to play a major role in this decreased bone mass during the onset of menopause, especially because it has a variety of protective effects on bone marrow and bone cells

Benefits and dietary vitamins

Two dietary vitamins, vitamin C (ascorbic acid) and E (α -tocopherol), can be used to thwart the onset of various disorders associated with an age-related decrease in estrogen. Rich in their antioxidant capacity, these vitamins scavenge free radicals and neutralize oxidative stress. One study assessing the effect of these vitamins on postmenopausal women found higher levels of the oxidative stress marker, malonaldehyde, and lower levels of the antioxidant enzymes, catalase and superoxide dismutase, in those who did not incorporate vitamin C and E in their diet. These vitamins were not only helpful in achieving a favorable redox balance in the body, but they also are associated with a

reduced risk of cardiovascular disease. This is mediated via their inhibition of cholesterol synthesis and LDL-cholesterol oxidation.

In regards to the symptoms of menopause, both vitamins have been shown to reduce the intensity and number of hot flashes via promotion of adrenal function. This allows for increased hormonal production, specifically estrogen, allowing for a greater antioxidant defense system in postmenopausal women. When considering vitamin C alone, its intake has been associated with a protective effect on bone. This can be seen through its suppressive action on osteoblast and osteoclast activity, which thereby prevents accelerated bone turnover and eventual bone loss.

However, at high doses, vitamin C and E have deleterious effects on the body. Specifically, large quantities of vitamin C (>2,000 mg/day) have been suggested to cause diarrhea, abdominal cramps, bloating, nausea, vomiting, and kidney stones. While high doses of vitamin E (>1,000 mg/day) may increase the risk of bleeding by having an anticoagulant-like effect on the body and may also increase the risk of birth defects. Thus, when using vitamin C and E to quell the adverse effects of menopause, it is important that appropriate dosages be used.⁹⁻¹⁰

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In India, the incidence of chronic kidney disease CKD is rising, and as per estimates from 2006, the age-adjusted incidence rate of end-stage renal disease (ESRD) is 229 per million population. Further, the number of new patients entering renal replacement programs annually is > 100,000.

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