

Sensitive skin: review of an ascending concept *

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Abstract: Sensitive skin is a condition characterized by stinging, burning and itching sensations. The diagnosis, pathophysiology and treatment of sensitive skin are still under discussion. In the last years, studies on its epidemiology have been performed, showing a high prevalence and impact on quality of life. Brazilian population was also considered in these studies. Cosmetics, climate changes and skin barrier impairment are the main factors that contribute for skin hyperreactivity. New studies are trying to bring new knowledge about the theme. This review will describe data on epidemiology, triggering factors, pathophysiology, diagnosis and treatment.

Keywords: Additives in cosmetics; Cosmetics; Cosmetic technology; Dermatitis; Contact Dermatitis; Hypersensitivity; Skin absorption; Skin care; Skin cream; Skin diseases

INTRODUCTION

Sensitive skin is defined as a sensory reaction triggered by contactors and/or environmental factors, usually without a visible clinical manifestation.^{1,3}

This entity was first described by Maibach in 1987 under the name of Cosmetic Intolerance Syndrome (CIS).⁴ In 1990, Fisher referred to the condition as "status cosmeticus".⁵ Literature reports have shown that this condition can also be triggered by environmental factors (cold, heat, sun, pollution, moisture) and therefore the term has been expanded to Sensitive Skin Syndrome (SSS).^{1,6} Possible synonyms for this condition are hypersensitivity, hyperreactivity, sensitivity, intolerance or skin irritation.⁷

Sensations described by patients vary largely: pruritus, burning, tingling, pungency, thickening or dryness of the skin. These symptoms may occur minutes to hours after contact with a cosmetic product/ environmental stimulant or even after several episodes of use of a topic product, triggering the conduction by cumulative effect.⁸

Sensitive skin syndrome can manifest itself in two forms: objective and subjective.⁷ The objective form is favored by a basic dermatitis that alters the protective skin barrier such as atopic dermatitis and acne. In these cases, clinical lesions may be visible, such as erythema, papules and vesicles.^{1,8} In the subjective form, the patient refers only to the symptoms, without visible dermatitis, and is thus usually self-diagnosed.

Presence of symptoms, in the majority of exclusively subjective cases, makes this entity a diagnostic challenge and some authors even consider a psychological origin for the picture. With the help of new technologies the presence of alterations in the cerebral stimulus in patients with this condition was demonstrated. However, it has not yet been possible to establish objective screening tests for the diagnosis of sensitive skin.^{1-3,6} Diagnosis, pathophysiology, epidemiology and treatment are still under discussion.⁹

EPIDEMIOLOGY

Although previously considered infrequent, sensitive skin syndrome has shown high prevalence in current studies. In a survey conducted in the United Kingdom, 51.4% of women and 38.2% of men considered themselves to be carriers of sensitive skin. Other European and North American studies showed similar rates.^{1,3,10}

In an European study, Misery *et al.* demonstrated a global prevalence of 38.4% of sensitive skin in the population, which shows the magnitude of the problem.⁹

Recently, a Brazilian population study found that 22.3% of men and 45.7% of women considered their skin sensitive.¹¹ Chart 1 shows the comparison between the frequencies of sensitive skin in different countries.¹¹

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CHART 1: Comparison of frequencies of sensitive skin in different countries

Country	Sensitive skin (%)	Little or not sensitive (%)
Japan	54.47	45.53
Italy	53.80	44.80
France	51.90	48.10
USA	44.60	55.40
Russia	39.72	60.28
Germany	35.60	64.20
Brazil	34.22	65.78
Spain	31.60	68.00
Switzerland	30.80	68.00
Greece	29.80	67.80
Portugal	27.40	72.40
Belgium	25.80	69.80

Source: Taieb C, et al, 2014.¹¹

PREDISONENT FACTORS

Ethnicity

Racial differences in the structure of the skin may be associated with the symptoms observed in those with sensitive skin. Higher sensitivity to capsaicin was demonstrated in Caucasians followed by Asians and then by blacks.^{3,6,9}

Thin skin is more prone to flushing due to barrier damage and increased vascular reactivity. Thus, in whites, reports of erythema are more common than in blacks and Asians. However, some authors found statistically insignificant differences between groups of different ethnic groups.^{3,6,9}

Gender

The perception of sensitive skin in women varies from 50% to 61% and, in men, from 30% to 44% according to epidemiological studies.^{12,13}

The entity was initially described in women and justified by its lower cutaneous thickness when compared with men, in addition to hormonal factors interfering in cutaneous hydration.^{13,14} However, a study conducted in 2010¹¹ showed a prevalence of sensitive skin in 68% of the interviewees, with no differences between the sexes. With the increased use of cosmetics by men, this condition has also been described in men.^{12,13}

Age

Sensitive skin is described in patients aged >18 years, probably due to the fact that research with epidemiological data has been performed on adults.^{1,3,6,11,15}

Studies have shown that young patients are more likely to have sensitive skin. On the one hand, elderly people have changes in the integrity of the skin tissue, which would favor sensitive skin. On the other hand, tactile sensitivity decreases with age, and irritability tests have diminished response.^{1,3}

Location

The main location is the face, mainly the nasolabial fold.⁷ Factors that contribute to this are probably the greater use of cosmetics in this area, the presence of thinner skin barrier and the exis-

tence of a greater number of nerve endings on the face.³

Other regions related to sensitive skin already described are: volar surface of forearms, hands, genital region and scalp.^{1,7}

Presence of other dermatoses

Atopic dermatitis and other dermatites, such as acne, rosacea, seborrheic dermatitis, contact dermatitis, psoriasis, and physical urticaria (dermographism) favor the picture described by altered skin barrier or the presence of inflammation. In these patients, sensitive skin is considered as an objective form, since the dermatitis can present with visible clinical lesions, erythema, cutaneous xerosis and eczema.^{1,3,7,16}

When there is erythema, the diagnosis of sensitive skin may be confused with several dermatitis. However, the presence of abnormal sensations, triggering factors and transient nature suggest the diagnosis of sensitive skin.^{9,17}

Environmental factors

Low temperature, humidity, wind, heat and sun exposure favor the manifestation of sensitive skin.^{1,3} Pollution, common in the industrialized world, has been one of the factors responsible for this entity.

Cosmetic products

Cosmetics are the main triggering factors of sensitive skin, especially in women, due to overuse and sometimes inappropriate use. Presence of potentially irritating substances in its composition (alpha-hydroxy acids, propylene glycol, alcohol, fragrances, etc.) increases the possibility of symptoms.³

Maintenance of cutaneous pH (5.5 on the surface) keeps the whole barrier and adequate hydration of the skin.¹ When the barrier is compromised, the penetration of substances leads to the inflammatory reaction with release of a series of cytokines. Thus, products that alter cutaneous pH favor sensitive skin.

The same way the irritants alter the function of the epidermal barrier, favoring sensitive skin, so the sensitizing substances, when phagocytized by Langerhans cells, lead keratinocytes and T lymphocytes to produce mediators of inflammation.¹

Sociocultural factors

Differences in the prevalence of sensitive skin could be attributed to varieties of habits (diet and body hygiene practices) and diversity in the perception of the symptomatology.^{1,3}

PATHOPHYSIOLOGY

Pathophysiology of sensitive skin is not completely elucidated; however it is recognized that this condition has no immunological or allergic origin.¹¹

Changing of the stratum corneum

The main hypothesis attributed to the occurrence of sensitive skin is the increase in the permeability of the stratum corneum, leading to greater penetration of substances and also to water loss. There is an inverse relation between corneal layer thickness and skin permeability.^{1,6}

The decrease in the thickness of the corneal layer facilitates the penetration of substances capable of inducing the release of cytokines, leukotrienes and prostaglandins. These mediators induce the formation of neurotransmitters which, in turn, stimulate the nerve endings.¹²

Measurement of transepidermal water loss (TEWL) has been used to aid in the diagnosis of sensitive skin. Individuals with increased TEWL are predisposed to intolerance to products in contact with the skin. Thus, adequate hydration of the skin improves the symptomatology of patients with sensitive skin.¹ Studies performed with menopausal women showed improvement of sensitive skin with the use of moisturizers and emollients.¹⁵

In addition, in the sensitive skin, a decrease in ceramide levels and decrease in capacitance were also detected.⁶

Dermatitis that lead to the alteration of the epidermis barrier, such as atopic dermatitis, seborrheic dermatitis and rosacea, act as factors predisposing to sensitive skin.²

Sensorineural change

Other evidence reported in the literature was dysfunction of the sensorineural activity of the cutaneous nerves. Current studies have demonstrated a thermal receptor of transient potential V1 (TRPV1) that would act as a facilitator of neurogenic inflammation.^{3,7}

Transient receptor potential (TRP) channels are expressed throughout the organism in various tissues and with diverse functions. Both the transient receptor potential melastatin 8 (TRPM8) and the transient receptor potential ankyrin 1 (TRPA1) are stimulated by cold and by certain substances, such as menthol. Transient receptor potential vanilloid 1 (TRPV1) is stimulated by chemicals, heat, cold, mechanical changes in the lipid layer and capsaicin; it acts as a cellular sensor, having an important role in pain and inflammation.

In patients with sensitive skin, the increase in sensorineural impulse is interpreted as unpleasant sensations. Neurotransmitters and their receptors that regulate the neuroendocrine system of the skin, present in keratinocytes, recognize the stimuli and lead to the release of neurotransmitters as substance P and calcitonin gene-related peptide (CGRP).¹⁸⁻²⁰ These neurotransmitters induce vasodilation and degranulation of mast cells, which also act on sensory perception through endothelin A and B (ETA and ETB) receptors.

Several published articles have demonstrated the participation of TRPV1 in rosacea and sensitive skin.²¹⁻²²

DIAGNOSIS

Clinical diagnosis

Symptoms (burning, pruritus, tingling, etc.) may or may not be accompanied by signs such as mild erythema, telangiectasias, xerosis, desquamation, or urticaria. However, in most cases, there are only subjective symptoms.^{1,3,6}

Patients with cosmetic intolerance usually have multiple subjective symptoms and therefore, the recording and evaluation of the history are fundamental.²³

Anamnesis and physical examination

It is essential to question the patient about personal, family and occupational history, as well as habits and use of cosmetic products. Complete physical examination should exclude signs of inflammation and the presence of other dermatitis, such as contact and atopic dermatitis.³

Due to the frequent absence of objective physical signs, self-assessment questionnaires are valid tools for identifying individuals with sensitive skin.¹⁰

A possible proposed questionnaire is shown in **chart 2**. Patients who meet one of the following criteria are considered compatible with sensitive skin:²⁰

- Positive answer in 2 of questions 1-3 (sensitive, reactive and irritative skin);
- Positive answer in 3 of questions 4-7 (reaction to cosmetics);
- Positive answer in 3 of questions 8-13 (reaction to the environment).

Complementary tests

Although research is being conducted, still no success have been achieved in the attempts to develop diagnostic tests for objective identification of the entire sensitive skin profile, probably due to the heterogeneity of the symptoms, the subjectivity of the discomfort reactions and the absence of visible signs.

Studies to identify active substances in sensitive skin focus on inflammatory mechanisms, such as vasodilation, edema, mast cell degranulation and release of TNF-alpha.

Some models use nerve cell cultures to assess the inhibition of capsaicin-induced CGRP peptide release by neurons. Clinical studies use the stinging test and TEWL to evaluate the epidermal barrier.

CHART 2: Sensitive Skin Questionnaire

1. Do you consider having sensitive facial skin?
2. Do you think you have sensitive facial skin that is prone to irritation?
3. Do you think you have reactive facial skin (which has a pungency, burning or itching, with or without redness)?
4. Do you avoid some cosmetics, which you think may cause reactive facial skin (which presents pungency, burning or itching, with or without redness)?
5. Do you consider your facial skin to be reactive (exhibiting pungency, burning or itching, with or without redness) as soon as you contact with cosmetics and toiletries?
6. Does any cosmetic or toiletry make your facial skin appear pungent, burning or itching?
7. Have you ever had any adverse reactions on the face due to the use of cosmetics or toiletries?
8. Does the expression "does not tolerate cold weather or cold environment" apply to your facial skin?
9. Does the expression "does not tolerate warm weather or warm environment" apply to your facial skin?
10. Does the expression "does not tolerate sudden changes in temperature" (e.g. leaving from a warm, indoor environment to a cold, outdoor environment) apply to your facial skin?
11. When coming into contact with the wind, does your facial skin show pungency, burning or itching?
12. When coming into contact with the sun, does your facial skin show pungency, burning or itching?
13. Is your facial skin reactive (pungency, burning or itching, with or without redness) to air pollution?

Source: Jourdain R, et al, 2005.²⁰

Because it is still a difficult condition to assess, several trials have been developed to improve the diagnosis of sensitive skin.²⁴

1. Sensory reactivity test

This is the cutaneous sensorineural evaluation of the application of chemical substances or physical stimuli. The stinging test consists of the application of 10% lactic acid in a nasolabial sulcus and saline solution in the other (control), evaluating the intensity of symptoms reported by the patient according to visual analog scale. Other substances can be used, such as capsaicin, ethanol, sorbic acid, among others.^{3,16,19,20,24,25} A patient-reported discomfort scale may be used:¹⁹

- 0: no discomfort or very mild discomfort
- 1: mild discomfort
- 2: moderate discomfort
- 3: severe discomfort

Such tests are quick and easy to perform, although they are subjective, lacking predictive value.^{3,15}

2. Magnetic Resonance

New studies aimed to evaluate brain activation during provocative tests of cutaneous sensory reactivity through nuclear magnetic resonance imaging, both in individuals with normal skin and in those with sensitive skin, by verifying differences between the two groups.²⁶

3. Irritation tests

These tests measure the signs of skin irritation after application of substances known as irritants (such as sodium lauryl sulfate), by means of colorimetry or electrical capacitance measurement, for example. They are noninvasive and objective exams. However, they require specific devices.³

4. Epidermal function tests

Epidermal function tests seek to measure structural or physiological changes in the skin after application of irritants. The most used parameters are: measure of transepidermal water loss, cutaneous pH, epidermal thickness.³

5. Dermoscopy

Recently, some authors have reported the presence of structural alterations in the sensitive skin visualized through dermoscopy (demonstrating capillary dilations) and confocal microscopy (showing epidermis with thinner than normal thickness).²⁷

6. Contact tests

Contact tests and contact phototests should always be considered in the investigation of the patient with sensitive skin, seeking to exclude allergic and photoallergic contact dermatitis. In addition to the standard and complementary batteries (according to the medical history), it is essential to test the patient's own cosmetic products.³

Unlike patients with allergic contact dermatitis, most of those with sensitive skin respond negatively to contact tests.²³

7. Other methodologies

One way to accentuate local conditions by increasing the irritative component of product use would be the behind-the-knee protocol in which the substance to be tested is applied in the popliteal fossa of the individual. Thus, a mechanical friction component to the traditional test.^{1,24}

In addition, evidence for type I hypersensitivity, such as prick tests, can be performed when considering the diagnosis of contact urticaria.

TREATMENT

The treatment of sensitive skin comprises several steps. In cases where there is a predisposing dermatitis to the symptomatology, the control of the disease contributes to the improvement of the condition.

In the acute phase, some active ingredients may be used to relieve symptoms such as: low and medium potency topical corticosteroids (to be used for a short period of three to four days) and topical immunomodulators such as pimecrolimus or tacrolimus (they can be indicated for a longer period).

In addition, the use of all cosmetics should be discontinued for a period of two weeks. After this period, the products are reintroduced one at a time.³ Next, the patient should be reassessed and perform complementary tests.^{3,6,8} Prior to the reintroduction of each patient's product, the open test should be performed for each patient.

Proper skin hydration helps to recover and maintain the skin protection barrier. Moisturizers with few components, without perfume and without substances that can irritate the skin (like urea), are indicated.

Photoprotectors should also be used in patients with sensitive skin, since, as already mentioned, ultraviolet radiation can trigger the symptomatology.

Regarding the formulation of products for sensitive skin, the type of vehicle and its components must be taken into consideration. In addition to the established tests to assess irritability and sensitivity of the products, it is necessary:

- To evaluate the stability of components;
- To eliminate unnecessary ingredients;
- To leave few active principles (minimum or unique for each product);
- To eliminate allergens and common irritants from the formulation. When this is not possible, to reduce the concentration of these substances;
- To avoid substances that increase the penetration of other substances into the skin, such as ethanol or propylene glycol;⁷
- To prefer powder cosmetics to those in cream or lotion;
- To use cosmetics easily removable with water;
- Not use fragrance products.

The study of the functions of TRPs, especially TRPV1, has led scientists to open up new perspectives for the treatment of pain. TRPV1 plays an important role in the symptoms of sensitive skin. Trans-4-tert-butylcyclohexanol was identified as a selective inhibitor of TRPV1, antagonizing its capsaicin-induced activation.³ Some protocols are already using antagonists of this receptor as a new line of treatment of sensitive skin symptoms.^{3,28-30} Another drug described as a TRPV1 inhibitor is furocoumarin, with properties of decreasing pain related to this receptor.³¹ However, there are still experimental studies without clinical trials in which these drugs were used as therapy for sensitive skin.

Demonstration of sensorineural changes through magnetic resonance imaging in previous studies with patients presenting with sensitive skin suggests that this is not only a subjective disease, but a dermatitis with a varied symptomatology and few clinical manifestations. The evolution of studies of this dermatitis will contribute in the future to new therapies and guidelines for patients with sensitive skin. □

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