

## Effect of Low Estrogen Hormone Level on Women in Menopause

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### **Abstract:**

Menopause is defined as the time of the last menstrual period which is followed by 12 months of amenorrhea. Menopause is a time in which hormonal fluctuations occur in the females` body. Estrogen is responsible for many mechanisms inside the body. The symptomatic changes begin since the perimenopause transition till the permanent cessation of menstrual cycle. Ovaries are the only source of estrogen and progesterone. Any surgical interfere or hanging of ovaries cause inappropriate estrogen production. There many risk factors that enhance an earlier menopause as toxic factors like smoking, being exposed to surgery on their ovaries or having a hysterectomy and exposure of retention of their ovaries also experience early menopause.

Main health concerns of menopausal women involve vasomotor symptoms, urogenital atrophy, osteoporosis, cardiovascular disease, cancer, psychiatric symptoms, cognitive decline and sexual problems. 75% of peri-menopausal women are affected with vasomotor symptoms.

The main sign that women are seeking for care and treatment is “Hot Flushes”. Women are suffering from hot flushes during sleep, at work and when doing their daily activities. This symptomatic change results in vaginal dryness, pruritus, dyspareunia, dysuria, and urinary urgency.

The cause behind this symptom is the reduced level of estrogen which cause reduced production of vaginal secretions that lubricants and moisturizes vagina. Women in menopausal period suffer from group of musculoskeletal symptoms, as backache, bone fractures on minimal trauma, the body height and mobility are decreased due to common cause which is osteoporosis. Although depression is not a common sign in menopause but in found to be relevant in 20% of menopausal women. Female sexual dysfunction after menopause is a complex problem with different reasons.

Hormone Replacement Therapy (HRT) is found to be effective in treating most of the menopausal symptoms. SSRI medications is found to be useful in treating depression-related menopause. Combination between calcium, vitamin D and HT is found to be very useful in preventing osteoporosis if started soon after menopause onset and used in long-term. Changing women lifestyle from time to another is very important to avoid depression, anxiety and to initiate sexual interest or desire. Also, using of vaginal lubricants is effective in relieving sexual activity uncomfortable.

**Keywords:** Estrogen Hormone, Hormone Level, Women, Menopause.

## **Introduction**

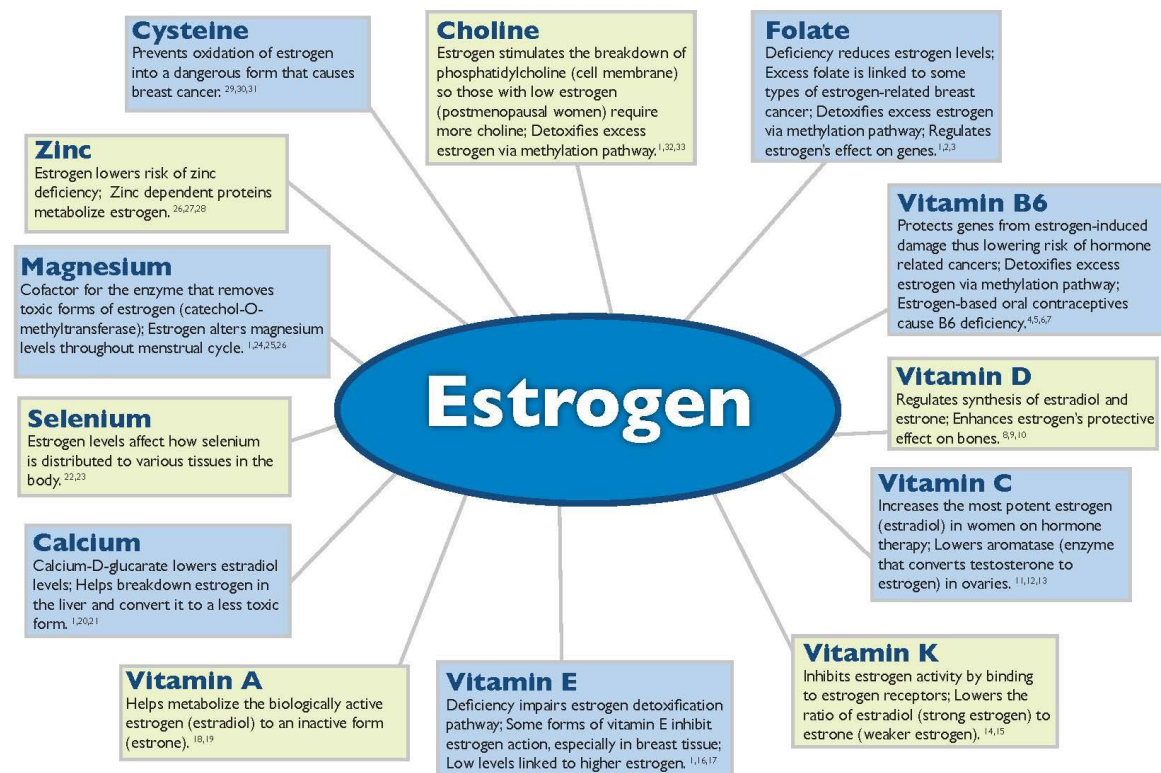
Menopause is one of the most important events in the women`s life in which it makes several permanent physiological changes in the woman. There are many symptoms which occur before, during and after the onset of menopause. The symptoms are called “post-menopausal syndrome”. These symptomatic changes had become a focus spot of researches recently. Menopause is defined as the permanent cessation of menstruation cycle of a woman, which results in the loss of ovarian follicle development.

The range of age which appears to be genetically controlled is not affected by race, socioeconomic status, age at menarche, or number of previous ovulations. There many risk factors that enhance an earlier menopause as toxic factors like smoking, being exposed to surgery on their ovaries or having a hysterectomy and exposure of retention of their ovaries also experience early menopause. Premature ovarian failure is the process of menopause before age of 40 years old and caused by idiopathic factors, toxic exposure, chromosomal abnormality or autoimmune disorders. [1]

Menstrual cycle is regulated by hypothalamus and pituitary glands. Pituitary hormones include two main ovary-regulating hormones which are follicle-stimulating hormone (FSH) and luteinizing hormone (LH). So, menopause is associated with hypothalamic and pituitary hormones changes which causes primary ovarian failure, which in return leads to ovarian follicles depletion. The ovary become no longer responding to FSH and LH. Also, the ovary stops its androgens production, which are ovarian estrogen and progesterone. Ovary androgen production continues beyond the menopausal transition due to sparing of the stromal compartment. Menopausal women have low estrogen hormone levels, especially from peripheral aromatization of ovarian and adrenal androgens. Because of the main site of aromatization is in the adipose tissue, so obesity affects clearly in menopause sequelae. [1]

The ovarian-hypothalamic-pituitary axis still in contact in the period of menopausal transition, which is called also perimenopause. Perimenopause is the period between onset of irregular menstrual cycles till the last occurred menstrual cycle. This transition is characterized by reproductive hormones fluctuation with different menstrual cycle length and missed menses. When ovarian failure occurs, FSH level increases and still elevated due to absence of the negative feedback of the ovary. Decreased level of estrogen and inhibin production due to follicular system atresia (especially granulosa cells). The reduced levels of inhibin and estrogen, and the increased level of FSH are the cardinal signs of menopause. Decreased estrogen levels in time of menopausal transition is characterized also by menstrual irregularities, prolonged and heavy menstruation intermixed with episodes of amenorrhea, decreased fertility, vasomotor symptoms and insomnia. These symptoms may emerge and continue for 4 years before the last menstrual cycle. [1]

The major consequences of menopause are deficiency of estrogen production. The increased chance of endometrial proliferation is due to decreased or no progesterone production. The other consequences of decreased progesterone are hyperplasia, and cancer associated with continued endogenous estrogen production. Main health concerns of menopausal women involve vasomotor symptoms, urogenital atrophy, osteoporosis, cardiovascular disease, cancer, psychiatric symptoms, cognitive decline and sexual problems. Many other symptoms are found in relation to postmenopausal syndrome, which include hot flashes, irritability, mood swings, dry vagina, difficulty concentrating, mental confusion, stress incontinence, urge incontinence, osteoporotic symptoms, depression, headache, vasomotor symptoms, and insomnia. Figure (1) shows what happens to other body elements and nutrients in case of estrogen deficiency. [1][2]



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Figure (1): Nutrient correlation wheel of estrogen. [2]

## Statement of the Problem

The problem of the research is the symptomatic changes which the women face in the period of menopause due to sharp decrease of estrogen hormone level produced from ovaries. This physiological and psychological changes are of great concern recently in research field. Although many women are having medications and supplements to avoid these changes, but they still suffer from such signs.

## Objectives

The research aims to focus on these main points:

- 1- Definition of menopausal transition.
- 2- Discuss the main physiological changes occur in menopause.
- 3- Mechanism of action of low ovarian estrogen level.
- 4- Complications of low circulating estrogen level on female`s body.
- 5- Recommendations for the woman to prevent or reduce the physiological and psychological effects of menopause.

## Study Questions

In this research, the researcher is answering the following questions:

- 1- What is the meaning of menopause?
- 2- How can low estrogen level affect negatively on the females?
- 3- What are the symptoms of menopausal transition?
- 4- What are the risk factors affecting on onset of menopause?
- 5- How can the woman avoid the changes?

## Discussion

In this part, we are discussing the main menopausal symptoms affecting almost all women. The symptoms are occurring mainly due to the reduced estrogen production from ovaries, so sharp decrease of circulating estrogen happens.

The symptoms are: Vasomotor symptoms, Urogenital atrophy, Osteoporosis, Depression, Cognitive functions, Sexual dysfunction, Problems with sleep and course of some important psychiatric disorders during menopause. Psychiatric disorders include schizophrenia, bipolar disorder, panic disorder and obsessive-compulsive disorder (OCD).

#### **A- Vasomotor Symptoms:**

75% of peri-menopausal women are affected with vasomotor symptoms. The symptoms can last for 1-2 years after onset of menopause in most of women and may continue for up to 10 years or longer in some women. The main sign that women are seeking for care and treatment is “Hot Flashes”. Women are suffering from hot flushes during sleep, at work and when doing their daily activities. Difficulties in concentration and emotional lability are also other signs of vasomotor symptoms. Treatment of vasomotor symptoms should improve these cognitive and mood symptoms if they are secondary signs to sleep disruption and daytime fatigue. At this time, the prevalence of thyroid diseases increases, so thyroid function tests should be performed. [1][3]

Mechanism of action of the hot flushes and what role that estrogen exactly plays in modulating these effects are unknown clearly, but it is known that these vasomotor effects are resulting from estrogen withdrawal not only estrogen deficiency. Many previous researches have supposed that the hypothalamus is the initial cause of these symptoms, in which noradrenergic, serotonergic or dopaminergic activation results in increased body temperature, metabolic rate and skin temperature ending with peripheral vasodilation and sweating in some women. [1]

Treatment this symptom includes systemic estrogen therapy, which is the most effective therapy available for vasomotor signs and showed great effect in relieving such symptoms. Oral contraceptives are beneficial solution for women in peri-menopausal transition (women who still menstruating but having hot flushes) or menopausal women. Low dose of oral esterified estrogen is effective. Selective serotonin reuptake inhibitors (SSRIs) also are effective in relieving hot flushes, as intake of paroxetine (12.5 and 25mg/day). Obese women and smokers have more severe vasomotor symptoms. [1]

### ***B- Urogenital Atrophy:***

This symptomatic change results in vaginal dryness, pruritus, dyspareunia, dysuria, and urinary urgency. Fortunately, these problems are responding good to systemic estrogen therapy. When peptic absorption is low, topical estradiol is recommended. Low-doses of estrogen cream (0.5g/1-3 times/week) are effective. Or, an estradiol vaginal tablet (25µg/twice/week), which may be less messy and easier to use than estrogen cream. Pay attention that vaginal lubricants are non-hormonal alternative to relief the intercourse discomfort. The cause behind this symptom is the reduced level of estrogen which cause reduced production of vaginal secretions that lubricants and moisturizes vagina. [1]

### ***C- Osteoporosis:***

Women in menopausal period suffer from group of musculoskeletal symptoms, as backache, bone fractures on minimal trauma, the body height and mobility are decreased due to common cause which is osteoporosis. Anovulation during the reproductive years (due to excess of exercising or an eating disorder), hyperthyroidism, hyperparathyroidism, chronic renal disease and diseases which require systemic corticosteroid use in its treatment, are all medical conditions increase the risk of osteoporosis in women in menopause. Treatment includes adequate intake of calcium and vitamin D. Hormone Therapy (HT) as estrogen therapy, is found to be effective in treating and preventing osteoporosis. It was found to reduce osteoporosis-related fractures by 50%. The latest researches shows that even very-low-dose estrogen therapy (as estradiol 0.25 mg/day, conjugated equine estrogen 0.3 mg/day with MPA 1.5 mg/day or transdermal estradiol 0.025 mg/day) in combination with calcium and vitamin D can produce significant advances in bone mineral density. [1]

### ***D- Depression:***

Although depression is not a common sign in menopause but in found to be relevant in 20% of menopausal women. A cohort study showed depressive symptoms increased during the menopausal transition and decreased after menopause.

The depressed mood is associated with reproductive hormone fluctuations, especially estrogen hormone. Depression mechanism of action is related strongly with fluctuating and decreased estrogen levels in peri- menopause and post-menopause respectively. Estrogen works by several mechanisms in the Central Nervous System (CNS), as it is stimulating the neurotransmitters synthesis, the expression of receptors and influencing the membrane permeability. Estrogen increases serotonin synthesis and norepinephrine activity in the brain. Serotonin and norepinephrine are thought to be the neurotransmitters which control motivation of depression in their reduction levels. Estrogen also decreases monoamine oxidase (MAO) activity, MAO responsible for breakdown of serotonin and norepinephrine in CNS, which leads to reduced degradation of both neurotransmitters, preventing depression prevalence. So, fluctuating or decreased estrogen levels clearly effects on serotonin and norepinephrine actions and uptake by their receptors. [1]

The risk of depression appears to be higher during perimenopause in which hormone levels are changing, than during post-menopause when estrogen and progesterone levels are low, but stable. Life stressors play an important role in controlling or directing the onset of depression, especially in menopausal transition. Life stressors that women can have include the following: [1]

1. Negative mood before menopause.
2. Negative behavior toward menopause and aging.
3. Smoking.
4. Lack of exercising.
5. No partner (single, widowed or divorced).
6. Poor self-perceived health.
7. Negative feelings toward partner.
8. Interpersonal stress or problems.
9. Care of aging parents.

Treatment of major depression involves standard antidepressants such as SSRIs, which is mostly used in treating perimenopausal depression syndrome. SSRIs is known to be safe and effective in treating such cases. Its effect begins after 4 to 6 weeks.



For mild depression, Hormone Replacement Therapy (HRT) alone may be appropriate. Estrogen is used when patients refuse psychic medications or fail in its action, or in cases which have significant vasomotor symptoms. [1]

#### ***E- Cognitive Difficulties:***

The relationship between the menopause transition and cognitive difficulties in some women suggests that cognitive disturbance may be related to the hormonal changes of the menopause. Memory problems are the most common cognitive complaints in perimenopausal transition and lately post-menopausal women. HRT had showed great advance in treating cognitive difficulties. There are specific cognitive functions that may be altered, as attention, verbal memory and learning capacity. In addition, menopausal women are at higher risk of developing Alzheimer disease, using of HT is found to decrease that risk. [1]

#### ***F- Sexual Dysfunction:***

Most of women are facing problems during sexual activity in after menopause, in which it doesn't have an exact reason for happening. Female sexual dysfunction after menopause is a complex problem with different reasons. Decreased sexual desire or interest and decreased ability to reach orgasm are the main signs of sexual dysfunction. The etiology includes psychological and physiological problems. [1]

### **Recommendations**

After visiting the physician or psychiatrist, there are some recommendations for peri-menopausal and post-menopausal women that should follow or consider to relief and avoid the symptoms of perimenopause and post-menopause side effects: [1][3]

- 1- Women should perform thyroid function tests to avoid atypical vasomotor signs, or resistant to treatment.
- 2- "Systemic Estrogen Therapy" is provided for women in menopause or peri-menopausal transition to relief vasomotor signs.

Very low dosage of oral esterified and conjugated estrogens (0.3mg/day), or transdermal estradiol (0.025mg/week), with minimal side effects and endometrial stimulation.

- 3- “Progestin Therapy” must be given beside low dose of estrogen, if a woman has not had a hysterectomy. Medroxyprogesterone acetate (MPA) (20 mg/day) and megestrol acetate (20 mg/twice/day) effectively treat vasomotor symptoms.
- 4- It's very important to advise women about making bone mineral density screening (calcium density) for high-risk women of osteoporosis.
- 5- Osteoporotic women should consider suitable intake of calcium and vitamin D in order to compensate the occurred osteoporosis and to avoid the musculoskeletal signs. In addition to that, smoking cessation, regular exercise and changing a sedentary lifestyle, in which is called changing the modifiable risk factors, may be helpful in reducing risk of osteoporosis.
- 6- Women should receive 1000–1500 mg of calcium and 400–800 IU of vitamin D daily through both healthy diet and mineral supplementation.
- 7- Combination between calcium, vitamin D and HT is found to be very useful in preventing osteoporosis if started soon after menopause onset and used in long-term.
- 8- SSRIs medications is found to be useful in treating depression-related menopause. Estrogen may be used in combination with SSRIs to gain significant effect in perimenopausal women.
- 9- Changing women lifestyle from time to another is very important to avoid depression, anxiety and to initiate sexual interest or desire. Also, using of vaginal lubricants is effective in relieving sexual activity uncomfortable.
- 10- Androgen therapy is very helpful in cases of sexual dysfunction. Estrogen therapy (in form of local or systemic vaginal estrogen) is used for eliminating dyspareunia and may improve sexual arousal and response, in addition to doses of intramuscular testosterone are used to increase sexual desire and orgasm.

## Conclusion

Decreased levels of estrogen can produce variety of health concerns and symptoms. Estrogen are produced only from ovaries of women. Eating disorders such as anorexia can affect negatively on estrogen level production, so those women are at higher risk to reach menopause early. There are several reasons for estrogen level declining, which are thyroid disorders that are affecting on metabolism, excessive exercise that consume the body, premature ovarian failure, chemotherapy, low-functioning pituitary gland and congenital diseases. Deficiency of estrogen lead to irregular periods, infertility, weak bones, painful sexual activity, hot flushes, increased urinary tract infections, cognitive difficulties, and depression. [4]

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