

Estrogens are essential for Good Health

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Received Date: April 26, 2024; Accepted Date: May 03, 2024; Published Date: May 13, 2024

Citation: P D Gupta, Shrishailappa Badami, (2024), Estrogens are essential for Good Health, *Clinical Medical Reviews and Reports*, 6(4); DOI:10.31579/2690-8794/210

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Abstract

Estrogens, the class of female steroid hormones are responsible for making a woman a woman. The imbalance of this hormone sometimes wreaks havoc in a person's life. The imbalance of this hormone may be due to pathophysiological and/or environmental exposure to xenoestrogens which are omnipresent in air, soil, and water including food, has become a serious cause of ill health. Unusual levels of estrogens in the circulatory system influence many organs and systems and cause certain systemic diseases and disorders.

Keywords: xenohormones; reproductive years; menopause; fluctuating estrogen levels

Introduction

Chemically estrogens are steroids produced from the precursor cholesterol. The type of steroid formed is dependent upon the attachment of hydroxyl groups. The three important natural estrogens in women are:

Estrone (E1): This is the primary type of estrogen present in menopausal females and normal males. From androgens, the ovaries, placenta, testicles, and fat tissue produce estrone.

Estradiol (E2): This is the most potent type of estrogen, both in terms of absolute serum levels as well as in terms of estrogenic activity. and in females of childbearing age its concentration is highest.

Estriol (E3): This is produced by the and peak levels are attained during pregnancy. The amount of secretion increases with foetus growth. In addition to these, there exists estrogen mimicking compounds, which are structurally or functionally related to the human sex hormone 17 β -estradiol (E2), not produced by our body, but bind the estrogen receptors (ERs) with various degrees of affinity and selectivity and called as xenoestrogens [1]. Several body systems are in part governed by estrogen and the libido, menstrual cycle, and vaginal functioning, such as lubrication and elasticity are regulated by it. It supports in maintenance of strong bones and preventing of cardiovascular disease. It also helps to the health of the breasts, muscles, skin and urinary tract [2,3]. Both natural or synthetic estrogens have a lot of clinical uses in the human female [4,5]. Estrogens are used in the treatment of excessive height, genital infections and gonadal dysgenesis in prepubertal females. They are also used in the management of disorders of menstrual cycle like amenorrhea, dysmenorrhea and menorrhagia, infertility symptoms like poor cervical mucus and anovulation, pregnancy like abortion and lactation suppression, acne vulgaris and hirsutism like dermatological disorders, for contraception as estrogen/progesterone combination and postcoital contraception. Menopause syndromes, breast cancer and several

genital disorders like atrophic vaginitis, genital prolapse and infections are also treated by estrogens during the postmenopausal years. Prostate carcinoma and sexual problems are treated in the human male by estrogens. However, research cautioned the use of estrogen therapy should be used with caution, and benefits should be weighed against the hazards and possible side effects and alternative forms of treatment should be considered [6,7].

Fluctuations of Estrogen Levels

Estrogen levels rise during puberty and healthy levels are maintained during her 40s and 50s, or the beginning of menopause [8]. Hence, fluctuation during women's lifetime are common. High reduction in estrogen production occurs during menopause, indicating stop of natural fertility and leading to anxiety, depression, diminished neuroprotection, memory loss, and mood changes which are due to the effects of estrogens on the brain functions. Menopausal drop in production of estrogen cause sudden and several times severe health problems on women. Research supports the use of estrogen in treating depression and other menopausal challenges. But effective treatments need to be explored and identified [9].

High levels

The high levels of estrogen levels cause anxiety, bloating, headaches, insomnia, low sex drive, memory problems, mood swings and swelling, resulting in shifting of the treatment by women [10].

Low levels

During the beginning of the menopausal period, the production of estrogens in the body get reduced leading to several symptoms including hot flashes, depression or mood swings, insomnia, low sex drive, night sweats, osteoporosis, memory and concentration disorders and vaginal dryness [10,11].

Effects of estrogens on Body Systems

Primarily estrogens induce the growth and development of female secondary sexual characteristics, regulate the menstrual cycle, and manage the reproductive system. Nevertheless, lately, it was found that in addition to male and female reproductive behavior, levels of estrogens also influence other systems, which is explained below.

a. The Skin

Estrogen helps to maintain skin thickness and elasticity by preventing a decrease in skin collagen and elastin contents. It also helps in skin moisturization; hence, post-menopausal skin is typically drier than it was before. It is also helping in increasing dermal matrix proteins such as mucopolysaccharides and hyaluronic acid [12].

b. Accelerated Bone Loss

Research support that osteoblasts, osteoclasts and osteocytes all express estrogen receptors [13] and increased osteoclast apoptosis through high production of transforming growth factor (TGF)-beta is seen in the estrogen-replete state. Estrogen deficiency is found to be high during estrogen treatment and it decreases the amount of bone loss during the remodeling cycle and the rate of bone remodeling [14]. The deficiency of estrogen affects both men and women equally. Inadequate bone formation combined with excessive bone resorption leads to bone loss. Estrogen deficiency increases the number of osteoclasts and decreases the number of osteoblasts resulting in overall bone resorption. Fracture risk in postmenopausal women inverse in proportion to the estrogen level [15].

c. Regulate Eyes Too

Frequent hormone fluctuations are common in women. Estrogen levels significantly change due to aging, menstrual cycles, puberty, birth control pills, pregnancy, perimenopause and menopause, and cause fluctuations also in eye sight [16]. Declining estrogen levels also cause decrease in lubrication of the oil glands in the eyes resulting in dryness and blurry vision [17]. The same effect is observed during extremely high levels of estrogen. Temporary blurry vision is also experienced by pregnant women. Estrogen causes the cornea to become more elastic and change the way light travels through the eye [18] leading to blurry vision and difficulty in contact lens wearing. The pathogenesis of glaucoma may be altered by the life time exposure to estrogen and such an exposure have a neuroprotective effect on the progression of primary open-angle glaucoma [19].

d. The brain

Estrogen also improves communication between neurons in the brain area of hippocampus, that is important for verbal memory. Estrogen receptors are present in women's brain cells, and the hormone has a nourishing and protecting role in the CNS. It also protects emotional well-being, anxiety and depression results when it plummets during menopause. Its neuroprotective effects are confirmed by its healing of brain after a stroke or traumatic brain injury and helping against degeneration leading to cognitive decline and dementia. Imbalance of estrogen levels results in many brain disorders, like Alzheimer's disease, autoimmune disorders and stroke. New drugs to target the hypothalamus might someday be the key to treatment. Sleep, though a function of the brain, is regulated by different conditions. Our studies have shown earlier that there is an inverse relationship between estrogen and the hormone melatonin which aids sleep [20]. Hence, menstruating and menopausal women suffer from sleep disorders [21].

e. Immunity

Estrogen influences our immunity by stimulating the production of immune-boosting cytokines which can protect us against certain autoimmune diseases, and curb the expression of Caspase-12, an enzyme that hinders the body's defense system against bacteria and viruses. Research suggest that during menopause due to declining estrogen an increase of inflammation takes place. Estrogen acts as anti-inflammatory and decreases the inflammation during other periods. This change can occur during any stage

of menopause. Estrogen influences our immunity by stimulating the production of immune-boosting cytokines which can protect us against certain autoimmune diseases, and curb the expression of Caspase-12, an enzyme that hinders the body's defense system against bacteria and viruses [22, 23].

f. The Heart and Circulatory System

Physiologically, estrogen regulates cholesterol levels [24] and a balance between estrogen and other sex hormones is needed for the human body for good health and sexual development. Disproportion of estrogen in the human body increases the risk of blood clots, leading to stroke, a heart attack, and even death. Declining estrogen levels cause an increase in LDL cholesterol and decrease in HDL cholesterol, resulting in fat and cholesterol build up along the arteries, which contribute to heart attack and stroke. It also makes heart and blood vessels stiff and less elastic leading to increase in blood pressure, which may damage blood vessels and cause the risk of stroke, heart disease and heart failure, suggesting decrease in estrogen's protective effect on the cardiovascular system [25]. Estrogen receptors ER-alpha and ER-beta mediate the direct and indirect effects of estrogens on the cardiovascular system [26]. The direct effects of estrogen occur through rapid nongenomic and longer-term genomic pathways by activation of endothelial nitric oxide synthase, causing arterial vasodilation. Long-term effects make changes in gene and protein expression, modulating the response to injury and atherosclerosis. The indirect effects of estrogen influence serum lipoprotein and triglyceride profiles, and the expression of coagulant and fibrinolytic proteins. Some of the protective effects of estrogens may be attenuated by advanced atherosclerosis and certain progestins. Women with premature menopause should be informed about likely development of heart failure or atrial fibrillation than their peers.

The fall in estrogen levels during perimenopause makes women more susceptible to circulatory problems. Poor blood circulation may cause leg pain and contribute to more severe problems, such as severe leg swelling, varicose veins, and restless leg syndrome. Estrogen Levels Tied to Risk for Sudden Cardiac Death [27].

g. Cause of Cancers

Certain cancers are caused by estrogen and hence, it acts like a carcinogen [28]; it increases the risk of certain cancers, specifically breast, uterine and vaginal cancers. They rely on estrogen to develop and grow [29].

The use of estrogen hormone therapy, though beneficial for menopausal symptoms like hot flashes, night sweats, and vaginal dryness, its use for treatment of these symptoms may increase the risk of estrogen-dependent cancers. Its use alone may increase the risk of uterine cancer and combination hormone therapy (estrogen and progesterone) is less likely to cause uterine cancer [30].

The breast cancer drug, tamoxifen, decreases the risk of breast cancer and its recurrence. It's a selective estrogen receptor modulator (SERM) that blocks estrogen's effects on breast tissue. In menopausal women, it acts like estrogen in the uterus [31] stimulating the growth of the uterine lining and hence increasing the endometrial cancer risk. However, there are less than 1% chances of developing endometrial cancer from tamoxifen per year. There's also a slightly higher risk of uterine sarcoma, a cancer that forms in uterine muscles or tissues.

h. Regulating Microbiota

The level of circulating estrogen via enterohepatic circulation is regulated by the gut microbiome. As well, estrogens regulate the gut-skin axis by increasing gut microbiome diversity to ensure the uptake of bile-excreted estrogen from the gut [32-34].

i. Other health conditions

Increased estrogen levels are associated with polycystic ovary syndrome (PCOS) [35], uterine fibroids [36], endometriosis, and insulin resistance. The positive role of estrogens in females v/s males was established during the recent pandemic of coronavirus. These differences raised possible therapeutic and protective actions of 17 β -estradiol against COVID-19 [37,38].

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Contribución de los autores :

Anthony Alvarez Morales: conducted the surveys and searched the bibliography. He chose the sampling method by selecting the study population and analyzed and discussed the content of the tables.

Yosniel Lugo Echevarría: he posed the objectives of the study, selected and triangulated the variables and carried out the translation into English and the final revision of the manuscript.

Anaisa León Mursuli: she helped fill out surveys and search for bibliography, performed statistical processing, calculated the arithmetic mean and standard deviation of the quantitative variables. She applied the Family Functioning Perception Test or FF-Sil Test.

Pedro Rolando López Rodríguez: Performed the statistical processing, calculated and interpreted the chi-square and associated variables according to Duncan's twelfth. He wrote the document.



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DOI:10.31579/2690-8794/212

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