Predictive methods exploring sensory irritation to surfacant-based products

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Abstract

The concept of sensitive skin is subject of rife controversies. Some authors consider sensitive skin as a sensory irritation without any visible clinical signs. Others extend this definition to some environmentally-induced dermatoses. This latter concept is at risk of introducing much confusion and overlapping with allergic and irritant contact dermatitis. The present review focuses on the restricted definition of invisible sensitive skin, and particularly on sensory irritation to surfactants. A series of biometrological assessments may reveal some aspects linked to sensory irritation.

Key words : surfactant, sensitive skin, sensory irritation

The so-called sensitive skin condition is reported to be steadily increasing in the populations of most Western countries. In some regions, the dermography suggested that one person out of two claimed to suffer from this ailment. The condition is frequently ascribed to an adverse effect of a skin care product or of any other formulation including cleaning and cleansing products [1]. However, it remains difficult to establish objectively the real causality link. On the overall, genetic influences, particularly ethnic differences might play a role the reactive susceptibility to diverse xenobiotics [2, 3]. In addition, there are strong cultural differences in the frequency of reporting sensitive skin between different populations.

According to authors, sensitive skin has two definitions. On the one hand, sensitive skin in its restricted sense corresponds to skin sensory irritation (SSI) that remains invisible at the clinical inspection. On the other hand, a broader concept includes a variety of clinical signs including erythema, xerosis, scaliness, … Indeed, this latter definition clearly encompasses allergic and irritant contact dermatitis, and exacerbation of other previous dermatoses.

The business market provides an ever growing diversity of products intended for individuals complaining from sensitive skin. However, there is currently no real consensus about the definition and recognition of the biology of sensitive skin. It likely represents a multifactorial process leading to skin discomfort [1, 4]. Sensitive skin means that the skin readily experiences either reduced tolerance or heightened response to external stress including physical factors and/or chemical xenobiotics. The initial perception of the adverse discomfort is immediate or delayed. It corresponds to SSI without any obvious clinical expression. It includes one or a combination of feelings including tightness, itching, stinging and burning sensations [4]. Overtime, the subjective

and subclinical symptoms may be followed by visible effects, including erythema as well as rough and dry-looking skin [4]. At that stage, the terms irritant or allergic contact dermatitis appear more relevant.

The aim of the present review was to revisit the concept of SSI and to summarize predictive methods allowing its assessment.

Mechanisms underlying SSI to surfactants

Several skin structures may be involved in the abnormal sensory response to surfactants. It is possible that the stratum corneum (SC) reactivity to any surfactant threat is impaired in a subset of individuals with SSI [1]. Two distinct mechanisms, acting either singly or in combination, are conceptualy involved in this process. On the one hand, surfactant interactions with corneocytes are abnormally intense releasing a variety of mediators including cytokines, prostaglandins and leukotrienes. In turn, these biomolecules help releasing neuromediators from other cells leading to the nerve ending stimulation [5, 6]. On the other hand, the barrier function to surfactants may be initially impaired allowing xenobiotics to directly stimulate sensory nerve endings. According to this latter hypothesis, SSI might be related to subtle variations in the structure of the SC. Thus, a thinner SC with or without alteration of the corneocyte desquamation may be involved [7]. Similarly, a reduced corneocyte size was put forward to explain increased penetration of water-soluble xenobiotics [8]. Still another possibility involves an individual lowered threshold for nerve stimulation. Indeed, free nerve endings and specialized nerve corpuscules receive both excitation stimuli and antagonist signals [5, 6]. When the latter activity is lowered, the efferent neurosensory input is amplified and perceived as a

manifestation of sensitive skin. As a result, lifestyle including psychological stress and emotions clearly influence this condition.

Some individuals with sensitive skin report unpleasant after-wash skin tightness. Unlike mild surfactant-based cleansers, some soaps and household cleaning products induce skin tightness, about 5-10 min after washing [4]. Such perception was ascribed to the physical stress created in the SC by the rapid water evaporation from the skin surface. Harsh surfactants actually create an immediate corneocyte overhydration and swelling, followed by the rapid water evaporation to reach a SC moisture level that is lower than the pre-surfactant treatment level [9, 10]. Such overhydration followed by a reduced hydration level is responsible for a higher rate of skin surface water evaporation. Thus, a differential stress is created inside the upper layers of the SC, leading to after-wash feeling of tightness. This condition parallels lipid removal as well as surfactant binding to proteins and subsequent change in the overall electrical charges at the skin surface [11].

In any case of surfactant-induced SSI, regional variability in the response to the offending agents may be prominent on different body areas. Moreover, the molecular nature of the surfactant is of importance because the individual overreactivity is often manifest for only a limited category of products. In addition, the SSI status varies with age, gender and ethnicity of individuals, as well as with specific environmental and seasonal geoclimatic conditions. In particular, the negative geoclimatic influence manifests itself when the environmental dew point modifications in winter alter the SC physiology [12, 13]. In general, women complain more frequently than men from sensitive skin. In the case of household cleaning products, women remain more frequently in contact with the triggering agents. As irritation reactivity commonly declines

with age, SSI to surfactants appears less frequent in middle-aged and older adults [14]. In general, fair skin is believed to be more susceptible to SSI than darker skin.

Experimental and predictive methods

Assessing SSI to surfactant-derived products calls for multipronged testing procedures. In addition, any investigative search targeting SSI, should consider the possibility of cumulative and boosting effects by chronic skin weathering [15]. The methods used for assessing both sensitive skin to xenobiotics and the efficacy of products aiming to protect against the unpleasant sensorial perceptions, are as many as the ingeniosity of skin experimentalists is vast. Selected and non limitative investigative procedures are listed below.

Subjective self-assessment of SSI is notoriously difficult to interpret, and is in time unreliable. One way to be more confident with the data relies on the use a blinded device for the subject who positions a cursor on a bland background. In a second step, the investigator reads the cursor position on a scale ranging from 0 (no sensorial stimulation) to 100 (upmost unpleasant sensorial stimulation).

The regular stinging test performed with application of lactic acid to the nasolabial fold may appear irrelevant when assessing SSI of the hands and forearms to surfactants. As another test, a chloroform-methanol 20:80 mixture, is deposited under an occlusion chamber affixed to the skin. The time for the first perception of unequivocal burning is recorded, followed by grading changes in burning sensation over the next few minutes. Burning is graded on a nominal scale for assessing the neurosensory reactivity. It is influenced by the structural integrity of the SC. Occult cracks indeed allow rapid permeation of the solvent mixture. In another procedure, dimethylsulfoxide (DMSO) is

applied for 10 minutes under occlusion. Five minutes after removal, whealing is scored clinically [16]. The flare surrounding the wheal is scored on a nominal scale and it represents an indirect measure of the SC permeability. This test detects a small proportion of subjects with sensitive skin to surfactant. It is influenced by previous subclinical challenges of the skin (preconditioning) by surfactants. Nicotinates are used similarly to explore alterations in transcutaneous xenobiotic penetration in subjects with sensitive skin [8].

Surfactants extract some compounds from the SC, in particular dansyl chloride previously applied on the skin [17]. The fluorescent dye is frequently removed more easily from the SC in some subjects claiming to have sensitive skin to surfactants.

The ex-vivo corneosurfametry bioassay [1, 18-20] is offered for assessing sensitive skin to surfactants. Human SC harvested from the forearms or dorsum of the hands using cyanoacrylate skin surface strippings (CSSS) is the test substrate. Diluted or neat surfactant formulations are sprayed over the CSSS which are kept for 2 h at room temperature in a humid environment. Samples are then thoroughly rinsed with tap water, dried and stained for 3 min with toluidine blue-basic fuchsin in 30% alcoholic solution. Their color is measured using reflectance colorimetry in the L*a*b* system (Chroma Meter® CR400 Minolta, Osaka, Japan). The L* and Chroma C* values are recorded. The difference between L* and Chroma C* corresponds to the so-called “colorimetric index of mildness” (CIM). Its value increases with the severity of interaction between corneocytes and surfactants. For a given surfactant-based product, the CIM value is typically increased in subjects complaining from sensitive skin to surfactants [20]. In other types of sensitive skin unrelated to surfactant, SSI does not show similar corneosurfametry characteristics [1]. The corneoxenometry bioassay is a variant to

corneosurfametry adapted to xenobiotics distinct from surfactants. It is performed ex vivo and provides information correlating with a series of in vivo tests [21]. The advantage of corneoxenometry over in vivo tests is the avoidance of discomfort and any other hazards for human volunteers. This test is performed and evaluated in a way similar to the corneosurfametry bioassay.

Testing skin sensorial perceptions is conveniently performed by electrical stinging stimulations [22]. The skin barrier function has no influence whatsoever on this evaluation. A weak continuous current is delivered by a dedicated device (Herpifix®, C+K electronic, Cologne, Germany). The time for the initial stinging perception is recorded. Some people complaining with sensitive skin detect the stinging sensation after a few seconds, well earlier than normal subjects [22].

A transient erythematous reaction to anionic surfactants such as sodium laurylsulfate (SLS) is assessed after applying 0.75% or less aqueous SLS for 24 hours in a chamber test to the forearms. Twenty-four hours after removing the chambers the reactions are clinically graded and quantified by reflectance colorimetry. The a*-value is informative. Immersion tests and in use tests are probably better suited for assessing sensitive skin to surfactants. A proportion of subjects with sensitive skin to surfactants develop intense erythema without or well before any SC alteration becomes perceptible. This situation likely corresponds to the rapid release of vasodilation mediators without full-blown irritation and influx of inflammatory cells. It is usually unrelated to a defect in the SC barrier function.

The blanching effect following topical applications of corticosteroids under occlusion is a measure of the SC barrier function [23]. A controlled amount of topical corticosteroid is applied to the forearms in test chambers affixed to the skin. After a 24 h-occlusion, the

chambers are removed and any residual product carefully wiped off. Two hours after occlusion removal, skin colorimetry records the L*-value which is a measure of skin lightness, and the a*-value representing the skin redness. For a given corticosteroid, the blanching effect is stronger when the SC barrier function is impaired.

Susceptibility to SSI has been reported to be correlated with increased baseline transepidermal water loss (TEWL) [24]. Accordingly, skin hypereactivity to water-soluble irritants is possibly related to increased permeation of the SC to these xenobiotics. Whether this condition is genuine or part of a self-exacerbating loop once irritation is already initiated and the SC damaged is unsettled.

Skin susceptibility to irritants has been reported to be associated with decreased SC capacitance. In our experience, this change is only present after preconditioning the SC, and it does not represent an initial step usually leading to sensitive skin. By contrast, measuring the passive sustainable SC hydration and the SC water holding capacity [25] following surfactant challenge might be a tool discriminating some sensitive and non-sensitive skins.

Sampling corneocytes using self-adhesive clear discs (Corneofix®, C+K electronic, Cologne, Germany) and staining the harvested material with a toluidine blue-basic fuchsin dye represent the initial steps of the squamometry test [26]. The squamometry index corresponds to the Chroma C* value as assessed by reflectance colorimetry. This test is available for different purposes. When it deals specifically with the interaction of surfactants with SC, the method is called squamometry S [26]. Indeed, after a preconditioning challenge with surfactants, the squamometry index increases. People with sensory irritation to surfactants may show increased reactivity. This finding is possibly related to the presence of so-called immature corneocytes in the SC [27].

Conclusions

In the vast majority of cases, sensitive skin to surfactant-derived products is a manifestation of SSI. Various tricks are conveniently used in order to assess this common condition. Any of the available methods only explores a limited aspect or one facet of the condition. A multipronged evaluation is therefore recommended for fully covering the topic.

Similar test procedures apply to the evaluation of products such as emollients used to improve sensitive skin. Indeed, among the marketed emollients, a significant proportion of them stays firmly in the purchased tube because of subjective variations in their tolerance and acceptability by the consumers. Assuming, however, that at least some of the emollients are actually used, the benefit provided is often difficult to objectivate. The effects of emollients and any other protective formulations on SSI are possibly assessed using subjective clinical investigation and the more rigorous objective assessments.

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