Probable Consequences of Menopause on body tissues and systems

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Abstract: Menopause, by definition, is the final menstrual period. It is a universal and irreversible part of the overall aging process as it involves a woman’s reproductive system. It is diagnosed after 12 months of amenorrhea and myriad of symptoms characterizing it. These include, among others, changes from regular, predictable menses; vasomotor and urogenital symptoms such as vaginal dryness, dyspareunia, sleep and mood dysfunction (Butler and Santoro, 2011; Santoro and Randolph, 2011). In this review we explored the physiology of menopause before dissecting its effects on other parts of the body.

Keywords: Menopause, dyspareunia, vaginal dryness, vasomotor and urogenital symptoms.

I. Physiology of Menopause

Menopause results from loss of ovarian sensitivity to gonadotropin stimulation, which is directly related to follicular attrition. The oocytes in the ovaries undergo atresia leading to a decline in both the quantity and the quality of follicles. Thus, the variable menstrual cycle length during the menopausal transition (MT) is due more to a shrinking follicle cohort size than to follicle failure. Anovulatory cycles and absence of cyclicity become common, with a highly variable pattern of gonadotropin and steroid hormone production, estrogen insensitivity, failure of the luteinizing hormone (LH) surge, the occurrence of the final menstrual period, and permanent amenorrhea (Butler and Santoro, 2011).

Hormonal fluctuation may not account for all irregular bleeding at this time (Ponjola, 2014). Uterine fibroids, uterine polyps, endometrial hyperplasia, or cancer become more prevalent at this age and must be ruled out. During the 5th decade of life, many women think that they are no longer fertile because they are so close to menopause. Although fertility declines, pregnancy can still occur as evidenced by a relatively high rate of unintended pregnancies in women aged 40-44 years. In fact, the number of unintended pregnancies in this age group has increased over the past decade (Henshow, 1998). Since functional follicles, which are stimulated by follicle-stimulating hormone (FSH) during the first part of the menstrual cycle decline in number, less recruitment of oocytes occurs, and follicular phase shortens. Once ovulation occurs, the luteal phase remains fairly constant, at 14 days.

Over time, as aging follicles become more resistant to gonadotropin stimulation, circulating FSH and LH levels increase. Increased levels of FSH and LH levels lead to stromal stimulation of the ovary, leading to increase in estrone levels and a decrease in estradiol levels. Levels of inhibins also drop during this period due to negative feedback of elevated FSH levels (Santoro and Randolph, 2011; Lanton et al, 1991).

II. Hormonal Changes in Menopause

With onset of menopause and loss of follicular function, there are significant changes in hormonal profile. These include:

- A dramatic decrease in circulating estradiol over a period of four years (starting 2 years before the final last menstrual period and stabilizing about 2 years after the final period).
- The level of estrone increases and becomes the major source of circulating estrogen in postmenopausal women.
- Total serum testosterone levels do not change during menopausal transition (MT). The dehydroepiandrosterone (DHEAS) levels do decline with age. A trend towards higher total cholesterol, low density lipoprotein (LDL) and apolipoproteinB levels in conjunction with loss of protective effect of high density lipoprotein (HDL) is characteristic in menopause (Smith and Judd, 1994).
III. The Urogenital System and Menopause

With loss of estrogen, the vaginal epithelium becomes redder as the epithelial layer thins and the smaller capillaries below the surface are more visible. Capillary number reduces further as vaginal epithelium atrophies, making the surface pale.

Malodorous discharge with pruritus results from bacterial flora colonization due to decrease in urine and vaginal pH. There is also reduced ruggeration with smooth vaginal wall. This leads to insertion dyspareunia which leads to sexual abstinence in some women if not treated. Within the pelvis, the uterus atrophies. Fibroids, if present become less symptomatic and can shrink. With the onset of menopause, endometriosis and adenomyosis are alleviated and so women with pelvic pain may achieve permanent relief.

There is general loss of pelvic muscle tone which may manifest as prolapse of reproductive or urinary tract organs.

In September 2013, The North American Menopause Society (NAMS) updated and expanded its recommendations concerning symptomatic vulvo-vaginal atrophy (VVA) in post menopausal women (Harding, 2013; NAMS, 2013). NAMS noted the following:

- vaginal micro-flora affect VVA symptom
- Therapy is based on the symptom severity and preference.
- Estrogen remains the most effective therapy for symptomatic VVA.
Atrophic cystitis, if present can mimic UTI. Women may report urinary frequency, urgency and incontinence. Atrophic cystitis renders the women more prone to UTI (Samantha, 2008).

Effects of Menopause on Bone

The main effect here is osteoporosis defined as a bone mineral density (BMD) greater than or equal to 2.5 standard deviation below the peak bone mass or T scores. Osteopenia is defined as a BMD that is 1.0-2.49 SDs below the T score (WHO Study Group, 1994). Grady and Cummings (2001), found a 27% reduction of non vertebral fractures in older women on hormone therapy. For hip and wrist fractures, the risk reduction was 40%, increasing to 55% in women less than 60 years. Data from Women`s Health Initiative (WHI) also demonstrated decreased bone fracture in these women.

The onset of menopause leads to rapid loss of BMD because bone resorption is accelerated while formation continues at the premenopausal rate. Trabecular bone is affected more than cortical bones hence bone loss is commoner at vertebral, coaxial and radial sites. Bone loss few years after onset of menopause may be as high as 20% of lifetime loss (Grady and Cumming, 2001).

IV. Risk Factors for Osteoporosis in Menopause

The overall effect of menopausal bone loss is reduction in bone strength leading to pathological fractures. However, there are risk factors for the development of osteoporosis and osteopenia in menopausal women. These include:

- BMD: The lower the woman’s bone mass at menopause, the more, the severity of the osteoporosis.
- Race: osteoporosis is more in whites than in Africans. It is least severe in women with dark complexion.
- Low serum estrogen
- Female sex
- Low serum androgen
- Smoking
- Physical inactivity
- Low body weight
- Little exposure to sunlight.

V. Menopause and Breast Cancer

Some studies have shown an increased risk of breast cancer with postmenopausal estrogen use; others showed a decrease (Rossouw et al, 2002). A possible link to cancer is also suggested by finding that breast cancer risk increased in women with early age at menarche and later age at menopause. However, a reduction in risk is observed with early age at pregnancy and interruption of menstrual hormonal changes. The role of estrogen in the development of breast cancer continues to be studied (Ponjola, 2014).

In women`s Health Initiative (WHI) study, the incidence of breast cancer increased in the estrogen and progestin versus placebo arm of the study (38 vs 30 per 10,000 person years); however, the incidence of breast cancer decreased in the estrogen only versus placebo arm of
the) study (26 vs 33 per 10,000 person years) (Rossouw et al, 2002; Anderson et al, 2004).

Breast cancer incidence and mortality were increased in the estrogen and progestin groups as compared to the placebo group (Chlebowski et al, 2010).

Central Nervous System and Menopause

The association between estrogen and memory function is an interesting area of research. Current data suggest that Alzheimer disease (AD) is more common in women than in men, taking the longer average life span of women into account (Anderson et al, 1999). In earlier studies, estrogen therapy appeared to reduce the relative risk of AD or to delay its onset (Karas et al, 1997).

The menopausal transition (MT) is usually a time of depressive symptoms due to hormonal changes and changes in life circumstances. It occur secondary to effects such as estrogen-related sleep disturbance and vasomotor symptoms. However, major depression is associated with the female sex at all ages.

Menopause and the Skin

In menopause, estrogen affects every organ system of the body including the skin. It appears that estrogen receptors are most abundant around the genitalia, face and lower limbs. Therefore these areas are especially vulnerable to reduced amounts of circulating estrogen hence skin conditions in these areas are common in menopause (Wines and Willstead, 2001). These changes include: facial hirsutism, clalopecia in approximately 1/3 of post menopausal women, menopausal flushing in 70-85% of women throughout menopausal stage. Keratoderma climactericum in which the skin on the palms and soles are thickened especially in obese postmenopausal women.

Cardiovascular Diseases and Menopause

Coronary artery disease (CAD) is the leading cause of morbidity and mortality in men and postmenopausal women. In the United States, about half of all cardiovascular deaths among women are due to CAD (Ariyo et al, 2002). Menopause increases the risk for women still further, independent of age. Prior to menopause, the risk of CAD for women lags behind the risk for men by about 10 years; after menopause, it catches up. As a result, mortality from CAD rises in women. The Framingham study showed the relation between menopause and increased cardiovascular mortality (Kannel et al, 1976).

The beneficial effect of estrogen on cardiovascular mortality is due to many factors. One mechanism appears to be estrogen’s effects on lipid metabolism, which includes reducing low density lipoprotein (LDL) and increasing high density cholesterol (HDL). Studies have suggested that the best predictors of CAD in men and women are different (Assmann et al, 1998) and that triglycerides, HDL, and lipoprotein (a) may be more significant in women (Erikson et al, 1999).

Women with elevated lipoprotein (a) levels should be treated more aggressively. A relationship between estrogen therapy and reduction in cardiovascular risk has been demonstrated in many studies. The risk reduction in women on estrogen therapy may be similar to the risk reduction in those lipid-lowering Drugs (Darling et al, 1997).

Hypercholesterolaemia is a major factor in the pathophysiology of atherosclerosis (Igweh et al, 2003). Indeed, it has been shown that in postmenopausal period, women have less cardiovascular friendly lipid profiles than in premenopausal state (Dowling, 2001).

VI. Conclusion

Menopause, a natural phenomenon, affects various tissues and organs of the body. Its effect is wide reaching not only on the reproductive system even to the bones and most hit is the cardiovascular system and disease related, especially due to changes in lipid profiles. In this review we succinctly explain menopause effect on the urogenital, skin, bone, breast, CNS and the cardiovascular system. Earlier in this study, we explored the physiology of menopause and hormonal changes.

References

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