Guest Editorial I

MENOPAUSE—SKIN & COLLAGEN AND ROLE OF MHT

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'An Aging Society is evolving, Which, for the most Part, is Female'

The health outcomes of demographic aging in terms of improved survival and changing patterns of morbidity are the product of changes in underlying economic, social and cultural determinants of health. Demographic aging not only brings about major changes in the duration of life course stages, but also in the social experience of these stages. Of all these changes, the increase in women's life course after age 50 is the most obvious; it is also the change that presents most challenges in achieving quality of life (QoL) for aging women over these years.

Average life expectancy is increasing globally and so is number of midlife women. So, women have to live longer in midlife or postmenopause. But menopause is a retrospective diagnosis when women have final period followed by amenorrhea for 12 months. Then women enter into postmenopause. Menopause occurs because of ovarian depletion and leading onto a state of hypoestrogenism. Hormonal changes start much earlier at about 4 to 5 years before menopause and this period is called perimenopause or climacteric. Estrogen depletion is affecting a large number of functions and organs of body, including cardiovascular, urogenital and musculoskeletal system.

Skin changes are one of the earliest changes which worry a woman and which can be perceived by woman herself and by onlookers. This has become a big social issue and is now drawing lots of attention from the dermatologists and as gynecologists are the first touch points for the care of midlife women, they can help a woman in prevention of skin problem and their treatment wherever possible.

Time is Now to Plan Ahead for Healthy Aging

Skin care is one of the earliest care which women would most likely to comply along with other systems like weight control.

Changes in the skin are the first one perceived by women as fine wrinkles or sagging of skin or dryness of skin. As women are becoming more professional and working women, it has become a great QoL issues for women how they perceive themselves or how they appear to others. Care of skin and cosmetology has become a billion dollar industry and as gynecologist, we have to updated on issues related to aging of skin.

Issues involved are whether skin changes are because of aging only or because of hormonal status and whether hormone replacement can help women in midlife. It has been postulated and proved also that skin changes are not only because of extrinsic factors but rather seven determinants of aging have been postulated. These determinants of skin aging are age, genetics, photoaging, hormonal like pregnancy and menopause, chronic debilitating diseased like kidney failure and gravity, life style like smoking, drugs, alcohol.

Skin is affected by estrogens and various other hormones is because it has been documented by the detection of estrogen receptors in normal skin, acne and hirsutism.

In immunohistochemical studies, estrogen-binding sites are detectable in the basal keratinocytes, sebaceous glands and skin vessel endothelia, and in fibroblasts—structures that are involved in the aging process. Therefore, it may be assumed that the stimulating estrogen influences on the skin decrease with depletion of estrogen receptors and decreasing levels of estrogens starting from perimenopause itself.

Subjective reports, cohort studies, experimental studies and even a few randomized controlled trials (RCTs) point toward adverse effects of menopause because of hypoestrogenic state to be detrimental to aging skin in the form of wrinkles, age spots, hydration and thickness of skin. Collagen and elastin are responsible for tensile strength and elasticity of skin and hydration and thickness along with glycosaminoglycans (GAGS). Collagen represents 70 to 80% of the dry weight of human skin, being the largest dermal component and it forms 30% of the total protein content in the human body.

Collagen tissue is linearly decreasing with menopause and there has been observed 29% decrease in the first 5 years after menopause and going at the rate of 2.1% per year for about 15 years. Large number of collagen types

have been described to date, the most abundant and well-studied types are I, II and III. Type I accounts for 90% of the total collagen in the body of a mammal. It is synthesized by fibroblasts and osteoblasts and forms thick and strong fibers.

Photoaging is seen in the form of melanoderma, but endocrine factors because of estrogen reduction are seen as dermal thinning, laxity, withering and wrinkling, so photoaging is superimposed by hormonal changes.

Various investigators have studied menopausal skin in relation to menopause, photoaging and menopause, tensile strength of skin, thickness, elasticity of skin, hydration and found effect of menopause as negative and effect of menopause hormone therapy (MHT) as positive effect.

The noticeable age of individuals is largely perceived from the appearance of facial skin. On sun-exposed areas, the main characteristics of the aging process are commonly referred to as photoaging. Typically, there are progressive changes leading to mottled subclinical melanoderma, followed by progressive laxity, withering, and wrinkling of the skin. The deleterious effect of ultraviolet light on specific skin structures is beyond doubt. In addition; endocrine factors are clearly involved in the dermal thinning that occurs during estrogen reduction in the climacteric period. Hence, hormonal aging with impaired tissue trophicity is likely superimposed on the effects of chronic sun exposure during the global process of facial skin aging. In fact, increasing atrophic skin withering and loosening is commonly associated with coarse wrinkling at different skin sites during climacteric aging.

In perimenopause viscoelasticity of skin changes and can be measured by various means. Hormone replacement therapy in particular has the potential to correct the functional damage seen in dermal tensile strength. A number of methods can be used to assess specific characteristics of the skin. Most investigators use the suction method. Skin dispensability appears to increase during menopause regardless of whether the woman is on hormone replacement therapy. This was studied by GE Pierard and described in his study in details.

In experimental studies in mice, it was seen in mice, oophorectomy alone was sufficient to accelerate skin aging and increase sensitivity to ultraviolet radiation.

Ultraviolet rays exposure caused further deterioration of skin quality and increased wrinkling. So, this again highlights influence of photoaging.

Skin Changes with Aging

Estrogen deprivation has a negative effect on skin in the form of reduced skin thickness, reduced elasticity and reduced hydration and increased aging spots. These are mainly because of effect on collagen and elastin and extracellular matrix. Histopathological changes in skin correlate with clinical signs. There is reduced collagen and elastin and thickness of three layers of skin epidermis, dermis and hypodermis or subcutaneous tissue is decreased. Collagen fibers which are tightly packed bundles change into loose fibrils and number is decreased and so is number of fibroblasts which are precursors of collagen. Blood vessels have decreased lumen, so skin becomes pale.

Correlation with Other Tissues

Another important factor, which has emerged, is correlation of effect on skin and other organs, which have collagen like in carotids, bones and intervertebral disks.

This is similar to what happens in bone matrix. Similarly, the media in the carotid has been shown to undergo the same change with the menopause and with estrogen therapy as the dermis. The carotid artery media is increased in menopausal women on estrogen therapy and is thinner in untreated women. Recently, new information has revealed that the menopause, i.e. estrogen deprivation, has similar effects on the connective tissue of intervertebral disks. Media thickness is decreased and intima increased in menopause but MHT has been shown to improve media thickness and decrease ratio of intima to media. Same way it has been noted that height of intervertebral disks is reduced in menopause and MHT increases intervertebral disk height from L1 to L3. In aged intervertebral disks, the predominant collagen is type III, not type I, which is the predominant collagen in skin and bone, although skin has additional type III. These negative changes are once again prevented or reversed with estrogen therapy.

This effect probably also extends to the extracellular noncollagenous matrix in all these systems, i.e. skin, carotid and intervertebral disks. The common thread is that estrogen has profound effects on connective tissue turnover, no matter the site. When we look into role of MHT, it has been seen that time of MHT and duration and selection of patients is very important. It has been seen that thigh collagen which is not exposed to sun damage has a better

response than in the skin in the face, which is damaged because of photoradiation. This raised the preventive effect of sunscreen starting early so that more beneficial effect of estrogen can be there. Various studies have seen beneficial effect of MHT by both routes oral and transdermal.

Type and progesterone is also important, as it has been found that androgenic effect of some progesterone may increase flare up of perimenopausal acne in sensitive individuals.

Perhaps time to consider seriously role of MHT in prevention of problems of skin aging along with other skin aging detriments like ultraviolet radiation, alcohol, smoking and proper diet.

If we start with MHT for any other indication and if woman reports subjective improvement is skin, as obstetricians with a proper follow-up, we can let her continue for 5 years or so and document our cases. This is just expert opinion and so far MHT not recommended for the sole purpose of skin effect.

We have to find exact dosage oral and transdermal, type of progesterone, when to start and how long.

BIBLIOGRAPHY

1. Asymmetric facial skin viscoelasticity during climacteric aging Gérald E Piérard, Trinh Hermanns-Lê, Ulysse Gaspard, and Claudine Piérard-Franchimont Clin Cosmet Investig Dermatol 2014;7:111-118.
2. Baron YM, Brincat MP, Galea R, Calleja N. Intervertebral disc height in treated and untreated overweight post-menopausal women. Hum Reprod 2005;20:3566-3570.
3. Brincat MP, Calleja-Agius J, Baron YM. The skin, carotid and intervertebral disc: making the connection! Climacteric 2007;10 (Suppl 2):83-87.
4. Brincat MP. Hormone replacement therapy and the skin. Maturitas 2000 May 29;35(2):107-117.
5. Piérard GE, Hermanns-Lê T, Paquet P, Piérard-Franchimont C. Skin viscoelasticity during hormone replacement therapy for climacteric ageing. Int J Cosmet Sci 2014;36(1):88-92.
6. Piérard GE. The quandary of climacteric skin ageing. Dermatology 1996;193(4):273-274.
7. Piérard-Franchimont C, Cornil F, Dehavay J, Deleixhe-Mauhin F, Letot B, Piérard GE. Climacteric skin ageing of the face—a prospective longitudinal comparative trial on the effect of oral hormone replacement therapy. Maturitas 1999 Jun 21;32(2):87-93.
8. Rittié L, Kang S, Voorhees JJ, Fisher GJ. Induction of Collagen by estradiol difference between sun-protected and photodamaged human skin in vivo. Arch Dermatol 2008;144(9):1129-1140.
9. Stevenson S, Thornton J. Effect of estrogens on skin aging and the potential role of SERMs. Clin Interv Aging 2007 Sep;2(3):283-297.
10. Women, ageing and health: Achieving health across the life span. WHO Publication, 2008.

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