

Article

Dermatological Changes during Menopause and HRT: What to Expect?

Bruna Bravo ¹, Lais Penedo ¹, Raquel Carvalho ¹, Carolina Dal Vesco ¹, Mariana Calomeni ¹,
Debra Gapanowicz ², Elaine Kemen ³, Raphaela Paes ³ and Guilherme Renke ^{3,4,*}

¹ Dermatology Department, Bravo Private Clinic, Rio de Janeiro 22240-032, Brazil; bruna@bravomed.com.br (B.B.); laispenedo@hotmail.com (L.P.); carolinadalvesco@gmail.com (C.D.V.); maricalomeni@gmail.com (M.C.)

² National Institute of Cardiology, Brazilian Ministry of Health, Rio de Janeiro 22240-006, Brazil

³ Nutrindo Ideais Performance and Nutrition Research Center, Rio de Janeiro 22411-040, Brazil

⁴ Clementino Fraga Filho University Hospital, Federal University of Rio de Janeiro, Rio de Janeiro 21941-617, Brazil

* Correspondence: renke@renke.com.br

Abstract: Menopause marks the end of a woman's reproductive life. It is well-known that skin aging is accelerated during this period, as declining estrogen detrimentally impacts the skin's extracellular matrix (ECM) which is the provider of strength and elasticity. Menopause also affects scalp hair, reducing hair diameter and leading to shorter hair growth. Objective: To evaluate the main dermatological complaints of Brazilian women during this period, comparing the compatibility of these complaints with similar studies that evaluated skin health at menopause. Methods: This study interviewed 463 postmenopausal women between 42 and 83 years old through a public electronic questionnaire in the SurveyMonkey app about their perception of the changes noticed in their hair and skin after menopause. All statistical analyses were performed in R v. 3.6.1. Results with p -values < 0.05 were considered significant. Results: Dermatological health in menopausal women, especially the quality of the skin, nails and hair may deteriorate with estrogen deficits. As life expectancy increases and hormone replacement therapy (HRT) becomes more common, a greater understanding of their dermatological effects in menopause is needed. Conclusions: Menopause strongly impacts skin quality and worsens women's self-esteem and quality of life. There is still a lack of knowledge about HRT and specific treatments for improving skin, hair and nails.

Keywords: menopause; skin quality; hormone replacement therapy; estradiol



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1. Introduction

Menopause is a marker of the end of a woman's reproductive life. It is defined as the permanent cessation of menstruation for 12 consecutive months due to the loss of ovarian follicular function [1]. The average age of menopause is approximately 51 years and is typically preceded by a transition period known as perimenopause, lasting an average of 2 to 8 years. During perimenopause, clinical and biological manifestations of the onset of menopause become evident, including 12 months after the last menstrual period [2]. Consequently, women spend approximately one-third of their lives in the postmenopausal period. The age at which this transition to menopause begins is influenced by a series of factors, including genetic components and environmental elements such as exposure to ultraviolet radiation and smoking. Furthermore, factors such as lifestyle, nutrition, alcohol consumption, stress levels and sleep deprivation also determine this process [2].

The skin is an endocrine organ and an essential target for estrogen, androgen hormones (such as testosterone) and cortisol [3]. Although vasomotor symptoms such as hot flashes and night sweats are more common and characteristic of menopause, skin and capillary

symptoms are often neglected concerning other manifestations of menopause. However, they have a significantly negative effect on quality of life.

Since one of the significant changes during menopause is the virtual cessation of ovarian estrogen production, it is well-known that skin aging is accelerated during menopause [3,4]. Declining estrogen detrimentally impacts the skin's extracellular matrix (ECM) which is the provider of strength, elasticity and resilience [4]. There is a decrease in collagen production, resulting in loss of elasticity and increased wrinkles, dry skin, itching, atrophy and sagging. In addition, the skin may be more prone to presenting dark spots and pigmentation irregularities, promoting a notable impact on women's self-esteem during this hormonal transition phase [4].

When it comes to hair and fur, menopause can also bring challenges. Changes in hair quality and structure, diffuse hair loss and hair thinning are observed, as there is a reduction in hair diameter and a faster transition from the anagen to the telogen phase, leading to a shorter hair growth phase [5]. Unwanted hair growth also occurs in facial areas during menopause. These hair changes can be distressing and impact self-image and perception of age [5].

Women must be aware of these changes and maintain the health and vitality of their skin and hair during menopause [5]. This may include using appropriate skin care products, protection against sun damage and dermatological treatments, always guided by healthcare professionals trained in treating these specific issues related to menopause to minimize unwanted effects and maintain well-being and women's health [5,6].

Hormone replacement therapy (HRT) is explored for its ability to alleviate the signs and symptoms caused by hormone deficiency as it aims to restore physiological levels of hormones in the body [5,6]. HRT consists of estrogen (17 β -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 Woman's Health Initiative (WHI) trial, some conditions were analyzed such as the fact that women with prior hysterectomy receiving only oral CEE for a median of 7.2 years presented an increased hazard for stroke and venous thrombosis [6]. However, HRT did not increase the risk for all-cause mortality [6], was neutral for coronary heart disease, cancer mortality and decreased hip fracture and diabetes rates [6]. In women under 60 years of age or within 10 years of menopause, statistically significant reductions of 20% in heart disease and 23% in breast cancer were observed after almost 6 years of CEE use and 12 years of follow-up. This benefit may not apply to populations at higher risk or with other risk factors for those conditions. Therefore, the increased risks of HRT, especially in breast cancer, were due to the progestogen component and not the CEE alone [6].

Estrogen helps maintain skin hydration, texture and overall appearance by increasing the production of collagen and elastin, which are proteins that keep the skin firm and elastic, helping to prevent the appearance of wrinkles and sagging [6,7]. Estrogen also helps to uniformize skin pigmentation, reducing the appearance of dark spots and preventing premature aging [7].

Estrogen increases blood circulation, contributing to healthier skin and playing an essential role in wound healing by reducing inflammation, stimulating granulation tissue formation and accelerating re-epithelialization [7]. Progesterone, another vital hormone in the female reproductive system, also affects the skin, although these effects are generally less pronounced than those of estrogen. Some of these include better hydration, regulation of sebum production and skin inflammation, which is beneficial in controlling acne and skin irritation. In most cases, the effects of progesterone are influenced by the body's balance between progesterone and estrogen [7].

Although menopause is associated with decreased hair density and female pattern hair loss, there is still a lack of research into the relevance of HRT in mitigating these changes [8]. Some studies indicate that it can help reduce hair loss in postmenopausal women, make hair thicker and healthier and improve hair quality.

HRT has been used for many years, however, its indications only include relieving menopausal symptoms and preventing osteoporosis. Generally, HRT is not recommended exclusively to treat skin and hair symptoms [5]. The decision to start must be individualized and consulted with a doctor, considering each woman's benefits and risks. It is crucial to discuss with patients the possible broader benefits of HRT, which go beyond the relief of vasomotor symptoms and encompass effects on the bones, breasts, heart and vascular system. This allows them to make informed decisions about managing menopause symptoms [5–8].

Considering this, systemic HRT has been recommended to treat skin aging [5]. We must explore how menopause and HRT affect skin aging to identify targets and develop drugs to improve skin health in midlife. Our objective was to define and quantify the main dermatological complaints of Brazilian women during this period, compare the compatibility of these complaints with similar studies that evaluated skin health during menopause and analyze the niche opportunity for cosmetics aimed at this phase of a woman's life.

2. Materials and Methods

2.1. Study Design

This study interviewed 463 postmenopausal women between 42 and 83 through a public electronic questionnaire in the SurveyMonkey app. The questionnaire consisted of 27 multiple-choice questions related to their menopause period and their perception of the changes in their hair and skin after menopause. The inclusion criteria were women after menopause, natural or surgically, and the exclusion criteria were men or women during reproductive age. All statistical analyses were performed in R v. 3.6.1. Results with p -value < 0.05 were considered significant.

2.2. Statistical Analysis

The primary analysis was descriptive and presented the observed data in tables. It was expressed by measures of central tendency and dispersion for numerical data, as well as by frequency and percentage for categorical data. Data were described as mean (standard deviation) for average variables and rates. The statistical program used for the analysis will be Statistical Package for the Social Sciences® (SPSS) version 21.0 (SPSS Incorporation). The Shapiro-Wilk normality test was used to verify the data distribution of all continuous variables. The Chi-squared test of independence was used to assess the association between the use of HRT and the use of androgen therapy with alterations in the skin, hair and period of menopause.

3. Results

There were 463 Brazilian women that answered a 27-question questionnaire. The questions covered information about the patient's age, skin type, age when menopause started, whether it was surgical or not and if they were treated with HRT (Table 1). Other questions about how this phase affected their quality of life were whether they noticed any skin and hair changes and whether there would be interest in cosmetic products mainly aimed at these specific complaints.

The patients' age ranged between 42 and 83 years old with a mean of 59.14 years, and their age of menopause onset ranged between 32 to 58 years. To better understand the results, we separated our interviewees into two groups: 15% (70) surgical menopause (SM)—women who have their uterus removed and then start menopause—and 85% (384) non-surgical menopause (NSM). In the SM group, the average age was 45.5 years, while in the NSM it was 50 years old. Regarding their skin type, 49% (229) of patients consider their skin mixed, 27% (124) dry, 11% (51) oiled and 10% (48) believe it is dry. Of the 458 responses obtained, 31% (144) fully agreed that menopause affected their quality of life, while 37% (171) partially agreed. Neither agreed nor disagreed, somewhat disagreed, or entirely disagreed had 10% (48) of responses each.

Table 1. General characteristics of the study participants. Values are expressed as *n* (%).

Variables	Total (<i>n</i> = 464)
Age (years)	59.1 ± 8.4
Elderly (≥60 years)—% (<i>n</i>)	46.8 (217)
Age at menopause—% (<i>n</i>)	48.9 ± 4.7
Skin type—% (<i>n</i>)	
Oily	11.0 (51)
Mixed	49.4 (229)
Dry	26.7 (124)
Sensitive	10.3 (48)
Others	2.6 (12)
Surgical menopause—% (<i>n</i>)	15.4 (70)
Menopause affected my quality of life—% (<i>n</i>)	
Totally agree	31.4 (144)
Partially agree	37.3 (171)
Do not agree nor disagree	10.3 (47)
Partially disagree	10.5 (48)
Totally disagree	10.5 (48)
Clinical symptoms after menopause—% (<i>n</i>)	
Vaginal atrophy	26.3 (122)
Fat increase	39.9 (176)
Tiredness or lack of energy	43.5 (202)
Hair growth on the face	22.4 (104)
Decreased libido	55.0 (255)
Hot flashes	56.3 (261)
Insomnia	51.7 (240)
Emotional lability	40.7 (189)
Osteoporosis	19.2 (89)
Weight gain	45.0 (209)
Skin dryness	1.3 (6)
Others	9.3 (43)
Sought medical treatment due to menopausal symptoms—% (<i>n</i>)	73.5 (341)
Change in skin	10.1 (47)
Hot flashes	42.7 (198)
Insomnia	26.9 (125)
Urogenital atrophy	9.1 (42)
Emotional lability	26.7 (66)
Other	14.2 (43)
Menopause affected your self-esteem—% (<i>n</i>)	
Totally agree	24.8 (114)
Partially agree	27.8 (128)
Do not agree nor disagree	14.1 (65)
Partially disagree	9.1 (42)
Totally disagree	24.1 (111)
Did you receive information about the effects of menopause on skin, hair and nails from your gynecologist and/or dermatologist?—% (<i>n</i>)	52.9 (243)
Do you feel comfortable talking to your dermatologist about menopause—% (<i>n</i>)	
Totally agree	70.6 (320)
Partially agree	9.9 (45)
Do not agree nor disagree	13.9 (63)
Partially disagree	2.0 (9)
Totally disagree	3.5 (16)
Menopause has affected the quality of your skin.—% (<i>n</i>)	
Totally agree	46.5 (212)
Partially agree	31.1 (142)
Do not agree nor disagree	11.4 (52)
Partially disagree	5.9 (27)
Totally disagree	5.0 (23)

Table 1. Cont.

Variables	Total (<i>n</i> = 464)
Skin changes—% (<i>n</i>)	
Skin thinning	29.5 (137)
Gloss loss	41.8 (194)
Increase in bruises, bruises (purple spots)	14.0 (65)
Sagging	66.8 (310)
Stains	34.1 (158)
More inflamed/irritated skin	8.6 (40)
More oily skin/acne	6.0 (28)
More sensitive skin	14.4 (67)
Dryness	51.3 (238)
Increased wrinkles	45.5 (211)
Worsening of dark circles	30.2 (140)
Other	3.7 (17)
Menopause affected the quality of your hair—% (<i>n</i>)	
Totally agree	43.8 (201)
Partially agree	28.3 (130)
Do not agree nor disagree	11.1 (51)
Partially disagree	5.9 (27)
Totally disagree	10.9 (50)
What changes have you noticed in your hair?—% (<i>n</i>)	
Thread thinning	36.4 (169)
Volume decrease	44.6 (2073)
Thicker yarn	4.7 (22)
More brittle	22.8 (106)
Many white threads	36.4 (169)
Gloss loss	25.4 (118)
Hair loss	46.3 (215)
Dryness	28.9 (134)
Others	1.7 (8)
Menopause affected the quality of your nails—% (<i>n</i>)	
Totally agree	39.0 (176)
Partially agree	28.2 (127)
Do not agree nor disagree	11.5 (52)
Partially disagree	6.4 (29)
Totally disagree	14.9 (67)
What changes have you noticed in your nails?—% (<i>n</i>)	
Peeling	35.8 (166)
Decrease in growth	18.5 (86)
Streaks on the nail	26.9 (125)
Fragile and/or brittle	55.8 (259)
Other	1.3 (6)
Treats or has already treated menopause symptoms with HRT—% (<i>n</i>)	46.6 (216)
HRT method uses/used—% (<i>n</i>)	
Pill	43.6 (98)
Transdermal gel	43.1 (97)
Hormone implant	10.7 (24)
Other	2.7 (6)
Did you take androgen therapy (DHEA, testosterone or gestrinone) after menopause?—% (<i>n</i>)	
Yes	21.5 (96)
No	78.0 (348)
I don't remember	0.4 (2)
You have been well advised by your gynecologist/endocrinologist about the risks and benefits of HRT—% (<i>n</i>)	
Totally agree	48.6 (211)
Partially agree	15.4 (67)
Do not agree nor disagree	18.0 (78)

Table 1. Cont.

Variables	Total (n = 464)	
Are you or were afraid to start HRT—% (n)	Partially disagree	7.6 (33)
	Totally disagree	10.4 (45)
You were informed that HRT would bring benefits to your skin, hair and nails—% (n)	Totally agree	36.5 (155)
	Partially agree	19.5 (83)
	Do not agree nor disagree	18.4 (78)
	Partially disagree	6.6 (28)
	Totally disagree	19.1 (81)
Improvement of symptoms after HRT—% (n)	Totally agree	42.6 (180)
	Partially agree	17.3 (73)
	Do not agree nor disagree	20.1 (85)
	Partially disagree	5.2 (22)
	Totally disagree	14.9 (63)
Have you had any adverse effects on your skin while taking HRT?—% (n)	Acne	3.9 (18)
	Seborrhea	1.5 (7)
	Increased body hair	9.3 (43)
	Spots on the face	5.4 (25)
	Weight gain or increased appetite	14.9 (69)
	Other	2.6 (12)
	There is a lack of cosmetic products aimed for menopausal women—% (n)	74.0 (309)
What specific menopause products would you use?—% (n)	Facial moisturizing creams	66.8 (310)
	Moisturizing body creams	59.5 (276)
	Intimate moisturizing creams	40.3 (187)
	Facial whitening creams	35.8 (166)
	Neck creams	53.9 (250)
	Eye area creams	50.0 (232)
	Nail strengtheners	48.1 (223)
	Shampoos and hair masks	43.1 (200)
	Facial sunscreens	47.6 (221)
	Facial soaps	34.7 (161)
	Other	2.4 (11)

The question that followed was about symptoms after menopause. Hot flashes were the number one symptom, and was mentioned by 57% (258) of women. In sequence, loss of libido was referred to by 56% (255), insomnia by 53% (240), increase in weight by 45% (206), tiredness by 44% (201), emotional lability by 42% (189), increase in visceral fat by 39% (175), vaginal atrophy by 27% (122), growth of facial hair by 23% (104) and osteoporosis by 19% (88) of the patients (Figure 1).

Regarding the influence of menopause on women's self-esteem, 53% (242) fully or partially agreed that their self-esteem was affected by this period of their lives. However, 47% of women reported that they had not been informed about the effects of menopause on their skin, hair and nails before this phase started.

Almost 70% (310) of patients pointed to skin laxity as a symptom that worsened after menopause, followed by 53% (238) with skin dryness, 47% (211) with skin rhytids, 43% (194) with loss of skin vigor, 35% (158) complained about skin hyperpigmentation, 31% (140) with dark circles worsening and 30% (137) with decreased skin thickness.

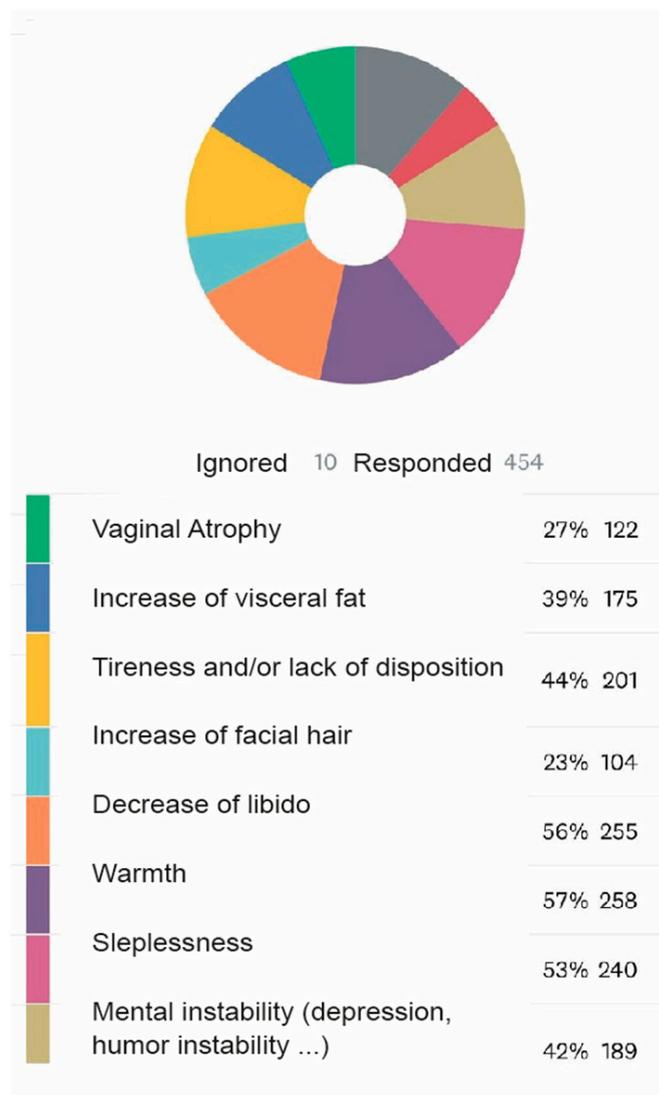


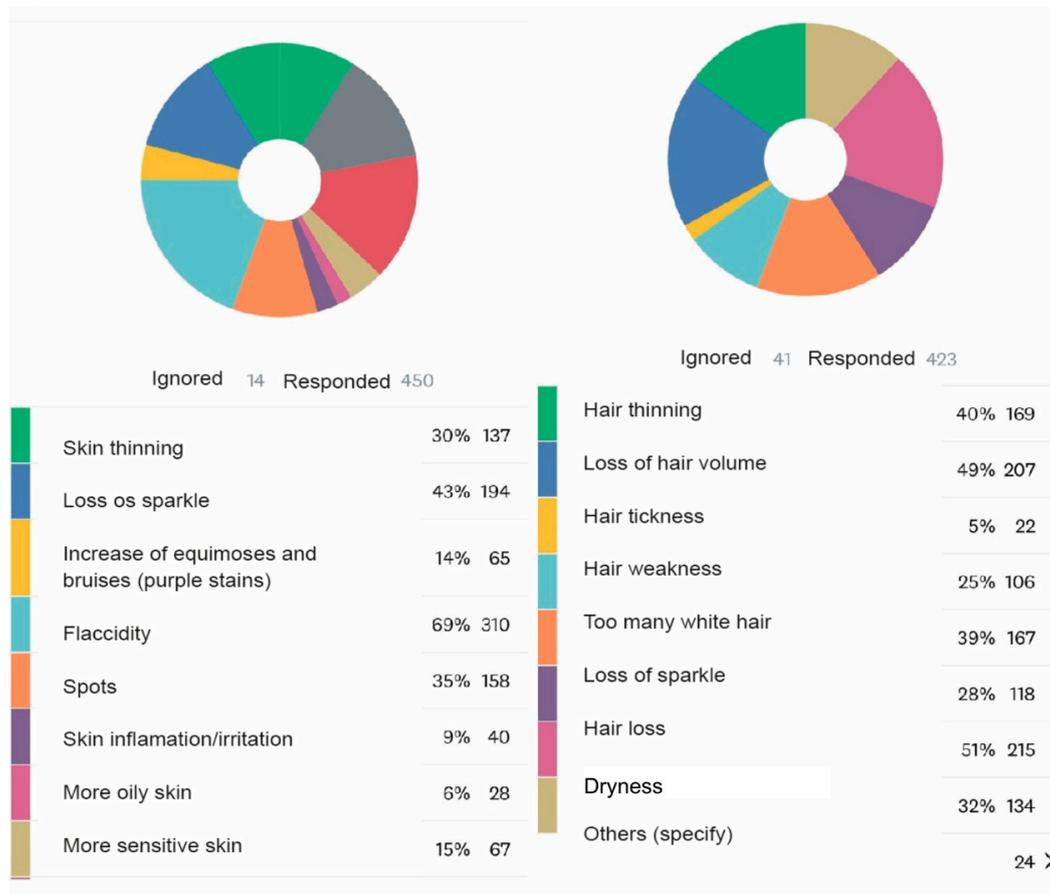
Figure 1. Clinical symptoms manifested after menopause. Values are expressed as *n* (%).

Concerning phaneros, 72% of patients fully or partially agree that menopause affects the quality of their hair and 67% fully or partially agree that the quality of their nails was also affected. Regarding their perception of hair changes, hair loss was pointed out by 51% (215) of the participants, followed by a decrease in hair volume (49%), an increase in white hair (39%), dryness (32%), hair fragility (25%) and loss of shine (28%). Regarding the nail symptoms, 66% (259) of the participants indicated that they felt their nails were weak and brittle, 42% (166) with peeling and 22% (86) noticed decreased growth speed (Figure 2).

Among the 216 women who underwent HRT, 91 were submitted to androgen therapy. Another interesting data was that although 211 patients agreed that their doctors advised them well on the risks and benefits of HRT, 155 feared adverse effects. The number one negative effect of HRT was weight gain (32%), followed by increased body hair (20%), hyperpigmentation (12%) and acne (8%).

In addition, it was observed that women who underwent HRT ($X^2 = 78.956/p < 0.001$) showed improvement in menopausal symptoms. Patients who sought care due to menopausal symptoms were encouraged to use HRT ($X^2 = 58.794/p < 0.001$) and showed improvement in symptoms ($X^2 = 16.984/p < 0.001$) (Table 2).

Finally, 309 patients (79%) pointed out an undersupply of cosmetic products aimed at menopausal women, and 414 women referred to the need for at least one class of menopausal dermocosmetics.



(a)

(b)

Figure 2. (a) Alterations noticed in skin after menopause; (b) alterations noticed in hair after menopause. Values are expressed as n (%).

Table 2. Assessment of association between study participants. Statistically significant p -value < 0.05 .

Variables	χ^2	p
HRT \times Skin Quality ($n = 102$)	0.292	0.589
HRT \times Hair Quality ($n = 104$)	3.307	0.069
HRT \times Nail quality ($n = 81$)	0.076	0.786
Androgen therapy \times Skin Quality ($n = 51$)	5.810	0.055
Androgen therapy \times Hair quality ($n = 53$)	6.519	0.038
Androgen therapy \times Nail quality ($n = 36$)	3.183	0.204
HRT \times Improvement of symptoms ($n = 159$)	78.956	< 0.001
Sought care due to symptoms \times HRT ($n = 197$)	58.794	< 0.001
Sought care due to symptoms \times Improvement in symptoms ($n = 158$)	16.984	< 0.001

4. Discussion

Estrogen is a steroid hormone that influences the growth, differentiation and function of many tissues. About 60% of circulating estrogen in ovulating women is in the form of estradiol (E2) and is produced primarily in the ovary, while 40% is made in extra-glandular

tissue from the androgen precursor androstenedione and is in the form of estrone (E1) and is not drastically altered by menopause. Therefore, E2 is the most functional estrogen during reproductive age and declines abruptly at menopause [9]. Vasomotor symptoms may begin during perimenopause and frequently persist for an average of 7.4 years or longer, affecting the patient's quality of life [10]. We observed the same trend in our study with 68% of patients fully or partially agreeing that menopause affected their quality of life. E2 therapy reduces weekly symptom frequency by 75% and significantly reduces symptom severity [10]. Curiously, we evaluated the same trend in our study, where 75% of postmenopausal women sought medical care with a specialist during menopause. Despite this, a smaller percentage of patients (40%) had common menopausal symptoms such as tiredness and lack of disposition, decreased libido, hot flashes, insomnia, emotional lability and weight or appetite gain.

In recent decades, health professionals have shown greater interest in the skin aging mechanism because, although the effects of estrogens on various organs are well established, the influence of these hormones on the skin is still poorly understood. It is known that in the perimenopause there is an acceleration of cutaneous aging. During this period, women report clinical signs and symptoms resulting from epidermal atrophy, a decrease in collagen and elastin, alterations in the proportion between type I and II collagen and alterations in vascularization. The speed of the process depends on several factors, including catabolic ones such as infections and tumors and others such as environmental exposure to ultraviolet light, pollution, lifestyle (poor nutrition, use of nicotine, alcohol, drugs) and hormonal causes [11,12]. However, despite all this knowledge, there seems to be a gap in the medical follow-up of perimenopausal patients where patients do not receive information about the dermatological effects of menopause. In our study, 47% of postmenopausal women reported not having been informed about the impact of menopause on their skin, hair and nails. These changes can interfere with a woman's self-esteem, especially in this perimenopause phase. We observed that more than 50% of women fully or partially agreed that their self-esteem was affected by menopause.

Skin and hair changes during menopause occur gradually and generally receive less attention than vasomotor symptoms. More than 60% of women report skin problems, and about half indicated that menopause had caused changes to their skin. According to 87 women from the Leicht C. study [13], the main symptom is dry skin [13]. However, according to a 2018 study with 1287 women, most health professionals cannot treat and monitor these patients. In this survey, similar to our findings, 50% of women felt that they had not been sufficiently informed about the dermatological symptoms of menopause and 72% reported noticing changes in their skin during perimenopause and menopause [14].

The visible signs of skin aging and loss of hair quality are of great concern to menopausal women. Increased sagging, dryness and wrinkles, especially on the face, contribute to an increase in the perception of aging and a decrease in attractiveness [15] significantly impacting a woman's quality of life. Furthermore, in Westernized societies, hair and skin quality reflects good health and well-being. Therefore, women at this stage are often judged which can cause a critical psychological burden [16].

Few studies evaluate dermatological symptoms (skin and capillaries) and their relationship with hormonal changes during menopause. Additionally, skin aging and wrinkles have been shown to correlate more closely with chronological age than with menopause. However, skin tightness (an inverse measure of dermal collagen density) has only been positively correlated with time since menopause [17,18]. During the perimenopause period, estrogen levels gradually decrease and the aromatization of androgens increases, leading to variations in sebum levels. Skin dryness can be noticed at the beginning of menopause, but initially, it can be somewhat compensated by hypertrophy of the sebaceous glands. Later, during menopause, when sebum production is markedly reduced by hypoestrogenism, the skin becomes increasingly dry, followed by sagging and atrophy. Skin atrophy from collagen loss is more pronounced in menopausal women [19–21]. In perimenopause, skin collagen levels decline rapidly, with a collagen reduction of approximately 30% in the

first five years, followed by a further decline of 2% per year for the next fifteen years [21]. An annual skin thickness reduction and constant collagen depletion of 1.1% and 2.1%, respectively, have been observed in menopausal women [22]. Interestingly, a significant complaint of sagging skin was observed in almost 70% of our study population.

In addition to the skin, hair changes and other problems are observed during menopause. Hair problems during menopause include (1) reduction of scalp hair and (2) unwanted increase in hair growth in some regions of the face, especially the upper lip and chin. Due to the sustained reduction of the hair cycle during menopause, diffuse effluvium may occur due to androgenetic alopecia or female pattern follicular rarefaction. Furthermore, existing hair becomes drier and thinner due to hormonal deficit and aging [16].

In the experience of our medical treatment centers specialized in menopause and dermatology—Nutrindo Ideais and Clinica Bravo—one of the biggest complaints of climacteric and menopausal patients is hair loss and loss of skin oil and appearance. Some patients experience improvements in these symptoms with endocrinological adjustment and HRT. However, most require intervention with a dermatologist with either injectable hair mesotherapy, platelet-rich plasma (PRP) or laser therapies.

Furthermore, due to the heterogeneity of hormonal changes and the repercussions of hypoestrogenism, our expertise demonstrates that all climacteric patients seek help not only from an endocrinologist but also from a dermatologist so that a personalized and multidisciplinary treatment can be instituted.

The questionnaire answers consist of patients' self-evaluation instead of dermatologists' diagnoses, which is a limitation of our study: the lack of correlations between patients' self-assessments and dermatological assessments made by a dermatologist's clinical examination. Therefore, our results confirm the impact on the quality of phaneros. We observed that more than 70% of patients fully or partially agree that menopause affects the quality of their hair, especially in hair volume (49%) and hair loss (51%). More than 65% of the patients stated that the quality of their nails was affected by this period, indicating that they felt their nails were weak and brittle.

The skin and hair are subject to structural changes with the gradual decline of hormones (estrogens and progesterone). Decreased estrogens negatively affect the ECM, which provides skin strength, elasticity and resilience. There is a rapid destruction of collagen and a decrease in the production of elastin fibers that make up the skin's supporting tissue, consequently accelerating aging. This leads to increased sagging, loss of skin tone and decreased hydration, resulting in thinner, dry, sagging and fragile skin [12,23]. This hormonal imbalance typical of this phase also favors the predominance of androgenic hormones in the circulation, favoring the oiliness of the face skin, a tendency to acne and the appearance of thick hair under the chin and on the sides of the face [23].

Nevertheless, we observed that patients pointed out skin dryness, skin laxity and accentuation of skin rhytids. Thus, studies show that about 30% of the skin's total collagen is lost during the first five years post-menopause, after which there is an average annual drop of 2.1%. This way, the aged skin becomes thinner due to the decrease in epidermal keratinocytes and the loss of connective tissue and the ground substance of the dermis, rich in glycosaminoglycans. These degenerative changes accompanying the aging process result in atrophy, sagging and skin wrinkling [23–25].

In this aspect, much research is being done on the effects of HRT and its anti-aging potential, especially on skin quality. The impact of HRT on skin quality and thickness is established; therefore, this hormonal therapy is already considered to alleviate skin atrophy and xerosis in menopausal women. Improvement in dermal density was demonstrated when estrogens were first used in menopausal women [26]. HRT appears to significantly affect skin quality and cosmetic benefits in women who have never used HRT. Women who receive long-term HRT at menopause have been observed to have less wrinkling and more elastic skin than women who have never used HRT [27]. Furthermore, a reduction in skin atrophy was demonstrated in those who received estrogen treatment for one year, thus providing further evidence for the potential use of estrogens in preventing skin aging.

However, no consensus has been established regarding the effects of HRT on dermal aging in menopause. Despite this, it has been reported that dermal collagen density, thickness and content are likely maintained in patients undergoing HRT compared to untreated women [26]. The hypothesis is that these changes are associated with changes in keratinocyte renewal. HRT partially restored both the barrier function and water retention capacity of the xerotic stratum corneum associated with menopause [28]. Finally, estrogen, specifically through increasing transforming growth factor-beta1 (TGF-beta1), has also been found to improve wound and skin healing rates with anti-aging effects [29].

Replacing other hormones, which can raise estrogen and androgen levels, such as dehydroepiandrosterone (DHEA) has shown several positive effects, including increased sebum production. This is especially useful for improving the skin of menopausal patients, as they are often physiologically hypo seborrheic [30,31]. A randomized clinical trial showed that skin atrophy significantly decreases due to increased epidermis thickness in postmenopausal women by oral DHEA replacement at a dose of 50 mg per day for 12 months, particularly on the dorsal surface of the hands [30]. Therefore, in addition to HRT with estrogens, the effects induced by oral DHEA supplementation can improve physical appearance and have an anti-aging effect on the skin.

Unlike DHEA, estrogen regulates several cellular functions, including proliferation, morphogenesis, differentiation and apoptosis. Estrogen receptors are present in every cell in our body, including epidermal keratinocytes, dermal fibroblasts, sebaceous glands, hair follicles and nails. The strong expression of these receptors in dermal fibroblasts suggests the direct participation of estrogens in the stimulation of collagen synthesis via transforming growth factor (TGF β). E2 stimulates the proliferation and DNA synthesis of keratinocytes, resulting in the thickening of the epidermis and greater skin hydration, reducing trans-epidermal water loss. The epidermal lipid layer and the content of glycosaminoglycans, mainly hyaluronic acid, are also increased by E2 stimuli [25,32,33]. Indeed, estrogen deficiency directly affects the quality of hair and nails.

Estrogen deprivation is associated with degenerative abnormalities of dermal elastic fibers, with reports of increased synthesis of these fibers after using a cream containing estriol. Most studies with estrogen replacement therapy, both oral and topical, show an increase in skin thickness and dermal collagen [34]. Studies have shown that the topical use of 17 β -estradiol in older people potentiates the expression of type I procollagen, especially in women. It has also been seen that the substance can stimulate collagen synthesis and decrease in vivo synthesis of MMP-1 (matrix metalloproteinase), preserving skin structure [35]. However, the use of estrogens in menopause for treating skin aging is still a controversial subject. Despite this, 64% of the patients agreed that their doctors advised them well about the risks and benefits of HRT. Still, they did not clarify the benefits of HRT for dermatological complaints.

Another exciting issue that still needs to be discovered is whether the use of topical estrogens on the skin would have the beneficial effects of attenuating aging without causing harm to the patient. Despite that, we observed that almost 65% of patients pointed out an undersupply of cosmetic products aimed at menopausal women. However, we agree that further studies are still needed to establish the minimum dose required to obtain the best results without systemic adverse effects of E2 [6,36–38].

Dermatological benefits or side effects with HRT vary depending on the hormone the patient receives during menopause (Table 3). Depending on the type of HRT, there may be an increase of up to 25% in the risk of dermatological side effects. HRT with non-bioidentical hormones appears to have a worse effect on cutaneous side effects than bioidentical hormones [39]. Most dermatological adverse events associated with HRT are androgenic and probably related to exacerbated testosterone levels and its derivatives [40,41]. Androgenetic alopecia has been associated with testosterone use. In two placebo-controlled clinical trials, testosterone replacement was associated with a 36% increase in hirsutism in a dose-dependent manner [42,43]. Another common side effect is acne, an adverse event

with a wide range of reported incidences of up to 50% in different studies, including case series, randomized clinical trials and literature reviews [42–45].

Table 3. Dermatologic benefits and side effects of HRT (DHEA: dehydroepiandrosterone; % prevalence).

Hormone Type	Dermatologic Benefit (%)	Dermatologic Side Effect (%)	References
Estradiol	Decreases skin atrophy and xerosis (31%).	Skin irritation (20%) (topical treatments only); Localized allergic reaction (<1%)	[26,27,30–32,39]
Testosterone	Decreases skin atrophy	Acne (5.6–50%); Increased facial hair growth (11.6–19.6%); Hirsutism (6–36%)	[39,42–45]
DHEA	Decreases skin atrophy (73%)	Acne (23%); Increased sebum production (64%); Skin oiliness and elasticity changes (41–89%)	[30,31,39]

Although melanoma is not associated with HRT, one case report suggested that sex hormones likely contribute to the pathophysiology of melanoma [46]. However, contradictory studies indicate an inhibitory effect of estrogen and progesterone on melanoma growth [47]. Furthermore, a randomized clinical trial found no increase in the incidence of non-melanoma skin cancer or melanoma in patients taking HRT during menopause [48]. In vitro experiments also reported autophagy and growth inhibition in melanoma cells induced by TRH.

Finally, melasma is associated with hormonal influences, such as menopause and HRT, although the etiology is not well studied at the molecular level [49–52]. The pathogenesis of hyperpigmentation may involve high estrogen, testosterone and progesterone levels, stimulating melanogenesis [49,52]. Although the literature does not mention melasma as a common side effect of HRT, it is crucial to consider it as a potential effect for anyone using HRT.

One of the study's limitations is the need for more statistical significance in the correlations between the use of HRT and improvement in skin quality, which may have been impaired due to the N of the analyzed sample.

5. Conclusions

Dermatological health in menopausal women, especially skin quality, nails and hair, may deteriorate with estrogen deficits. As life expectancy increases and estrogen and androgen replacement therapy becomes more common, a greater understanding of their dermatological effects in menopausal women is needed.

The self-perception of the studied population substantially impacted the skin and worsened self-esteem and quality of life in the postmenopausal period. The main complaint was the need for more precise information about the risks and benefits of HRT and specific treatments for improving skin, hair and nails.

HRT increases epidermal and dermal thickness, increases collagen and elastin content and improves skin moisture with fewer wrinkles. Although menopause is associated with a decrease in hair density and female-pattern hair loss, research on the role of HRT in mitigating these changes is lacking. Future research is needed to evaluate new dermatological treatments for perimenopausal women and, in general, patients were open to understanding treatment options for this phase in an attempt to improve their quality of life and self-esteem.

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