SENSITIVE SKIN: A NEW ENTITY PERSPECTIVE

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Abstract:

The phenomenon of “sensitive skin” is a relatively recent terminology in certain populations reporting sensory complaints that are more intense and more frequent than the normal population, especially after using cosmetic products. The incidence of sensitive skin is increasing along with the rapid widespread of skin care products availability. Various studies have been conducted but the pathophysiology of sensitive skin is still unclear. Physiological changes in sensitive skin are influenced by two main factors such as dysfunction in skin barrier and neurosensory. There are various quantitative sensory tests that can be done to determine skin sensitivity. Until now, there is no guideline for treating sensitive skin. Contributing factors, quantitative sensory tests, relation to skin diseases, and managements will be discussed in this literature review.

Keywords: Dysfunction; Neurosensory; Sensitive skin; Skin barrier
Introduction

The phenomenon of “sensitive skin” is a relatively new term in certain populations who complain about more intense and more frequent sensory than the normal population, especially after using cosmetic products.¹

Along with the increasing subjective phenomenon of sensitive skin, surveys have become one of the popular approaches to evaluate the prevalence of this condition in the general population worldwide. Overall, it was found that 60–70% of women and 50–60% of men reported having sensitive skin. Epidemiological studies conducted in several countries in Europe, the United States, Russia, and Japan show that sensitive skin conditions occur in about 60% of women and 40% of men and affect the quality of life.² Sensitive skin is also associated with geographical conditions, namely in areas with lighter-skinned people (Fitzpatrick skin types II-III) tend to experience sensitive skin more often than dark skin.³ Ages over 50 years often report the incidence of sensitive skin in the genital area, especially women.

According to the International Forum for the Study of Itch, sensitive skin is an uncomfortable sensation, such as a stinging, burning, pain, itching, and tingling sensation that can sometimes be accompanied by erythema. This condition occurs not only on the face but can also affect the scalp and hands. Trigger factors can be physical, chemical, psychological and hormonal factors.⁴

The pathophysiology of sensitive skin is still not fully understood. Decreased skin tolerance threshold, skin barrier dysfunction, increased transepidermal fluid loss, release of neurotransmitters due to neurogenic inflammation, activation of Transient Receptor Potential (TRP) protein receptors, and involvement of endothelin and its receptors are some of the things that are thought to be associated with sensitive skin conditions.²,³,⁵ This literature review discusses the classification of sensitive skin types, contributing factors and various sensory tests to detect sensitive skin.

The Classification of Sensitive Skin

Sensitive skin has two forms of clinical manifestations, subjective and objective types. Subjective type is characterized by self-perception of patients who feel they have sensitive skin without any lesions. The objective type is characterized by a disruption of the skin barrier and clinical signs that can be observed, for example, erythema, papules, and vesicles, as in atopic dermatitis patients.³

A validated questionnaire has been developed, skin characteristics based on the Baumann Skin Typing System (BSTS) in 2004. The development of the cosmetic industry increases the production of various types of beauty products with varied content, which can be found in the market. This makes it difficult for consumers and doctors to determine safe cosmetic products. Through scientifically BSTS, it is hoped that it can become a specific guide for doctors and patients/consumers to find the content of skin care products that are suitable by considering the characteristics of the user's skin. Sensitive skin has 4 subtypes according to Baumann: the type of stinging, allergy, acne, and rosacea, all subtypes are based on the inflammatory process.⁶

a. Stinging Type

This subtype is characterized by a burning, stinging or itching sensation without visible clinical changes caused by application of topical cosmetics or drugs. Symptoms are generally seen within hours of application of the suspect substance to susceptible individuals.⁶ In groups of people who have a tendency to develop a stinging sensation, they are referred to as stingers. This sensitive skin subtype is not always accompanied by clinical symptoms of redness, but a severe stinging sensation is the main complaint.⁷ Until now
there is no universally accepted skin test to identify patients who are prone to stinging sensations, this is presumably because each ingredient produces different levels in each individual. Patients with rosacea and retinoid-associated dermatitis report that a stinging sensation is present even in contact with water. Some ingredients that often cause a stinging sensation in this sensitive skin type include glycolic acid, benzoic acid, bronopol, components of cinnamic acid, formaldehyde, lactic acid, propylene glycol, sodium lauryl sulfate, sorbic acid, urea, ascorbic acid, and plant extract of witch hazel.6,7

b. Allergy Type

This sensitive skin subtype is very easy to develop contact dermatitis due to exposure to various allergens which are characterized by clinical symptoms of redness accompanied by itching and peeling skin. The skin patch test is a test that is often used to determine whether ingredients in skin care products can cause allergies. Increased immune response in contact dermatitis or skin barrier dysfunction is the cause of this subtype sensitive skin condition because allergens enter the skin layer more easily. Fragrances and preservatives are the most common allergens causing this condition.6

c. Acne Type

This sensitive skin subtype is the most common type. Adolescents and women are vulnerable groups to have this subtype. Factors that influence the pathogenesis of acne are increased sebum production, accumulation of desquamated keratinocytes in hair follicles, the role of Propionibacterium acnes, and inflammation.7 This makes it easier for acne lesions to form, such as papules, pustules, comedones and cysts. Sensitive skin acne type will be more difficult to treat if accompanied by dry skin conditions than oily skin, this is because most acne treatments will cause dry skin.6

d. Rosacea Type

The clinical symptoms of rosacea can overlap with acne because in rosacea papules and pustules may appear, accompanied by redness of the face and flushing and telangiectasia. This sensitive skin subtype should avoid triggering factors such as spicy and hot foods, alcohol, skin exfoliating products, and extreme weather (too hot or too cold).7

Several other sensitive skin classifications have also been proposed including by Muizzuddin et al, Pons-Guiraud, and Löffler et al which are presented in Table 1.8-10

Pathogenesis of Sensitive Skin

There are two characteristics associated with the incidence of sensitive skin, namely skin barrier dysfunction and skin neurosensory dysfunction which can be seen in Table 2.3

The decrease in skin barrier function causes the nerve fiber endings to become unprotected so that irritants or allergens can easily penetrate into the stratum corneum. Both of these will facilitate the recognition by antigen-presenting cells that can induce the inflammatory process. This mechanism also occurs in atopic skin conditions. The study by Chen et al showed that some subjects with sensitive skin showed signs of high vascular reactivity in the absence of skin barrier dysfunction.31 Subjects who believed their skin was sensitive were more likely to be stingers than nonstingers.

The variety of sensory manifestations reported by patients with sensitive skin without strong objective signs indicates a neurosensory defect in sensitive skin. In this condition the neural response becomes faster with a decrease in the sensitivity threshold. Neurosensory dysfunction of the skin is getting more and more that there is a relationship with sensitive skin, especially in the aspect of neurogenic inflammation and nerve response dysfunction. In sensitive skin
there is a decrease in the threshold for sensory perception (conducted by unmyelinated C nerve fibers and a small number of A-δ nerve fibers). This suggests that the imbalanced function of nociceptor C nerve fibers has a role in the abnormal sensory perception of sensitive skin. Neurogenic inflammation is mediated by the action of substance P (SP) and calcitonin gene-related peptide (CGRP) on vascular endothelium and smooth muscle cells so that in sensitive skin, an increase in SP and CGRP expression can be found.¹²

Transient receptor potential vanilloid-1 (TRPV1) is a receptor that, when activated, produces sensations of pain, itching, and burning. TRPV1 is expressed on keratinocytes, fibroblasts, mast cells, endothelial cells, and C- and A-δ fiber sensory nerves. These receptors are activated under conditions of low pH and excessive heat. Study by Ehnis-Pérez et al on 31 subjects who declared themselves to have sensitive skin by means of lactic acid test and skin biopsy. The pathogenesis of sensitive skin, but this is still being investigated today.¹³ The study results showed higher TRPV1 expression in subjects with sensitive skin based on the biopsy results of both nasolabial folds with the first sample for qualitative analysis and the second sample for quantitative analysis of TRPV1 expression using real-time PCR. TRPV1 is considered to play an important role in the pathogenesis of sensitive skin but this is still being studied until now.¹³

Table 1. Several other sensitive skin classifications

<table>
<thead>
<tr>
<th>Classifications dan Definitions</th>
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<tbody>
<tr>
<td>Muizzuddin⁸</td>
<td>Delicate: The skin barrier is easily disrupted without a rapid or intense inflammatory response</td>
</tr>
<tr>
<td></td>
<td>Reactive: Strong inflammatory response without significant increase in skin permeability</td>
</tr>
<tr>
<td></td>
<td>Stingers: Enhanced neurosensory perception of minor skin stimulation</td>
</tr>
<tr>
<td>Pons-Guiraud⁹</td>
<td>Very Sensitive: Reactive to various endogenous and exogenous factors accompanied by acute and chronic clinical symptoms and strong psychological conditions</td>
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<td></td>
<td>Environmentally Sensitive: Clean, dry, and thin skin with a tendency to blush or flush and reactive to environmental factors</td>
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<td></td>
<td>Cosmetically Sensitive: Transient reactive to certain cosmetic products</td>
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<tr>
<td>Löffler¹⁰</td>
<td>Very sensitive: Subjects who declared themselves to have increased skin sensitivity</td>
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<tr>
<td></td>
<td>Irritable: Subjects with strong objective skin reactions after exposure to irritants or allergens</td>
</tr>
<tr>
<td></td>
<td>Stingers: Individuals who consistently experience pain responses to chemicals</td>
</tr>
</tbody>
</table>

Table 2. Pathophysiological characteristics of sensitive skin³

<table>
<thead>
<tr>
<th>Skin barrier dysfunction</th>
<th>Neurosensory dysfunction</th>
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<tr>
<td>1. Changes in <strong>Transepidermal Water Loss (TEWL)</strong></td>
<td>Increased innervation of the epidermis</td>
</tr>
<tr>
<td>2. Thinning of the stratum corneum</td>
<td>Decreased intraepidermal nerve fiber density (C peptidergic nerve fibers)</td>
</tr>
<tr>
<td>3. Decreased hydration of the stratum corneum</td>
<td>Increased neural sensor input</td>
</tr>
<tr>
<td>4. Decrease in skin fat layer</td>
<td>Increased expression of transient receptor potential vanilloid-1 (TRPV1)</td>
</tr>
<tr>
<td>5. Decrease in ceramide levels</td>
<td>Genetic variation in TRPV1 associated with susceptibility to capsaicin</td>
</tr>
<tr>
<td>6. Increased neutral lipids and decreased sphingolipids</td>
<td></td>
</tr>
<tr>
<td>7. Increased activity of sweat glands</td>
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</tr>
</tbody>
</table>
Contributive Factors on Sensitive Skin

Women more often report sensitive skin conditions than men, this is because the epidermis in women is thinner than men and especially the facial skin in women tends to be more often exposed to various types of treatment products that can trigger uncomfortable sensations. Fluctuating female hormonal conditions can also make skin more sensitive. Falcone et al reported that some premenopausal subjects felt that their skin became more sensitive when they started having a menstrual cycle, whereas 70% of postmenopausal women experienced an increase in skin sensitivity. Physiological changes in the form of aging can cause the skin to become more sensitive, especially in the genital area.

Differences in skin type and ethnic group have been known to influence skin structure and susceptibility to certain irritants. Skin differences between different ethnic groups have been reported in several epidemiological studies. In a study by Jourdain et al, it was found that European-Americans have a higher susceptibility to wind than other ethnic groups. Asian ethnicity is more sensitive to spicy food while Hispanic ethnicity has low reactivity to alcohol. African-Americans tend to report more frequently in the form of sensory stimuli responses, while Caucasians report more often than not with visible visual effects.

Jourdain et al reported that sensitive skin can occur due to several environmental conditions, health and beauty products, household cleaning products, personal hygiene products, and clothing materials. Environmental influences include sun exposure, hot or cold weather, dry air, humidity, wind, and air conditioning. Health and beauty product ingredients that can cause sensitive skin include soap, shampoo, hair dye, other hair products, eye cosmetics, facial cosmetic ingredients, facial moisturizers, facial astringents, facial cleansers, fragrances, body moisturizers, anti-aging creams, sunscreen, deodorant, antiperspirant, and loose powder. Some household cleaning agents that can cause sensitive skin include floor cleaning products, dishwashing liquid, detergents, and fabric softeners. Personal hygiene products include sanitary napkins, pantyliners, diapers, tampons, wipes, and douching products. Clothing materials that can cause sensitive skin include underwear and rough clothing. In addition, individuals with sensitive skin have a tendency for one of their family members to also have sensitive skin.

Lifestyle and culture also directly influence the perception of sensitive skin. Older women with incontinence are more likely to report irritation from tampons. The increasing prevalence of facial or body care products intended for men has increased the incidence of sensitive skin reported by male subjects. Women who work in the industrial sector are also more likely to report the incidence of sensitive skin.

Quantitative Sensoric Test

1. Temperature Sensation Test
   This test aims to assess the function of free nerve fibers and their association with myelinated and unmyelinated nerve fibers. This method can quantitatively measure thresholds for sensations of heat, cold, and pain due to both. This technique was also used by Yosipovitch et al to assess differences in sensory irritation and pain perception in 49 subjects with 3 different ethnicities (Chinese, Malay, and Indian). Subjects were given heat stimuli with a gradual increase using a thermal sensory analyzer at two locations, namely the forehead and arms. above the ventral side near the antecubital fossa. The results of this study did not show differences in the perception of pain due to heat or cold between these ethnic groups.

2. Stinging Test
This test is widely used to assess the sensitivity of the skin nerves. Stinging (stinging sensation) is a variant of the sensation of pain that arises and disappears quickly when the sensory nerve is stimulated. The stinging sensation occurs as a result of a decrease in the threshold for sensory perception, which is transmitted mostly by unmyelinated C nerve fibers and to a lesser extent by A-δ nerve fibers. This test assesses the intensity of the stinging sensation induced by a chemical that is applied to the most sensitive area, namely the nasolabial folds.

**a. Lactic Acid**

The 10% lactic acid solution was applied using a cotton swab on the test area and for the control area on the contralateral side, saline solution was applied at room temperature of 21°C and 40% relative humidity. After 5 minutes of application, subjects were then asked to describe the intensity of the pain sensation using a visual analogue pain scale (VAS) with points 0–10. Score 0 if there is no uncomfortable sensation, score 1–4 if there is a tolerable uncomfortable sensation, score 5–9 if there is an increase in uncomfortable sensation that cannot be tolerated, score 10 if the worst uncomfortable sensation has ever been felt. An intensity score of more than one (≥1) indicates a positive lactic acid stinging test (LAST) and is classified as sensitive skin. Subjects with negative LAST results were grouped as controls.

**b. Capsaicin**

The examination procedure using the capsaicin test is considered accurate for the diagnosis of sensitive skin. After cleansing the face, the concentration of capsaicin was increased fivefold in 10% ethanol solution applied to the nasolabial folds. Capsaicin provides an assessment of a stronger relationship to the incidence of sensitive skin when compared to the lactic acid test.

**c. Dimetil sulfoksida (DMSO)**

This test uses a 98% DMSO solution that has been diluted in saline. The test part is generally in the forearm where the flexor is exposed to the test material for 10 minutes, then rinsed and dried with a tissue. The assessment was carried out twice, at the 30th minute and at 60th minute after the DMSO solution was rinsed from the test part. The total value of the two assessment times is expressed as the total DMSO score. After application, there may be an intense burning sensation, painful hives, and persistent erythema in the stingers group.

**3. Nicotinate and Sodium Lauryl Sulfate Occlusion Test**

This test applies methylnicotinate as a potent vasodilator to the third distal of the flexor upper arm. The concentration of the liquid used ranged from 1.4 to 13.7% and allowed to stand for 15 seconds. The vasodilating effect was assessed by observing erythema and using laser Doppler velocimetry (LDL). Increased vascular reaction to methylnicotinate and similar analyzes at various concentrations of sodium lauryl sulfate have been reported in subjects with sensitive skin.

**4. The Evaluation of Itching Responds**

The sensation of itching is mediated by type C nerve fibers with a slow response rate and insensitivity to mechanical stimulus. Thus far, no individual susceptibility to itching sensation has been identified without an underlying dermatitis. The itch response can be induced by the injection of various topical or intradermal substances, eg proteolytic enzymes, mast cells, and vasoactive products. An example of such a substance is the intradermal injection of histamine dihydrochloride (100 g in 1 ml of normal saline solution) into one arm. The patient was asked to record the intensity and duration of the itching sensation. All information obtained was a subjective assessment of the patient. In comparison between the cumulative score of the lactic acid test and the histamine-induced itching score, it was shown that the stingers group complained of a more intense itching sensation than the nonstingers group.
5. **Washing and Exaggerated Immersion Tests**

This test aims to identify a subpopulation with a tendency for increased skin response. In the washing test, subjects were asked to wash their face with special soap or detergent. Overtreatment in the form of an immersion test was carried out by immersing the subject's hands and arms into a solution containing an anionic surfactant at 40°C for 20 minutes. Then the hands and forearms are rinsed under running water and dried with a tissue. This procedure was repeated three times with an interval of two hours between immersion for two consecutive days. In this test, evaluation of the sensation of tightness, burning, itching, and stinging using a rating scale was carried out before the start of the test, two hours after the third and sixth immersion, and 18 hours after the last immersion. Evaluation is carried out after completion of immersion for at least 30 minutes at a temperature of 21°C.\(^{17}\)

6. **Behind-the-Knee Test**

This method is performed by overexposure to induce sensitive skin in the popliteal fossa. The test product is affixed behind the knee and closed using an elastic bandage so that when performing daily activities, it will increase mechanical friction. Evaluation was carried out after using the test product for one day using visual grading of erythema. The level of irritation produced by the test product was found to be higher than the conventional test due to chemical irritation.\(^{17}\)

**Sensitive Skin in Several Skin Disease**

Sensitive skin conditions have a complex relationship and are not yet fully understood in relation to various skin diseases. Individuals with eczematous contact dermatitis have higher skin sensitivity than normal skin people. People with allergic contact dermatitis are more susceptible to environmental exposures such as chemical or mechanical irritants, weather conditions, and skin care products. Sensitive skin can occur in individuals with various skin diseases, both eczematous and non-eczematous disorders.\(^{18}\)

Eczematous skin diseases associated with sensitive skin conditions include atopic dermatitis, allergic contact dermatitis, irritant contact dermatitis, and seborrheic dermatitis. Non-eczematous skin diseases associated with sensitive skin conditions are rosacea, perioral dermatitis, and dry skin. The most important factor in sensitive skin is skin barrier dysfunction.\(^{19}\)

**The Management of Sensitive Skin**

Management of sensitive skin conditions is not easy because it is necessary to determine a skin care regimen that does not aggravate patient complaints, including the selection of appropriate care and medical products.\(^{20}\)

1. **Skin Care**

Repair of the skin barrier is of utmost importance in the management of sensitive skin. The use of moisturizers with oil-in-water emulsions containing occlusive ingredients is considered very important to repair the skin barrier by increasing the hydration of the stratum corneum. Patients with sensitive skin should use products with a minimum amount of active ingredients. The use of an unscented, foam-free and alcohol-free facial cleanser (ethanol or propylene glycol) intended for sensitive skin is the first choice for patients with this condition.\(^{20}\) Types of cosmetics that can be given for sensitive skin conditions in the form of products made from powder and easy to clean with water.\(^{5}\)

Discontinuation of all substances that can irritate the skin should also be done for at least two weeks. Irritants cosmetic products containing tretinoin, alcohol, benzoyl peroxide, and glycolic acid. Then need to be re-evaluated if there is a skin disease underlying this sensitive skin condition, such as seborrheic dermatitis, atopic dermatitis, psoriasis, acne, rosacea, or perioral
dermatitis. Evaluation of skin physiological parameters can also be assessed using corneometer, evaporimeter, sebumeter, and pH meter.\textsuperscript{21}

2. Medicine

The active ingredients that are still being studied for the treatment of sensitive skin conditions are trans-4-tert-butylcyclohexanol and 1\% pimecrolimus to treat or prevent clinical symptoms of sensitive skin. According to Kueper et al, trans-4-tert-butylcyclohexanol has potential bioactive ingredients for the treatment of sensitive skin.\textsuperscript{22} The vanilloid receptor TRPV1 is known to have a role in sensitive skin by facilitating neurogenic inflammation and sensitivity to capsaicin, which is an activator of TRPV1. Pimecrolimus 1\% cream has been shown to be effective as an anti-inflammatory for atopic dermatitis.\textsuperscript{23} Pimecrolimus can rapidly inhibit itching or burning sensations in patients with sensitive skin.

A study by Seite in France in 2013 found that the use of thermal spring waters (TSW) which contains moisturizing and anti-irritant ingredients can reduce the symptoms of sensitive skin on the face. TSW has been widely used in aerosol form which has an anti-inflammatory effect and can destroy radical oxygen species (ROS) induced by exposure to ultraviolet light.\textsuperscript{24} The split-face comparison study by Barolet et al. tested the clinical efficacy and safety of TSW after fractional photothermolysis in 20 patients with bilateral dermal melasma. On one side of the test area, TSW was sprayed at least six times a day while the other side of the face was used as a control. The results of the study showed that the sensation of pain, dryness, and redness of the skin decreased significantly on the side of the test area in the first 10 minutes, second day, and fourth day after photothermolysis. In Indonesia, TSW is widely available, for example Eau Thermale Avène Thermal Spring Water\texttrademark, Bioderma Hydrabio Brume\texttrademark, Evian Brumisateur Facial Spray\texttrademark, and Bio-essence Miracle Bio Water\texttrademark. The use of TSW can be one of the treatment options for sensitive skin.\textsuperscript{24}

Conclusions

Until now, various studies have been carried out but the pathological mechanism of sensitive skin is still unclear. Barrier and neurosensory dysfunction of the skin are the most important in sensitive skin conditions. Various quantitative sensory tests can be performed, the most common of which is the stinging test using lactic acid and capsaicin tests.

Sensitive skin is also closely related to several diseases, both eczema and non-eczematous. The management of sensitive skin conditions does not yet have clear guidelines, but the discontinuation of irritants and the selection of an appropriate skin care product regimen are top priorities. An understanding of the new entity "sensitive skin" is important for clinicians to know in order to provide education and appropriate treatment options according to patient complaints.

References
