Hormonal Management for Aging Females

Yaşlanan Kadınlarda Hormon Kontrolü

Merih BAYRAM[a]

[a]Kadın Hastalıkları ve Doğum AD,
Gazi Üniversitesi Tıp Fakültesi,
ANKARA

Yazışma Adresi/*Correspondence:*
Merih BAYRAM
Gazi Üniversitesi Tıp Fakültesi,
Kadın Hastalıkları ve Doğum AD,
ANKARA
mbayram@gazi.edu.tr

ABSTRACT Ovarian senescence , a gradual process of decreasing in ovarian function that begins at around 35 years of age and reaches its culmination at the menopause at about 51 years of age is evidenced by a progressive decline in fecundity and increases in spontaneous miscarriages and menstrual irregularities in the second half of the 4th decade of life and the years that follow. The consequences of ovarian ageing and resulting estrogen deprivation have many phenotypic effects on tissue regeneration and maintenance. Collagen homeostasis in skin, bone and supportive ligaments of generative tract is generally affected. Epithelial thinness of the vagina and bladder trigone result in dyspareunia associated with vaginal dryness and urinary urgency and frequency, respectively. Neural plasticity and neural transmission are other vulnerable targets of estrogen deficiency and may result in irritability, depressive moods, insomnia, poor concentration and declining memory. Estrogen induces nitric oxide synthase and improves lipoprotein metabolism, which are fundamental mechanisms in promoting a healthy arterial tree. The earlier the age at which menopause occurs, the more profound its effects on the incidence of cognitive impairment and indeed on the incidence of coronary heart disease. The diagnosis and management of ovarian senescence is highly easy and effective with individualised hormonal replacement. Although comorbidity of ovarian senescence (stroke, coronary disease, dyslipidemia, dementia, osteoporosis,diabetes) is more harmful than breast cancer, risk/benefit relationship with HRT should be analyzed comprehensively.

Key Words: Female senescence, quality life, HRT

ÖZET Overin yaşlanması , 35 yaşlarında başlayan 51 yaşlarında menapoz ile sonuçlanan over fonksiyonlarında kademeli bir azalma sonucu yaşamın 4. dekat ikinci yarısı ve sonrasında düşük doğurganlık,yüksek spontan düşük ve mensturasyon bozuklukları ile karakterize yaşam değişiminin fizyopatolojik adıdır. Over yaşlanması sonucu gelişen östrojen düşüklüğü doku rejenerasyonu ve idamesi üzerinde fenotipik bir çok etkiye sahiptir.Genel olarak deri, kemik ve üreme sistemi destek bağlarında kollajen homeostasisi bozulur.Vajina ve mesane trigon epitelinde incelmeye bağlı vajinal kuruluk, disparonia, sık ve ağrılı idrar yapma olur. İrritabilite, depresyon, uykusuzluk, konsantrasyon eksikliği ve unutkanlığa neden olabilen nöral plastisite ve transmisyon östrojen eksikliğinin hassas diğer bir etkisidir.Sağlıklı bir arteriel sistemin gelişmesinde önemli mekanizmalar olan östrojen ile nitrik oksit sentaz stimülasyonu ve lipoprotein metabolizması üzerindeki olumlu etki azalır. Overin yaşlanması ne kadar erken yaşda olur ise algılama ve koroner arter hastalığı üzerindeki etkileri de o kadar fazla olur. Over yaşlılığında tanı kolay ve tedavi bireysel hormon replasman tedavisi ile oldukca etkindir. Over yaşlılığında komorbidite (inme, koroner hastalığı, dislipidemi, demans, osteoporoz ve diabet) her ne kadar meme kanserinden daha zararlı ise de HRT'nin kar/zarar ilşkisi tedavide tümüyle dikkate alınmalıdır.

Anahtar Kelimeler: Kadında yaşlanma, yaşam kalitesi, HRT

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Ovarian senescence is a gradual process that begins at around 35 years of age and reaches its culmination at the menopause at about 51 years of age. This decreasing in function is evidenced by a progressive decline in fecundity and increases in spontaneous miscarriages and menstrual irregularities in the second half of the 4th decade of life and the years that follow. The consequences of ovarian ageing and resulting estrogen deprivation have many phenotypic effects on tissue regeneration and maintenance.[1] Collagen homeostasis in skin, bone and supportive ligaments of generative tract is generally affected. Epithelial thinness of the vagina and bladder trigone result in dyspareunia associated with vaginal dryness and urinary urgency and frequency, respectively. Neural plasticity and neural transmission are other vulnerable targets of estrogen deficiency and may result in irritability, depressive moods, insomnia, poor concentration and declining memory. The earlier the age at which menopause occurs, the more profound its effects on the incidence of cognitive impairment and indeed on the incidence of coronary heart disease.

Estrogen induces nitric oxide synthase and improves lipoprotein metabolism, which are fundamental mechanisms in promoting a healthy arterial tree. The menapouse and its management have attracted a great deal of interest in the last century for a number of reasons. Increasing number of women who are being exposed to long term estrogen deficiency, definitions for quality of life and general wellbeing have been underlined by high expectations. The present perimenopausal population adopts the anti-ageing culture and turns away from strictly biologistic, negative, and ageist ideas.

The diagnosis of the menopause is easy and its management with individualised hormonal replacement is highly effective.

a) Estrogen deficiency: pathophysiology and semptomatology

The gradual decline in ovarian estrogen production in the years prior to the complete cessation of menstruation;

-Fewer granulosa cells being generated

-Less effective synthesis of estradiol per growing follicle

-Less inhibin production reduced negative feedback on FSH release

-At the menopause, a dramatic decline in plasma estradiol level occurs. Postmenopausal ovary cease to contribute to estradiol levels in blood. Peripheral conversion of androstenedione into estrone becomes prominent. 5% of thus formed estrone is converted to estradiol through the action of 17 beta hydroxysteroid dehydrogenase.[2]

b) Androgen deficiency: pathophysiology and semptomatology:

-Dehydroepiandrosterone (DHEA) is produced in both the ovaries and the adrenal glands under the influence of luteinising hormone and adrenocorticotropic hormone

-DHEAS is exclusively produced by the adrenal glands and is converted to DHEA by steroid sulphatase. Their declining plasma levels are due to age-related reduced steroid synthesizing capasity of the zona reticularis and due to ovarian ageing.[3]

In a recent study, the results revealed that approximately 37% of the African-American women died from comorbid conditionsinstead of breast cancer, while only 32% of the Caucasian women died from comorbid conditions instead of breast cancer. The researchers found that the two most common comorbid conditions among the women were diabetes and hypertension.[4]

HRT and beneficial effects:

There may be benefits in taking this medication that reduce the risk of comorbid diseases shown to be more harmful from this perspective, than breast cancer. Some studies have shown that ERT in hysterctomyzed women or short-term use of CHRT for less than 5 years in women with an intact uterus carries no increased risk for breast cancer.

HRT for its possible benefits:

Related findings demonstrate that CHRT is an effective way to manage unwanted postmenopausal symptoms and to prevent long-term health problems such as stroke, coronary disease, dyslipidemia, dementia, and osteoporosis. To reduce risks for osteoporosis, improve glycohemoglobin, improve cardiovaskuler health, reduce risks for colorectal cancer, and in treatment of hot flashes. ERT promoted better glysemic control in type II diabetics.[6] Reduction of HbA1c has been shown to reduce other comorbid complications related to diabetes.5 Evaluated cardiovascular benefits of both ERT and CHRT in postmenopausal women:[7]

-Lowered circulating norepineprine

-Lowered blood pressure

-Lowered cholesterol levels, specificially low-density lipoprotein (LDL) levels while increasing high-density lipoprotein (HDL) levels

Effects of menopause on quality of life:

-Hot flushes were the most common complaint 98%

-Sleep disturbances 77%

-Mood swings 69%

-Vaginal dryness 51%

-Atrophic vaginitis is one of the many unpleasant effects associated with estrogen decline.[8]

Harmfull effects of HRT:[9]

-The deep vein thrombosis risk is increased with HR=1.47 in the whole population

-Significant decrease in women's desire, arousal, orgasm and frequency of sexual activity, and a significant increase in vaginal dryness/dyspareunia with a rate of sexual dysfunction that ranged from 42% to 88% throughout the menopausal transition. Both age and declining estradiol levels have significant detrimental effects on sexual functioning, desire and sexual responsiveness.10 Testosteron levels are relative effects of hormonal and relationship factors in sexual function during the natural menopausal transition. The minimum effective dose of estradiol needed to increase sexual response by 10% (700 pmol1-1) is twice that needed to decrease dyspareunia, supporting the notion that other hormonally mediated mechanisms, modulating physical and mental well-being are involved in sexual functioning across the menopause transition.

Treatment with testosterone:

Many of the concerns about potential risks and side effects of testosterone treatment for women are a result of problems that had been documented in women in hyperandrogenic status. Appropriate assessment of long-term safety of the new testosterone preparations specifially designed for women is difficult.[11] The most commonly reported side effects of testosterone treatment in women are dose related androgenic skin problems-hirsutismus. In the large 300 μg/day testosterone transdermal patch trials, androgenic adverse event are similar in the placebo and testosterone groups. There is non-significant increase in unwanted hair growth.[12] Testosterone treatment in low-dose regimens has beneficial effects on many facets of sexuality, including desire, arousal, orgasm and responsiveness, as well as frequency and satisfaction.[13]

Changes in urogenital tract in menopause:

Estrogen and progesterone receptors are found throughout the urogenital tract and are sensitive to any hormonal changes occuring around the menopause. Estrogen deficiency after the menopause causes atrophic changes. The vaginal epithelium becomes thin and loses its rugae and pale or erythematous with fine petesial hemorrhages. An increase in vaginal pH, due to lower production of lactic acid, permits the growth of pathogens. Vaginal and cervical secretions also decrease, leading to reduce lubrication during sexual arousal.[14]

Treatment with estrogen:

Estrogen therapy, improves the symptoms of urgency but has a lesser effect on stress incontinans. Maintaining patients' quality of life requires a holistic vision of each woman's problems, especially in this society where appereance, age and ageing are of utmost importance.[15]

The most common osteoporotic fractures are those of the hip, spine, and wrist. Hip fracture incidence is assumed to be reduced by 75% for women treated with either HRT regimen.

The influence of hormone replacement therapy on breast cancer incidence remains uncertain. Unopposed estrogen use is associated with an increased risk of breast cancer, which increases with duration of use.

Epidemiological studies have consistently found that unopposed estrogen use is associated with lower risk of coronary heart disease. A 35% risk reduction in coronary heart incidence is assumed and the benefit of treatment continues for only 2 years beyond termination of therapy.

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