Climacteric

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/icmt20

Skin, hair and beyond: the impact of menopause

C. C. Zouboulis, U. Blume-Peytavi, M. Kosmadaki, E. Roó, D. Vexiau-Robert, D. Kerob & S. R. Goldstein

To cite this article: C. C. Zouboulis, U. Blume-Peytavi, M. Kosmadaki, E. Roó, D. Vexiau-Robert, D. Kerob & S. R. Goldstein (2022) Skin, hair and beyond: the impact of menopause, Climacteric, 25:5, 434-442, DOI: 10.1080/13697137.2022.2050206

To link to this article: https://doi.org/10.1080/13697137.2022.2050206

Published online: 04 Apr 2022.

CLIMACTERIC
2022, VOL. 25, NO. 5, 434–442
https://doi.org/10.1080/13697137.2022.2050206

Taylor & Francis
Taylor & Francis Group

REVIEW

Skin, hair and beyond: the impact of menopause

C. C. Zouboulis[a], U. Blume-Peytavi[b], M. Kosmadaki[c], E. Roó[d], D. Vexiau-Robert[e], D. Kerob[f] and S. R. Goldstein[g]

[a]Departments of Dermatology, Venereology, Allergology and Immunology, Dessau Medical Center, Brandenburg Medical School Theodor Fontane and Faculty of Health Sciences, Brandenburg, Germany; [b]Department of Dermatology, Venerology and Allergology, Charité Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Germany; [c]Dermoiatriki Athens, Athens, Greece; [d]Clider Clínica Dermatológica Roó, Universidad Francisco de Vitoria, Madrid, Spain; [e]Gynecology, Saint-Louis Hospital, Paris, France; [f]Laboratoires Vichy, Levallois-Perret, France; [g]School of Medicine, New York University Grossman, New York, NY, USA

ABSTRACT

The skin is an endocrine organ and a major target of hormones such as estrogens, androgens and cortisol. Besides vasomotor symptoms (VMS), skin and hair symptoms often receive less attention than other menopausal symptoms despite having a significant negative effect on quality of life. Skin and mucosal menopausal symptoms include dryness and pruritus, thinning and atrophy, wrinkles and sagging, poor wound healing and reduced vascularity, whereas skin premalignant and malignant lesions and skin aging signs are almost exclusively caused by environmental factors, especially solar radiation. Hair menopausal symptoms include reduced hair growth and density on the scalp (diffuse effluvium due to follicular rarefication and/or androgenetic alopecia of female pattern), altered hair quality and structure, and increased unwanted hair growth on facial areas. Hormone replacement therapy (HRT) is not indicated for skin and hair symptoms alone due to the risk–benefit balance, but wider potential benefits of HRT (beyond estrogen's effect on VMS, bone, breast, heart and blood vessels) to include skin, hair and mucosal benefits should be discussed with women so that they will be able to make the best possible informed decisions on how to prevent or manage their menopausal symptoms.

ARTICLE HISTORY
Received 26 August 2021
Revised 4 January 2022
Accepted 25 February 2022
Published online 4 April 2022

KEYWORDS
Menopause; perimenopause; exposome; hair; skin; mucosa; hormones; hormone replacement therapy

Introduction

The median menopausal age is 51 years and is generally preceded by a course of perimenopause (around 2–8 years) when the clinical and biological features of approaching menopause commence (this includes the 12 months following the last menstrual cycle) [1,2].

The age of onset of the menopause transition is multifactorial and is influenced by genetics [3] and exposome factors, including environmental factors like UV radiation and tobacco smoke and lifestyle factors like hormones, nutrition/alcohol consumption, stress and sleep deprivation [4,5].

In this review, we mainly focus on manifestations of skin and mucosa as well as hair changes at perimenopause and menopause, discussing which hormones play a role and how their clinical consequences can be prevented or managed.

Symptoms of menopause

Perimenopausal symptomatology is variable in different women. Generally, within 4–5 years of menopause, 80% of women will be devoid of symptoms or have only mild symptoms, while 20% may have symptoms for up to 10 years or longer. The most common climacteric symptoms in around 75% of women are vasomotor symptoms (VMS), including hot flashes, night sweats and sleep disturbance, that may start during perimenopause. VMS will often lead women to consult a physician. A multiethnic study in 3302 women enrolled at seven US sites found that the median total VMS duration was 7.4 years [6]. Risks for hot flashes include early or iatrogenic menopause, females with skin of color or Hispanic ethnic groups, high body mass index or sedentary lifestyle, smoking, anxiety, depression, psychosocial stress and use of selective estrogen receptor modulators (SERMs) or aromatase inhibitors [7].

Other common physical symptoms include genitourinary syndrome of menopause (GSM), palpitations, headaches, bone/joint/muscle pain, asthenia, tiredness, insomnia, breast tenderness, dyspareunia and skin aging/hair/mucosal disorders, while psychological symptoms include memory loss, irritability, poor concentration and loss of confidence [8]. Insomnia may contribute to neurological symptoms that emerge during perimenopause. Other risks to health associated with menopause include bone loss/osteoporosis, heart disease, diabetes, obesity and cognitive decline.

CONTACT C. C. Zouboulis Christos.zouboulis@mhb-fontane.de Departments of Dermatology, Venereology, Allergology and Immunology, Dessau Medical Center, Brandenburg Medical School Theodor Fontane and Faculty of Health Sciences, Brandenburg, Dessau, Germany

Skin, hair and mucosal changes during menopause

Besides VMS, skin and hair symptoms often receive less attention than other menopausal symptoms. In a survey of 87 women attending a menopause clinic, 64% reported skin problems and around half indicated that the menopause had caused skin changes, with dry skin being the main symptom [9]. Additionally, in a survey from 2018 in 1287 French women, 72% reported they noticed changes in their skin at perimenopause/menopause, while 50% felt they had been insufficiently informed about these symptoms, highlighting the need for educating women and healthcare professionals on the impact of menopause on the skin [10]. The visible signs of dryness, wrinkles and sagging, especially on the face, contribute to an increased perception of aging and decreased attractiveness [11] with a significant impact on quality of life (QoL). Furthermore, a woman is frequently judged, particularly in westernized societies, by the quality of her skin and hair (including hair color), both of which are seen to reflect health and well-being, and may cause a great psychological burden [12].

Large longitudinal studies have investigated the onset and duration of VMS but there is a paucity of information on studies evaluating skin, mucosal and hair symptoms and hormonal changes at different stages in menopausal women. Furthermore, it may be difficult to distinguish between so-called menopausal symptoms from loss of ovarian function or from natural aging or psychosocial factors. Actinic lentigines ('dark spots') are common in women of menopausal age but are caused almost exclusively by photodamage rather than hormonal changes. However, one pilot study reported that in photo-exposed areas, such as the face, menopausal women acquire a higher degree of pigmentation than premenopausal women after equal exposure time [13]. Wrinkling has been shown to correlate most closely with chronologic age and skin color rather than menopause, whereas skin rigidity (an inverse measure of dermal collagen density) was only positively correlated with the time since menopause in women with white skin [14].

During the perimenopause course, peripheral estrogen levels do not steadily decline but fluctuate around the normal range, since aromatization of androgens increases, leading to variations in sebum levels. Skin dryness may be noticed in early perimenopause, but it may initially be somewhat compensated by sebaceous gland hypertrophy. Later in menopause when sebum production is markedly reduced, the skin becomes increasingly dry and itchy, followed by sagging and atrophy.

Skin atrophy due to collagen loss is more pronounced in menopausal women [15–17]. In early menopause, skin collagen levels decrease fairly rapidly with a collagen reduction of approximately 30% in the first 5 years, followed by a further decline of 2% per year for the next 15 years [17]. A steady depletion of collagen and reduced skin thickness with yearly reductions of 2.1% and 1.1%, respectively, was observed in menopausal women [18].

Diffuse effluvium due to follicular rarefication and/or androgenetic alopecia of female pattern may be observed later in menopause due to sustained reduction of hair cycling, while the existing hair becomes thinner and drier due to aging. However, thinning may be noticeable at perimenopause in women predisposed to develop centroparietal alopecia. Hair issues at menopause include reduced scalp hair but increased (unwanted) hair growth in certain areas on the face [12].

GSM with changes in the bladder, vulva and vagina due to vulvovaginal atrophy affects almost half of postmenopausal women. Symptoms of vaginal dryness, vaginal irritation and itching may be followed by reduced elasticity, dyspareunia, urinary urgency, dysuria and recurrent urinary-tract infections, which will deteriorate with time from the menopausal transition if left untreated [19–22].

In addition, oral mucosa dryness [23] and conjunctival dryness may increase as menopause progresses.

The skin is an endocrine organ

Skin cells produce sex hormones and other steroids, such as estrogens, androgens and glucocorticoids from systemic steroid hormones originating from the adrenals [24]. In menopause, changes of sex hormones occur. The androstenedione/sex hormone-binding globulin ratio, cortisol, melatonin, insulin-like growth factor-1 (IGF-1) and norepinephrine are also related to the pathophysiology of menopause [24,25].

Role of hormones on skin, hair and mucosal menopausal symptoms and conditions

In addition to the effects of chronological aging, sun exposure and other environmental or lifestyle factors affect the menopausal skin biology.

Estrogens

Hypoestrogenism may affect various systems and plays important roles in the immune function, cancer development and other biological processes related to health and well-being [26]. Estrogens (specifically 17β-estradiol) are primarily synthesized in the ovaries in premenopausal women, while estrone comes from non-ovarian sites in menopausal women, including the adrenal glands, skin, brain, adipose tissue and pancreas [27,28]. Human skin is a major target of hormones [24,29] with glucocorticoids, cAMP analogs, growth factors and cytokines modulating local estrogen synthesis via aromatase, mainly expressed in the pilosebaceous unit [30,31]. Estrogen receptors (ERs) are abundant in both dermis and epidermis, and are most dense in the genitalia, face and lower limbs [32,33]. In human skin, there is no gender difference in the pattern or distribution of ER. Two isoforms of ER are known (i.e. ERα and ERβ). Whereas a large number of natural and synthetic estrogens show a similar binding affinity to both receptors, other ligands are more selective, such as genistein or daidzein, which induce a stronger activation of ERβ. ERα is expressed exclusively in basal and partially differentiated cells of normal sebaceous glands and is seen in only a small portion of the eccrine gland

epithelia. In the axillary apocrine glands, a strong nuclear expression of ERα is seen in the secretory epithelium [34]. ERβ is expressed by sebaceous glands (in the same distribution as ERα) and by human eccrine sweat glands. ERβ is widely expressed in the skin, namely in dermal papilla cells and dermal fibroblasts, sebocytes, adipocytes, melanocytes and keratinocytes of the outer root sheath [35].

The impact of estrogen decline at menopause on aging skin has been extensively reviewed [11,15,17,33,36–38]. Estrogen deficiency during menopause alters certain skin functions: impaired skin barrier function causes skin dryness from diminished skin moisture and decreased sebum production on the face and scalp; decreased antioxidant function and impaired wound healing [15,39]; decreased collagen and elastin synthesis leading to wrinkling and dermal thinning on both skin and genital mucosa, and decreased glycosaminoglycans in the extracellular matrix, such as hyaluronic acid, leading to decreased skin turgescence and reduced hydration [40]; and thermoregulation function with pallor, reduced vascularity and hot flashes caused by vasodilation deep within the blood capillaries in the papillary dermis.

Estradiol can significantly alter both the growth and life cycle of the hair follicle by binding to ERs, thus influencing aromatase activity, which is responsible for converting androgen into estrogens [41]. Estradiol prolongs the anagen phase of the hair cycle, which enhances hair growth by increasing the synthesis of essential growth factors stimulating the proliferation of follicular keratinocytes, explaining the reduction of hair renewal, growth and thickness, and rarefication of hair observed during menopause [27].

Estrogen induces glycogen production by vaginal and cervical epithelial cells. Menopausal decline in estrogen results in urogenital atrophy and a loss of vaginal epithelial cells [21]. The resulting reduction in epithelial glycogen in menopause also leads to low levels of lactobacilli as they are unable to proliferate without glycogen, hence they no longer produce antimicrobial and anti-inflammatory products leading to an increased susceptibility to mucosal injury [19].

Androgens

Unlike estrogen and progesterone which decline rapidly, androgen secretion, which is already relatively low in women, declines gradually with menopause and aging. Androgens play a role in modulating hair growth and sebum production in the pilosebaceous unit. The relative increase of androgens during the menopause leads to clinical hyperandrogenism manifesting as sebaceous gland hypertrophy and androgenetic alopecia of female pattern due to regional reduction of hair renewal and growth, which can be aggravated by genetic and exposome factors [42].

Aging, concomitant diseases, genetic factors, environmental factors and medication, in conjunction with hormonal changes occurring during menopause, can all affect hair quality and result in cessation of hair growth activity, hair thinning, loss of trio or duo groups and hair density decline [12,43]. Androgens, such as testosterone, dihydrotestosterone and their prohormones, may play a role in miniaturization of hair follicles and a decrease in body and scalp hair or transform small, fair vellus hairs in hormone-sensitive areas on the face to darker terminal hair follicles [12,41]. Relative peripheral hyperandrogenism, secondary to androgen, estrogen and progesterone imbalance, may impact the hair growth pattern [12,44]. However, most women presenting with alopecia, particularly of the female pattern, do not have elevated androgen levels, indicating that the androgen/estrogen ratio and not androgen-dependent mechanisms may be involved [12,45,46].

Dehydroepiandrosterone (DHEA; much of which is sulfated DHEA-S) in the skin is mainly produced in the adrenal glands from cholesterol by two cytochrome P450 enzymes. DHEA is converted in sebocytes to testosterone and, finally, in all skin epithelial cells to 5α-dihydrotestosterone (DHT), which are skin active androgens with diversified activity, whereas its aromatization leads to the synthesis of skin active estrogens (estradiol and estrone) and more potent androgens, which have greater impact on skin. DHEA and DHEA-S are the most abundant sex steroids in plasma. Circulating levels of DHEA decline dramatically with age, albeit with large variability on a scale from 1 to 8 in different women, which may explain the large disparity of symptoms [47]. DHEA is the cardinal source of both androgen and estrogen synthesis for all tissues except the uterus following menopause. Supplementation has been shown to increase skin thickness, hydration and sebum production. Local synthesis of the sex steroids in the skin affects the eccrine sweat glands and hair follicles.

Cortisol

The synthesis of cortisol in the adrenal gland is stimulated by the anterior lobe of the pituitary gland with adrenocorticotropic hormone (ACTH). The release of corticotrophin-releasing hormone (CRH), ACTH and cortisol from skin cells may explain some skin aging signs [48,49]. Stress hormones negatively affect the epidermal barrier [50] and cortisol suppresses the pro-inflammatory cytokines IL-1 and TNF-α, resulting in deficient cutaneous repair. The clinical effects of cortisol on the skin are dryness, inflammation and wrinkles.

Overnight urinary cortisol levels were found to increase during the late stage of perimenopause in some women, especially if they had severe hot flashes [51]. Furthermore, increased salivary cortisol levels were observed in women in menopause [52].

Another stress hormone, norepinephrine, released by the adrenal medulla, inhibits epidermal proliferation and reduces blood perfusion via α-adrenergic-induced vasoconstriction [53]. Finally, stress may also hamper hair growth, although studies in menopausal women are lacking [54].

Vitamin D

Vitamin D is a fat-soluble vitamin, characterized by synergic action of its two main metabolites: 25-OH-D_2, which is obtained from plant sources, and 25-OH-D_3, which comes from animal products and endogenous synthesis in skin

through exposure to sunlight. While the prevalence of vitamin D insufficiency is more common in older, frailer women, vitamin D supplementation was not shown to affect overall health outcomes in several clinical studies [55,56], but may improve vaginal health outcomes in menopausal women with vulvo-vaginal atrophy symptoms [57] and metabolic syndrome risk profile [58]. Furthermore, in several clinical studies on vitamin D insufficiency supplementation in menopausal women, calcifediol was found to be superior to cholecalciferol in improving vitamin D status [59] and was associated with a concomitant greater improvement in muscle strength after oral supplementation for 6 months [60].

Melatonin

Melatonin declines with menopause and/or aging and changes in melatonin concentrations related to the menopausal transition may be associated with VMS, mood, sleep and QoL [61].

Prevention and management of menopausal symptoms

Studies have shown that only 25% of women who experience symptoms consult a physician, highlighting the need to improve awareness concerning the management of menopausal symptoms [7,62]. Decisions about therapy for perimenopausal and menopausal women should be individualized and will depend on symptomatology, health status, immediate and long-term health risks, personal life expectations and availability of therapies [63,64].

Hormone replacement therapy

Since the Women's Health Initiative (WHI) trial results in 2002 in older women (mean age 63 years) led to a dramatic reduction in the number of women receiving hormone replacement therapy (HRT), it has now become clear that the risks of HRT are low for healthy women (<60 years of age or within 10 years of menopause onset) [64–69]. HRT remains the most effective treatment for VMS, GSM (local vaginal hormone therapies for some patients) and bone protection, as well as for improving QoL [70–72]. HRT should be started early for hot flashes and painful intercourse and there is no maximum length of treatment time. For women with primary ovarian insufficiency (due to genetic, iatrogenic [e.g. surgery, chemotherapy], infectious or autoimmune causes) [2] without contraindications, HRT is recommended until at least the average age of natural menopause as the benefits on bone, heart, cognition, GSM, sexual function and mood outweigh the risks [72].

The ancillary Women's Health Initiative Memory Study of Magnetic Resonance Imaging (WHIMS-MRI) study measured subclinical small vessel cerebrovascular disease to possibly explain the negative cognitive findings reported by the WHIMS [73,74].

HRT consists of estrogen (17β-estradiol or conjugated equine estrogen [CEE]) and, in women with an intact uterus, progestogen (micronized progesterone) is also required to protect the endometrium. In the WHI trial, women with prior hysterectomy receiving only CEE for a median of 7.2 years did not exhibit increased risk for all-cause mortality, coronary heart disease or cancer mortality, did present decreased hip fracture and diabetes rates, but presented increased stroke and venous thrombosis [75]. In women <60 years of age or within 10 years of menopause, statistically significant reductions of 23% in breast cancer and 20% in heart disease were observed after 5.9 years of CEE use and 11.8 years of follow-up; this benefit may not apply to populations at higher risk [75,76]. Hence, the increased risks of HRT were due to the progestogen and not the CEE (used in the USA but not in Europe) [64,75].

As an alternative to progestogen, SERMs are synthetic non-steroidal agents that have variable estrogen agonist and antagonist activities in different target tissues [77]. For example, bazedoxifene may provide endometrial [78] and breast protection [79] in menopausal women with a uterus, while conjugated estrogen [77,80] reduces bone loss [81,82], VMS [83] and vaginal atrophy [84]. Furthermore, CEE may exhibit SERM-like properties such as reduced breast cancer incidence and mortality.

Efficacy data are lacking on compounded bioidentical hormones for correcting menopausal hormonal imbalances and there are safety concerns about dose and purity [85].

Until there is a better understanding amongst all physicians of the minimal risks of HRT when individualized with regular evaluations, many women will continue to suffer a reduced QoL unnecessarily [86]. Furthermore, HRT may offer wider benefits, including the management of skin, hair and mucosal symptoms, as discussed below.

Non-hormonal therapies

Estrogen therapy is the gold standard for menopausal symptoms and there is limited evidence for the efficacy of non-hormonal therapies. Some efficacy in reducing hot flashes has been observed with cognitive behavioral therapy, clinical hypnosis, low-dose selective serotonin-reuptake inhibitors and serotonin–norepinephrine reuptake inhibitors, drugs that lower blood pressure (clonidine), antidepressants (paroxetine salt) and gabapentinoids [7,87]. They may be preferred by women who have contraindications to hormone therapy (e.g. a history of or an elevated risk of breast cancer, chronic venous disease or deep vein thrombosis) or unacceptable side effects with HRT.

Effects of HRT on skin

Clearly, HRT is not indicated solely for skin and hair benefits, but these should be considered in individual patient discussions concerning the treatment of menopausal symptoms. Improvements in skin surface texture, hydration, collagen content of the dermis and viscoelasticity have been shown in women receiving HRT/estrogen (oral and transdermal)

[15,17,33,36,37,88]. A randomized controlled trial in menopausal women with 12 months of oral estrogen increased dermal thickness by 30% [89] and, similarly, 6 months of HRT increased skin collagen by 6.5% [90]. Minor improvements in skin elasticity, hydration and thickness, but not surface lipids, were observed after 7 months of HRT [91]. HRT appeared to mitigate the progressive enlargement of pores after menopause [92].

Results on wrinkles are less clear. In a cross-sectional analysis, improvements in skin elasticity and wrinkle severity were observed after 5 years of HRT [93]. A 24-week study reported a statistically significant improvement with CEE versus placebo for skin thickness and fine wrinkles [94]. However, other HRT studies did not show a significant improvement in wrinkles [95,96]. In a randomized controlled trial, HRT showed some benefits on skin but did improve skin wrinkles or rigidity at most facial locations when women within 36 months of their last menstrual period were treated for 4 years with HRT (oral CEE or transdermal estradiol with micronized progesterone) versus placebo [97]. The authors suggested that confounding in non-randomized studies may occur due to race/ethnicity as women with skin of color had the lowest wrinkle scores even without HRT [97].

The observation that improvement in wrinkles with HRT only occurs in non-photoaged skin highlights the importance of photoprotection. A study of 40 postmenopausal women (mean age 75 years) receiving topical estradiol or vehicle showed that principally sun-protected skin on the hip, but not photoaged forearm or facial skin, benefited from HRT [98].

Studies have also been conducted with SERMs [15,33,99,100]. Raloxifene, a SERM which is used successfully to prevent and treat postmenopausal osteoporosis, as well as reduce breast cancer risk, was also shown to increase collagen biosynthesis in human skin fibroblasts [101]. In a 12-month trial with 17 postmenopausal women (mean age 66 years), raloxifene had a similar effect to estradiol treatment (patch plus cyclic medroxyprogesterone acetate) in increasing skin elasticity [102].

Summarizing, HRT, SERMs, topical estrogens, topical isoflavones (soy-derived compounds that interact with ERs) and phytoestrogens may improve estrogen-deficient skin [37,38,99]. However, prospective, placebo-controlled clinical studies to document the efficacy and potential risks of therapeutic interventions for the skin and hair problems during menopause are required.

Finally, tibolone is a synthetic selective tissue estrogenic activity regulator used for HRT in some countries. In the tibolone patient information leaflet, unusual hair growth is listed under common side effects and itchy skin under rare ones. However, a Cochrane systematic review on short-term and long-term effects of tibolone did not report any skin and hair side effects [103].

Effects of HRT on hair

Data are lacking on the effect of HRT on hair quality and sebum production during menopause [104]. A recent review on the impact of micronized progesterone (topical or oral, with or without estradiol) found no publications on menopausal scalp hair quantity and quality or on female pattern hair loss in perimenopausal/menopausal women [105].

Management of skin, hair and mucosal symptoms

Dermo-cosmetics and adapted skin care for facial skin and other areas may be used alone or combined with HRT (if prescribed for other symptoms).

Photoprotection

Photoprotection (sunscreen, clothes, sunglasses, seeking shade) can prevent photoaging and may reduce the prevalence of premalignant and malignant skin lesions (melanoma, non-melanoma skin cancer).

Dermo-cosmetic ingredients can compensate hormonal changes on the skin

Pro-xylane. A C-xylopyranoside derivative (pro-xylane) has been shown to stimulate the synthesis of mucopolysaccharides in the dermis and epidermis to improve skin elasticity and tonicity. Reduced visible signs of skin aging and changes in sebum composition were observed in postmenopausal women after applying topical serum containing pro-xylane 3% daily for 60 days [106].

Cassia extract. Cassia extract, from a traditional medicinal plant, has anti-aging effects on skin by reducing the impact of cortisol on collagen and hyaluronic acid synthesis to stimulate extracellular matrix synthesis [107].

Hyaluronic acid. Hyaluronic acid, or hyaluronan, in the skin extracellular matrix has viscoelastic and hygroscopic properties [108], and may be a suitable alternative to vaginal estrogens for the treatment of symptoms of vaginal atrophy in women with contraindications to HRT [109].

Other ingredients. Dermo-cosmetics for skin hydration to treat dry skin may include collagen stimulators, antioxidants, or estrogen.

Dedicated dermo-cosmetics for hair and scalp conditions

Alopecia may be difficult to manage during the menopause, especially since loss of hair volume/density is age-dependent [12,110]. Dedicated shampoo may be used in combination with or after using a prescription medication. Aminexil and Stemoxydine (an antioxidant) are active dermo-cosmetic ingredients shown to decrease the percentage of hair in the resting telogen phase to maintain hair density [111,112].

Holistic approach

Increased awareness of symptoms and prevention/treatment/coping strategies might help women during menopause. The skin aging process is accelerated by menopause but also by

Table 1. Expert recommendations for prevention/treatment/coping strategies for symptoms of menopause, including skin, hair and mucosal symptoms.

Symptom	*Recommendations*		*References*
Vasomotor symptom management	Gynecologist follow-up and start HRT early when needed (annual follow-up if continuing after 5 years)	Estrogen and progesterone HRT Estrogen and SERM HRT	[72] [84]
	Non-hormonal therapies if HRT contraindicated	Acupuncture therapy Behavioral therapy	[64]
Genitourinary and mucosal symptoms	Gynecologist follow-up and start HRT early when needed	Estrogen and progesterone HRT Estrogen and SERM HRT	[72]
	If only genitourinary symptoms without VMS	Local vaginal estrogen therapy	[7,115,116]
Skin symptoms	Dermatologist follow-up, photoprotection to avoid/reduce photodamage and photoaging	Daily sunscreen of appropriate sun protection factor Protective clothing, sunglasses	[114]
	Adapted skin care for facial skin and other areas	Pro-xylane Cassia extract Antioxidants Other collagen stimulators Hydration for dry skin Avoid chronic application of topical corticosteroids	[106] [107] [117,118]
	HRT (if prescribed for other symptoms)	Not indicated for skin symptoms alone due to the risk–benefit balance	
Hair symptoms	Dermatologist follow-up if significant androgenic alopecia	Local minoxidil medication (solution or foam)	[119,120]
	Loss of volume/density is age dependent	Specific hair dermo-cosmetics to increase volume (Aminexil, Stemoxydine) Nutricosmetics to enhance hair quality	[111,112]
	Management of facial hypertrichosis	Epilation techniques Local eflornithine	[121]
All symptoms and general well-being	Stress reduction, psychological support and improving sleep quality	Cognitive behavior therapy Mindfulness and meditation	[7]
	Advise lifestyle changes (physical exercise, weight loss, healthy eating, reduce stress, quit smoking)	Quitting smoking is essential before receiving HRT	[72]

HRT, hormone replacement therapy; SERM, selective estrogen receptor modulator; VMS, vasomotor symptoms.

the exposome [113]. Calcitrol (vitamin D) is synthesized in the skin exposed to UV radiation and is important for bone health; however, photoprotection is essential for preventing skin premalignant and malignant lesions and skin aging signs [114]. Photoprotection, reducing stress, healthy nutrition, weight loss, physical exercise and discontinuation of smoking early in the perimenopausal period may help to alleviate symptoms and reduce the risk of further decline before menopause is established.

Expert recommendations

Recommendations for physicians (including dermatologists and gynecologists) based on clinical literature, information from professional menopause societies and expert opinion of the authors are summarized in Table 1.

Conclusions

Most previous reviews about menopause, its physiologic changes and various therapies included a paucity of information about the role of sex steroids and their replacement from a dermatologic perspective. Although HRT is not indicated for skin and hair symptoms alone due to the risk–benefit balance, a better understanding of skin, hair and mucosal changes at menopause and how to manage or prevent them will reduce the burden and improve the well-being and QoL of women at this stage in their lives. Further efforts are needed to educate physicians on these wider potential benefits of HRT on skin, hair and mucosa (beyond the benefits for VMS, bone, breast, heart and blood vessels), and this information should be discussed with women to help them make the best possible informed decisions as soon as they have any menopausal symptoms.

Acknowledgements

Writing and editorial assistance for the preparation of this manuscript were provided by Helen Simpson, PhD, ISMPP CMPP™, of My Word Medical Writing and funded by Vichy Laboratoires. Advisory board and editorial assistance were supported by Vichy Laboratoires.

Potential conflict of interest D.K. is an employee of Vichy Laboratoires and all other authors received honoraria as advisory board members for Vichy Laboratoires.

Source of funding None.

ORCID

C. C. Zouboulis http://orcid.org/0000-0003-1646-2608
U. Blume-Peytavi http://orcid.org/0000-0003-3528-3752
S. R. Goldstein http://orcid.org/0000-0001-9600-5866

References

[1] Research on the menopause in the 1990s. Report of a WHO scientific group. World Health Organ Tech Rep Ser. 1996;866:1–107.
[2] Brambilla DJ, McKinlay SM. A prospective study of factors affecting age at menopause. J Clin Epidemiol. 1989;42(11):1031–1039.
[3] de Bruin JP, Bovenhuis H, van Noord PA, et al. The role of genetic factors in age at natural menopause. Hum Reprod. 2001;16(9):2014–2018.
[4] Midgette AS, Baron JA. Cigarette smoking and the risk of natural menopause. Epidemiology. 1990;1(6):474–480.
[5] Fleming LE, Levis S, LeBlanc WG, et al. Earlier age at menopause, work, and tobacco smoke exposure. Menopause. 2008;15(6):1103–1108.
[6] Avis NE, Crawford SL, Greendale G, et al. Duration of menopausal vasomotor symptoms over the menopause transition. JAMA Intern Med. 2015;175(4):531–539.
[7] Pinkerton JV. Hormone therapy for postmenopausal women. N Engl J Med. 2020;382(5):446–455.
[8] Pimenta F, Leal I, Maroco J, et al. Menopause symptoms' predictors: the influence of lifestyle, health- and menopause-related, and sociodemographic characteristics. J Women Aging. 2012;24(2):140–151.
[9] Leitch C, Doherty V, Gebbie A. Women's perceptions of the effects of menopause and hormone replacement therapy on skin. Menopause Int. 2011;17(1):11–13.
[10] LePillouer-Prost A, Kerob D, Nielsen M, et al. Skin and menopause: women's point of view. J Eur Acad Dermatol Venereol. 2020;34(6):e267–e269.
[11] Lephart ED. A review of the role of estrogen in dermal aging and facial attractiveness in women. J Cosmet Dermatol. 2018;17(3):282–288.
[12] Blume-Peytavi U, Atkin S, Gieler U, et al. Skin academy: hair, skin, hormones and menopause – current status/knowledge on the management of hair disorders in menopausal women. Eur J Dermatol. 2012;22(3):310–318.
[13] Akiba S, Shinkura R, Miyamoto K, et al. Influence of chronic UV exposure and lifestyle on facial skin photo-aging-results from a pilot study. J Epidemiol. 1999;9(6 Suppl):S136–S42.
[14] Wolff E, Pal L, Altun T, et al. Skin wrinkles and rigidity in early postmenopausal women vary by race/ethnicity: baseline characteristics of the skin ancillary study of the KEEPS trial. Fertil Steril. 2011;95(2):658–662.e1-3.
[15] Thornton MJ. Estrogens and aging skin. Dermatoendocrinol. 2013;5(2):264–270.
[16] Calleja-Agius J, Muscat-Baron Y, Brincat MP. Skin ageing. Menopause Int. 2007;13(2):60–64.
[17] Brincat MP, Baron YM, Galea R. Estrogens and the skin. Climacteric. 2005;8(2):110–123.
[18] Brincat M, Kabalan S, Studd JW, et al. A study of the decrease of skin collagen content, skin thickness, and bone mass in the postmenopausal woman. Obstet Gynecol. 1987;70(6):840–845.
[19] Mac Bride MB, Rhodes DJ, Shuster LT. Vulvovaginal atrophy. Mayo Clin Proc. 2010;85(1):87–94.
[20] Portman DJ, Gass ML. Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the international society for the study of women's sexual health and the North American Menopause Society. Menopause. 2014;21(10):1063–1068.
[21] Calleja-Agius J, Brincat MP. The urogenital system and the menopause. Climacteric. 2015;18(Suppl 1):18–22.
[22] Santoro N, Komi J. Prevalence and impact of vaginal symptoms among postmenopausal women. J Sex Med. 2009;6(8):2133–2142.
[23] Suri V, Suri V. Menopause and oral health. J Midlife Health. 2014;5(3):115–120.
[24] Slominski A, Zbytek B, Nikolakis G, et al. Steroidogenesis in the skin: implications for local immune functions. J Steroid Biochem Mol Biol. 2013;137:107–123.
[25] Su HI, Freeman EW. Hormone changes associated with the menopausal transition. Minerva Ginecol. 2009;61(6):483–489.
[26] Somasundaram A, Rothenberger NJ, Stabile LP. The impact of estrogen in the tumor microenvironment. Adv Exp Med Biol. 2020;1277:33–52.
[27] Barakat R, Oakley O, Kim H, et al. Extra-gonadal sites of estrogen biosynthesis and function. BMB Rep. 2016;49(9):488–496.
[28] Fuentes N, Silveyra P. Estrogen receptor signaling mechanisms. Adv Protein Chem Struct Biol. 2019;116:135–170.
[29] Zouboulis CC. The human skin as a hormone target and an endocrine gland. Hormones. 2004;3(1):9–26.
[30] Emoto N, Ling N, Baird A. Growth factor-mediated regulation of aromatase activity in human skin fibroblasts. Proc Soc Exp Biol Med. 1991;196(3):351–358.
[31] Makrantonaki E, Vogel K, Fimmel S, et al. Interplay of IGF-I and 17beta-estradiol at age-specific levels in human sebocytes and fibroblasts in vitro. Exp Gerontol. 2008;43(10):939–946.
[32] Thornton MJ, Taylor AH, Mulligan K, et al. Oestrogen receptor beta is the predominant oestrogen receptor in human scalp skin. Exp Dermatol. 2003;12(2):181–190.
[33] Reus TL, Brohem CA, Schuck DC, et al. Revisiting the effects of menopause on the skin: functional changes, clinical studies, in vitro models and therapeutic alternatives. Mech Ageing Dev. 2020;185:111193.
[34] Wollina U, Abdel-Naser MB, Ganceviciene R, et al. Receptors of eccrine, apocrine, and holocrine skin glands. Dermatol Clin. 2007;25(4):577–588, ix.
[35] Zouboulis CC. Human skin: an independent peripheral endocrine organ. Horm Res. 2000;54(5–6):230–242.
[36] Hall G, Phillips TJ. Estrogen and skin: the effects of estrogen, menopause, and hormone replacement therapy on the skin. J Am Acad Dermatol. 2005;53(4):555–568. quiz 569–572.
[37] Rzepecki AK, Murase JE, Juran R, et al. Estrogen-deficient skin: the role of topical therapy. Int J Womens Dermatol. 2019;5(2):85–90.
[38] Lephart ED, Naftolin F. Menopause and the skin: old favorites and new innovations in cosmeceuticals for estrogen-deficient skin. Dermatol Ther. 2021;11(1):53–69.
[39] El Mohtadi M, Whitehead K, Dempsey-Hibbert N, et al. Estrogen deficiency – a central paradigm in age-related impaired healing? Excli J. 2021;20:99–116.
[40] Wilkinson HN, Hardman MJ. A role for estrogen in skin ageing and dermal biomechanics. Mech Ageing Dev. 2021;197:111513.
[41] Grymowicz M, Rudnicka E, Podfigurna A, et al. Hormonal effects on hair follicles. IJMS. 2020;21(15):5342.
[42] Khunger N, Mehrotra K. Menopausal acne – challenges and solutions. Int J Womens Health. 2019;11:555–567.
[43] Messenger AG. Hair through the female life cycle. Br J Dermatol. 2011;165(Suppl 3):2–6.
[44] Duarte GV, Trigo AC, Paim de Oliveira M. D. F. Skin disorders during menopause. Cutis. 2016;97(2):E16–E23.
[45] Mirmirani P. Hormonal changes in menopause: do they contribute to a 'midlife hair crisis' in women? Br J Dermatol. 2011;165(Suppl 3):7–11.
[46] Bienenfeld A, Azarchi S, Lo Sicco K, et al. Androgens in women: androgen-mediated skin disease and patient evaluation. J Am Acad Dermatol. 2019;80(6):1497–1506.
[47] Labrie F, Martel C, Balser J. Wide distribution of the serum dehydroepiandrosterone and sex steroid levels in postmenopausal women: role of the ovary? Menopause. 2011;18(1):30–43.

[48] Peters EM. Stressed skin?-A molecular psychosomatic update on stress-causes and effects in dermatologic diseases. J Dtsch Dermatol Ges. 2016;14(3):233–252; quiz 253.
[49] Slominski AT, Zmijewski MA, Skobowiat C, et al. Sensing the environment: regulation of local and global homeostasis by the skin's neuroendocrine system. Adv Anat Embryol Cell Biol. 2012; 212v, vii, :v, vii, 1–115.
[50] Maarouf M, Maarouf CL, Yosipovitch G, et al. The impact of stress on epidermal barrier function: an evidence-based review. Br J Dermatol. 2019;181(6):1129–1137.
[51] Woods NF, Mitchell ES. The Seattle midlife women's health study: a longitudinal prospective study of women during the menopausal transition and early postmenopause. Womens Midlife Health. 2016;2:6.
[52] Prasad N, Jabbar PK, Jayakumari C, et al. Late-night salivary cortisol in healthy, community-dwelling Asian Indians assessed by second-generation ECLIA. J Clin Endocrinol Metab. 2020;105(8): dgaa269.
[53] Kahan V, Andersen ML, Tomimori J, et al. Stress, immunity and skin collagen integrity: evidence from animal models and clinical conditions. Brain Behav Immun. 2009;23(8):1089–1095.
[54] Peters EMJ, Müller Y, Snaga W, et al. Hair and stress: a pilot study of hair and cytokine balance alteration in healthy young women under major exam stress. PLoS One. 2017;12(4): e0175904.
[55] Nudy M. Jiang X, Aragaki AK, et al. The severity of vasomotor symptoms and number of menopausal symptoms in postmenopausal women and select clinical health outcomes in the women's health initiative calcium and vitamin D randomized clinical trial. Menopause. 2020;27(11):1265–1273.
[56] Ozsoy-Unubol T, Candan Z, Atar E, et al. The effect of vitamin D and exercise on balance and fall risk in postmenopausal women: A randomised controlled study. Int J Clin Pract. 2021;75(12): e–14851.
[57] Kamronrithisorn T, Manonai J, Vallibhakara A-O, et al. Effect of vitamin D supplement on vulvovaginal atrophy of the menopause. Nutrients. 2020;12(9):2876. doi:10.3390/nu12092876.
[58] Ferreira PP, Cangussu L, Bueloni-Dias FN, et al. Vitamin D supplementation improves the metabolic syndrome risk profile in postmenopausal women. Climacteric. 2020;23(1):24–31. doi:10.1080/13697137.2019.1611761.
[59] Pérez-Castrillón JL, Dueñas-Laita A, Brandi ML, et al. Calcifediol is superior to cholecalciferol in improving vitamin D status in postmenopausal women: A randomized trial. J Bone Miner Res. 2021;36(10):1967–1978. doi:10.1002/jbmr.4387.
[60] Corrado A, Rotondo C, Cici D, et al. Effects of different vitamin D supplementation schemes in post-menopausal women: A monocentric open-label randomized study. Nutrients. 2021;13(2): 380 doi:10.3390/nu13020380.
[61] Toffol E, Kalleinen N, Haukka J, et al. Melatonin in perimenopausal and postmenopausal women: associations with mood, sleep, climacteric symptoms, and quality of life. Menopause. 2014;21(5):493–500.
[62] Vaccaro CM, Capozzi A, Ettore G, et al. What women think about menopause: an Italian survey. Maturitas. 2021;147:47–52.
[63] Davis SR, Lambrinoudaki I, Lumsden M, et al. Menopause. Nat Rev Dis Primers. 2015;1:15004.
[64] Baber RJ, Panay N, Fenton A. 2016 IMS recommendations on women's midlife health and menopause hormone therapy. Climacteric. 2016;19(2):109–150.
[65] Langer RD, Hodis HN, Lobo RA, et al. Hormone replacement therapy – where are we now? Climacteric. 2021;24(1):3–10.
[66] Rossouw JE, Manson JE, Kaunitz AM, et al. Lessons learned from the women's health initiative trials of menopausal hormone therapy. Obstet Gynecol. 2013;121(1):172–176.
[67] Palacios S, Stevenson JC, Schaudig K, et al. Hormone therapy for first-line management of menopausal symptoms: practical recommendations. Womens Health. 2019;15:1745506519864009.
[68] Manson JE, Bassuk SS, Kaunitz AM, et al. The women's health initiative trials of menopausal hormone therapy: lessons learned. Menopause. 2020;27(8):918–928.
[69] Lobo RA. Hormone-replacement therapy: current thinking. Nat Rev Endocrinol. 2017;13(4):220–231.
[70] Schneider HPG, Birkhäuser M. Quality of life in climacteric women. Climacteric. 2017;20(3):187–194.
[71] Mehta J, Kling JM, Manson JE. Risks, benefits, and treatment modalities of menopausal hormone therapy: current concepts. Front Endocrinol. 2021;12(564781):564781.
[72] The 2017 hormone therapy position statement of the North American Menopause Society. Menopause. 2017;24(7):728–753.
[73] Haring B, Liu J, Rapp SR, et al. Heart rate, brain imaging biomarkers and cognitive impairment in older (≥63 years) women. Am J Cardiol. 2020;129:102–108.
[74] Coker LH, Espeland MA, Rapp SR, et al. Postmenopausal hormone therapy and cognitive outcomes: the women's health initiative memory study (WHIMS). J Steroid Biochem Mol Biol. 2010;118(4–5):304–310.
[75] Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the women's health initiative randomized trials. JAMA. 2013;310(13):1353–1368.
[76] Anderson GL, Chlebowski RT, Aragaki AK, et al. Conjugated equine oestrogen and breast cancer incidence and mortality in postmenopausal women with hysterectomy: extended follow-up of the women's health initiative randomised placebo-controlled trial. Lancet Oncol. 2012;13(5):476–486.
[77] Pinkerton JV, Conner EA. Beyond estrogen: advances in tissue selective estrogen complexes and selective estrogen receptor modulators. Climacteric. 2019;22(2):140–147.
[78] Mirkin S, Komm BS, Pan K, et al. Effects of bazedoxifene/conjugated estrogens on endometrial safety and bone in postmenopausal women. Climacteric. 2013;16(3):338–346.
[79] Pinkerton JV, Harvey JA, Pan K, et al. Breast effects of bazedoxifene-conjugated estrogens: a randomized controlled trial. Obstet Gynecol. 2013;121(5):959–968.
[80] Komm BS, Mirkin S. Incorporating bazedoxifene/conjugated estrogens into the current paradigm of menopausal therapy. Int J Womens Health. 2012;4:129–140.
[81] Lindsay R, Gallagher JC, Kagan R, et al. Efficacy of tissue-selective estrogen complex of bazedoxifene/conjugated estrogens for osteoporosis prevention in at-risk postmenopausal women. Fertil Steril. 2009;92(3):1045–1052.
[82] Komm BS, Mirkin S, Jenkins SN. Development of conjugated estrogens/bazedoxifene, the first tissue selective estrogen complex (TSEC) for management of menopausal hot flashes and postmenopausal bone loss. Steroids. 2014;90:71–81.
[83] Pinkerton JV, Utian WH, Constantine GD, et al. Relief of vasomotor symptoms with the tissue-selective estrogen complex containing bazedoxifene/conjugated estrogens: a randomized, controlled trial. Menopause. 2009;16(6):1116–1124.
[84] Pickar JH, Boucher M, Morgenstern D. Tissue selective estrogen complex (TSEC): a review. Menopause. 2018;25(9):1033–1045.
[85] Pinkerton JV. Hormone therapy for postmenopausal women. Reply. N Engl J Med. 2020;382(24):e91.
[86] Manson JE, Kaunitz AM. Menopause management-getting clinical care back on track. N Engl J Med. 2016;374(9):803–806.
[87] Nonhormonal management of menopause-associated vasomotor symptoms: 2015 position statement of the North American Menopause Society. Menopause. 2015;22(11): 1155–1172. quiz 1173–1174.
[88] Piérard GE, Humbert P, Berardesca E, et al. Revisiting the cutaneous impact of oral hormone replacement therapy. Biomed Res Int. 2013;2013:971760.
[89] Maheux R, Naud F, Rioux M, et al. A randomized, double-blind, placebo-controlled study on the effect of conjugated estrogens on skin thickness. Am J Obstet Gynecol. 1994;170(2):642–649.

[90] Sauerbronn AV, Fonseca AM, Bagnoli VR, et al. The effects of systemic hormonal replacement therapy on the skin of postmenopausal women. Int J Gynaecol Obstet. 2000;68(1):35–41.
[91] Sator PG, Sator MO, Schmidt JB, et al. A prospective, randomized, double-blind, placebo-controlled study on the influence of a hormone replacement therapy on skin aging in postmenopausal women. Climacteric. 2007;10(4):320–334.
[92] Piérard-Franchimont C, Piérard GE. Postmenopausal aging of the sebaceous follicle: a comparison between women receiving hormone replacement therapy or not. Dermatology. 2002;204(1):17–22.
[93] Wolff EF, Narayan D, Taylor HS. Long-term effects of hormone therapy on skin rigidity and wrinkles. Fertil Steril. 2005;84(2):285–288.
[94] Creidi P, Faivre B, Agache P, et al. Effect of a conjugated oestrogen (premarin) cream on ageing facial skin. A comparative study with a placebo cream. Maturitas. 1994;19(3):211–223.
[95] Phillips TJ, Symons J, Menon S. Does hormone therapy improve age-related skin changes in postmenopausal women? A randomized, double-blind, double-dummy, placebo-controlled multicenter study assessing the effects of norethindrone acetate and ethinyl estradiol in the improvement of mild to moderate age-related skin changes in postmenopausal women. J Am Acad Dermatol. 2008;59(3):397–404.e3.
[96] Yoon HS, Lee SR, Chung JH. Long-term topical oestrogen treatment of sun-exposed facial skin in post-menopausal women does not improve facial wrinkles or skin elasticity, but induces matrix metalloproteinase-1 expression. Acta Derm Venereol. 2014;94(1):4–8.
[97] Owen CM, Pal L, Mumford SL, et al. Effects of hormones on skin wrinkles and rigidity vary by race/ethnicity: four-year follow-up from the ancillary skin study of the Kronos Early Estrogen Prevention Study. Fertil Steril. 2016;106(5):1170–1175.e3.
[98] Rittie L, Kang S, Voorhees JJ, et al. Induction of collagen by estradiol: difference between sun-protected and photodamaged human skin in vivo. Arch Dermatol. 2008;144(9):1129–1140.
[99] Stevenson S, Thornton J. Effect of estrogens on skin aging and the potential role of SERMs. Clin Interv Aging. 2007;2(3):283–297.
[100] Verdier-Sévrain S. Effect of estrogens on skin aging and the potential role of selective estrogen receptor modulators. Climacteric. 2007;10(4):289–297.
[101] Surazynski A, Jarzabek K, Haczynski J, et al. Differential effects of estradiol and raloxifene on collagen biosynthesis in cultured human skin fibroblasts. Int J Mol Med. 2003;12(5):803–809.
[102] Sumino H, Ichikawa S, Kasama S, et al. Effects of raloxifene and hormone replacement therapy on forearm skin elasticity in postmenopausal women. Maturitas. 2009;62(1):53–57.
[103] Formoso G, Perrone E, Maltoni S, et al. Short-term and long-term effects of tibolone in postmenopausal women. Cochrane Database Syst Rev. 2016;10(10):Cd008536.
[104] Desai K, Almeida B, Miteva M. Understanding hormonal therapies: overview for the dermatologist focused on hair. Dermatology. 2021;237(5):786–786.
[105] Gasser S, Heidemeyer K, von Wolff M, et al. Impact of progesterone on skin and hair in menopause – a comprehensive review. Climacteric. 2021;24(3):229–235.
[106] Bouloc A, Roo E, Moga A, et al. A compensating skin care complex containing pro-xylane in menopausal women: results from a multicentre, evaluator-blinded, randomized study. Acta Derm Venereol. 2017;97(4):541–542.
[107] Limtrakul P, Yodkeeree S, Thippraphan P, et al. Anti-aging and tyrosinase inhibition effects of cassia fistula flower butanolic extract. BMC Complement Altern Med. 2016;16(1):497.
[108] Nusgens BV. Hyaluronic acid and extracellular matrix: a primitive molecule?. Ann Dermatol Venereol. 2010;137(Suppl 1):S3–S8.
[109] Dos Santos CCM, Uggioni MLR, Colonetti T, et al. Hyaluronic acid in postmenopause vaginal atrophy: a systematic review. J Sex Med. 2021;18(1):156–166.
[110] Blume-Peytavi U, Bagot M, Tennstedt D, et al. Dermatology today and tomorrow: from symptom control to targeted therapy. J Eur Acad Dermatol Venereol. 2019;33(Suppl 1):3–36.
[111] Loussouarn G, Courtois M, Hourseau C. A new approach to the prevention and cosmetic treatment of alopecia: aminexil. BEDC. 1997;5(1):1–5.
[112] Reygagne P. Evaluation clinique de la stémoxydine à 5% en lotion sur la densité capillaire. Annales de dermatologie et vénérologie. 2013;140:9–12. [French].
[113] Passeron T, Krutmann J, Andersen ML, et al. Clinical and biological impact of the exposome on the skin. J Eur Acad Dermatol Venereol. 2020;34(Suppl 4):4–25.
[114] Krutmann J, Schalka S, Watson REB, et al. Daily photoprotection to prevent photoaging. Photodermatol Photoimmunol Photomed. 2021;37(6):482–489.
[115] Lethaby A, Ayeleke RO, Roberts H. Local oestrogen for vaginal atrophy in postmenopausal women. Cochrane Database Syst Rev. 2016;2016(8):Cd001500.
[116] Constantine GD, Graham S, Lapane K, et al. Endometrial safety of low-dose vaginal estrogens in menopausal women: a systematic evidence review. Menopause. 2019;26(7):800–807.
[117] Jung S, Lademann J, Darvin ME, et al. In vivo characterization of structural changes after topical application of glucocorticoids in healthy human skin. J Biomed Opt. 2017;22(7):76018.
[118] Kim BJ, Lee NR, Lee CH, et al. Increased expression of 11β-hydroxysteroid dehydrogenase type 1 contributes to epidermal permeability barrier dysfunction in aged skin. Int J Mol Sci. 2021;22(11):5750.
[119] Trüeb RM. Aging of hair. J Cosmet Dermatol. 2005;4(2):60–72.
[120] Ahluwalia J, Fabi SG. The psychological and aesthetic impact of age-related hair changes in females. J Cosmet Dermatol. 2019;18(4):1161–1169.
[121] Somani N, Turvy D. Hirsutism: an evidence-based treatment update. Am J Clin Dermatol. 2014;15(3):247–266.