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ORIGINAL ARTICLE

Prevalence of sensitive skin and its biophysical response in a Mexican population

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Abstract

AIM: To describe the frequency and biophysical response of sensitive skin in Mexican subjects, using the lactic acid test.

METHODS: The lactic acid stinging test was applied to 250 healthy volunteers, both sexes, 18 years of age or older, without any active dermatoses on the test site. Volunteers were university students, workers of public institutions, and general population from San Luis Potosi, Mexico. Participants were not excluded based on socioeconomic status. Demographic data were obtained through a questionnaire. Skin phototype was obtained through colorimetry. Subjects were randomized to receive 10% lactic acid on one nasolabial fold and placebo on the other side. The presence and intensity of adverse sensations, such as itching, burning, or stinging, was evaluated through a 10-point Visual Analogue Scale (VAS) prior to treatment and at 3, 5, 8 and 10 min after the intervention. Subjects with a VAS of 2 or higher were considered positive for the test. A VAS lower than 2 was considered a normal response to skin manipulation. Simultaneously, biophysical changes and barrier function were assessed by colorimetry, transepidermal water loss (TEWL), and capacitance. To decrease measurement variations by skin manipulation, the nasolabial fold was segmented in four areas of 1 cm^2 for each time measurement. Descriptive analyses were made using central tendency measures. Analyses of data were performed using two-tailed χ^2 test, Fisher's test, *t*-test, logistic regression, or Mann-Whitney *U* test for non-parametric values between groups.

RESULTS: Of the included 246 subjects, 68% were women and the mean age was 32 years. The most frequent skin phototype was Ⅴ (ranges Ⅱ-Ⅴ). Thirty-six percent of the subjects identified themselves as having sensitive skin. Fifty-two percent of the subjects were positive to the lactic acid stinging test, with a mean VAS of 4.5 at 3 min. Subjects with the self-diagnosis of sensitive skin were more likely to be positive for the test (80% *vs* 36%, $P < 0.001$). Lighter skin phototypes (types Ⅱ and Ⅲ) showed a higher response to the test compared to darker skin tones (type Ⅴ; OR = 0.88, $P < 0.001$). There were no statistical differences in baseline biophysical measurements. At 3 min, TEWL was significantly higher in subjects positive to the test (27.5 *vs* 23.7, $P < 0.05$). At 5 min, TEWL and capacitance showed statistical differences (26.0 *vs* 22.4, $P < 0.05$, and 239 *vs* 179, $P < 0.05$, respectively). After 5 min, values tended to return to baseline levels in both groups.

CONCLUSION: Sensitive skin is frequent in our population. Darker skin phototypes have a lower prevalence of this syndrome, probably due to inherent differences in skin barrier function.

Key words: Sensitive skin; Lactic acid test; Transepidermal water loss; Colorimetry; Capacitance

Core tip: Self-diagnosed sensitive skin can be found in one-third of Mexican subjects, but using the lactic acid stinging test, we identified a prevalence of 50%. Baseline biophysical measures did not predict the test response, but alterations in subsequent measurements support the hypothesis of a dysfunctional skin barrier. One subgroup presented a slow response to the test, suggesting that other pathways, such as an altered neurosensitive response, are involved. This study indicates a higher prevalence of sensitive skin in subjects with lighter skin phototypes compared to darker ones. These findings suggest that pigmentation may confer a protective mechanism against sensitive skin.

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INTRODUCTION

Sensitive skin is defined as the presence of stinging, burning, itching or other unpleasant sensations after physical (light, ultraviolet radiation, heat, cold, air), chemical (cosmetics, soap, water), hormonal, or possibly psychological stimuli[1-5]. Therefore, an exaggerated reactivity to external factors without any evidence of skin lesions or erythema is the main hallmark of this disease[2,4,6]. It is frequently a self-diagnosed condition, and there are no accurate tests to recognize or quantify it because of the individual variations in perception and intensity of the related symptoms[7,8].

Although the pathogenesis of sensitive skin syndrome is not completely understood, the most accepted theory is the presence of an altered barrier function[9-12]. Irritation results from the abnormal penetration of substances to deeper layers of the skin, where they can induce vasodilatation and stimulate c-type neuronal fibers[2,12,13]. Also, changes in the pH of the stratum corneum have been found to induce skin sensitivity through the activation of the transient potential receptor vanilloid (TRPV) neuronal receptors[14-16].

Multiple methods eliciting subclinical irritation of the skin have been explored to objectively diagnose this condition. Some methods include application of lactic acid[17,18], capsaicin[14], sodium-lauryl-sulphate[19], cross-polarized light[20], and quantification of interleukins in sebum[21]. However, the 10% lactic acid test, also known as the lactic acid stinging test (LAST), is considered the most reliable and reproducible of all[13,17]. This lactic acid irritation test creates a more acidic skin environment (pH 4-6), eliciting irritative symptoms in subjects with sensitive skin usually within the first five minutes[17,22].

Epidemiological studies based on self-assessment of sensitive skin to cosmetic or environmental factors from Europe, North America, and Japan have indicated a varied prevalence of this condition ranging between 50%-85% in women and 30%-40% in men[1,2,5,8,23,24]. The importance of sensitive skin syndrome is well-recognized in the clinical setting, especially in regards to patient intolerance to topical prescriptions that would usually be well-tolerated (*i.e.,* glycolic acid, azelaic acid, sunscreens). Some patients also reject the use of soap, moisturizers, and makeup without objective signs of cutaneous disease. Poor compliance to skin treatments due to these factors supports the presence of the syndrome. Although sensitive skin is frequent among Caucasians, its prevalence in Latin-American populations is unknown, and none of the suggested diagnostic tests have been explored so far in that population. Therefore, the aim of this study was to use the lactic acid stinging test to objectively describe the biophysical response and frequency of sensitive skin in Mexican subjects.

MATERIALS AND METHODS

Study design and test subjects

The study was a randomized, placebo-controlled, double-blind test conducted in San Luis Potosi, Mexico, from August 2011 to September 2012. We included healthy volunteers, between 18 and 70 years of age, regardless of their self-assessment of sensitive skin. Exclusion criteria were pregnancy or nursing, known allergy to lactic acid, use of any topical medication for the past 4 wk, and the presence of active dermatoses on the test site. Subjects were university students, workers of public institutions, and the general population who were asked in a random modality to participate. Demographic data included age, sex, skin phototype, previous dermatoses, and the self-diagnosis of sensitive skin. Skin phototype was assessed through the melanin angle in accordance to Chardon *et al*[25] using the following classification: phototype Ⅰ, > 55°; phototype Ⅱ, 41°-55°; phototype Ⅲ, 28°-41°; phototype Ⅳ, 10°-28°; phototype Ⅴ, 0°-10°. All subjects signed an informed consent. The study was approved by our Institution's Ethics Committee and is registered at the United States National Institutes of Health Clinical Trial Register (NCT01591993).

Sensitive skin test with lactic acid

The lactic acid stinging test was performed according to the protocol established by Frosch and Kligman[17], where 10% lactic acid is applied to the nasolabial fold with no thermal induction of sweating. The peak response in subjects with sensitive skin syndrome is consistently reported within the first three minutes, followed by a gradual decline to near baseline values at 10 min[13,17,22]. For this study, we randomly applied 10% lactic acid (Sigma Aldrich, United States) in an aqueous solution on one nasolabial fold and simultaneously applied a 0.9% saline solution as placebo on the other side by a second investigator. Solutions were absorbed in a cotton swab at a constant weight of 0.2 g and applied by a gentle

stroke on each side. Testing was blinded for subjects and investigators. Temperature and acidity of the interventions were measured and controlled for each test. The pH parameters were set at 2.1 for lactic acid and 6.9 for placebo, both at room temperature. The intervention was carried out under controlled environmental conditions of humidity (40%) and temperature (22 ℃).

Volunteers were evaluated initially and at 3, 5, 8 and 10 min after the application of lactic acid or placebo. To obtain biophysical measurements, the nasolabial fold was segmented downwards in four consecutive areas of 1 cm^2 each. This was done to decrease the possibility of inducing changes by the sequential registrations on the skin site.

The primary outcome was a verbally declared sensation of discomfort that included stinging, itching, burning, tingling, tightening, or pain on the site of application. The intensity was measured using a Visual Analogue Scale (VAS) of 10 points, where 0 meant no discomfort, 1-4 meant an increasing but tolerable discomfort, 5-9 meant an increasing and intolerable discomfort, and 10 meant the worst discomfort ever experienced[26]. Subjects declaring a VAS intensity of two or greater at any point of the study were considered positive to the test and categorized consequently with "sensitive skin". We considered that a value below 2 could be attributed to the manipulation and application of a liquid substance. Therefore, subjects with VAS of 0 or 1 were considered negative for the test and had "normal skin". Visual changes (erythema, rash, or other) were evaluated by investigators and documented by digital photography.

Biophysical measurements

Skin pigmentation and erythema were evaluated by a reflectance spectrophotometer (ChromaMeter CR-300, Minolta, Japan). It assesses color in three dimensions: *L* (luminance), which gives the relative brightness, ranging from black to white; *a*, which represents the color range from red to green; and *b*, which represents the color range from yellow to blue. The *a* axis was used to evaluate clinical or subclinical erythema. All measurements were performed without excessive pressure to the skin to avoid modifications of the blood flow.

Transepidermal water loss (TEWL) was calculated using the Evaporimeter DermaLab (Cortex Technology, Denmark), which evaluates the vapor pressure gradient of the skin. The water loss was recorded in g/m^2 per hour. Skin surface hydration was determined by capacitance using the Corneometer DermaLab Moisture Module (Cortex Technology, Denmark). This instrument measures the electrical capacitance of the stratum corneum, reflecting its water content in arbitrary units.

Statistical analysis

The sample size needed was calculated using a minimal expected sensitive skin prevalence of 20% in a large sample population (*i.e.*, ⩾ 100 000). Assuming a confidence level of 95%, at least 246 subjects were needed. Permuted block randomization was used to assign the left or right nasolabial fold to test. Descriptive analyses were made using central tendency measures. Analyses of data were performed using two-tailed χ^2 test, Fisher's test, *t*-test, Mann-Whitney *U* test for non-parametric values between groups, logistic regression, or odds ratio (OR); *P*-values < 0.05 were considered significant. All were performed using the JMP software 8.0 (Cary, NC, United States) at 95%CI.

RESULTS

The study recruited 250 subjects, of which four subjects were eliminated from analysis due to incomplete data. The remaining 246 subjects were included in all of the analyses. The mean age was 32 years (range, 18 to 66 years), 68% were women, and the most frequent skin phototype was Ⅴ (49%), followed by Ⅳ (35.4%) and Ⅲ (12.6%). Eighty-nine subjects (36%) considered themselves as having sensitive skin. The demographic characteristics of the study group are shown in Table 1.

Lactic acid test

A total of 128 subjects (52%) were positive for the LAST during the test period of 10 min. A positive response in the first three minutes was observed in 101 subjects (41%). The mean VAS of this group was 4.5 ± 2.1. Twenty-seven subjects (11%) exhibited a delayed response, demonstrating irritation five to 10 min after the start of the test. Thirty-three subjects (13%) described discomfort at 3 min on the placebo side; eleven of these subjects (63%) were also sensitive to lactic acid. In all of these subjects, discomfort on the placebo side was graded as 2 or lower in the VAS and discomfort disappeared after three minutes. The most common response was stinging (58%), followed by itching (40%), and other sensations (8%). None of the subjects presented clinical erythema during the study, even in the cases of high VAS scores.

Concerning the self-diagnosis of sensitive skin, 80% (n = 71) of individuals were positive to the LAST. On the other hand, only 36% (n = 57) of those that did not consider themselves as sensitive exhibited a positive response to the challenge (P < 0.001), as shown in Figure 1. We found a higher prevalence of responders among women compared to men (60% *vs* 34%, P < 0.001). There were also significant differences in the test outcomes among skin phototypes. We found that lighter skin tones (types Ⅱ or Ⅲ) showed a higher response to the LAST compared to the darker skin tones (type Ⅴ), as seen in Figure 2 (P < 0.001). Logistic regression analysis confirmed this relationship, suggesting that the higher pigmentation was associated with decreased prevalence of positive tests (P < 0.001, OR = 0.88). No significant differences were found among the groups by age (Table 2).

Biophysical measurements

Basal values for all the biophysical measurements did not differ between sensitive and non-sensitive subjects in response to the LAST. However, after the lactic acid challenge, significant differences were observed for all parameters in subjects who were positive relative to those subjects who were negative for the test. Colorimetric measures

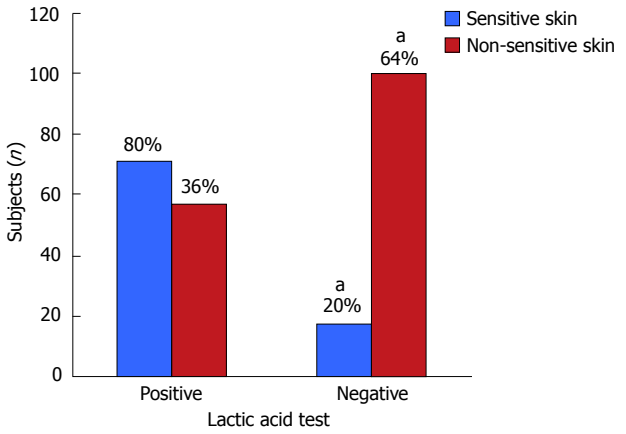

Figure 1 Relationship between the lactic acid stinging test response and self-diagnosis of sensitive skin in study subjects. Of the 246 subjects, 128 were positive and 118 were negative for the test. Bars represent the proportion of subjects with self-diagnosis of sensitive (n = 89) and non-sensitive skin (n = 157) and their results to the test. χ^2 test, $^aP < 0.05$ *vs* positive for the test.

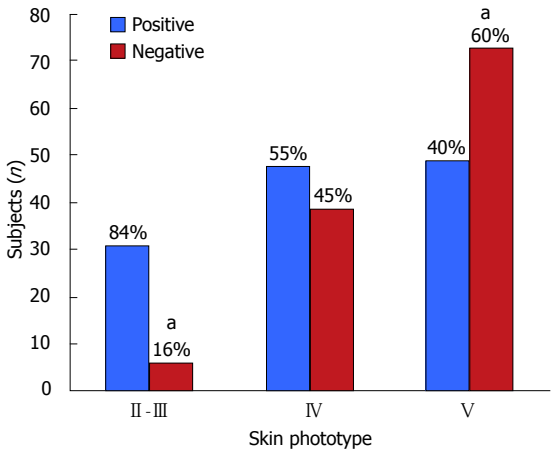

Figure 2 Relationship between skin phototype and lactic acid stinging test response. Subjects with lighter skin phototypes were more prone to display a positive response to lactic acid stinging test (84%), than subjects with the darker skin phototype in the sample population (40%). χ^2 test, $^aP < 0.05$ *vs* positive for the test.

showed statistical differences in the a^* value between onset and at 3 min and 5 min ($P = 0.006$ and $P = 0.017$, respectively), being greater in subjects negative to LAST. TEWL showed an increased water loss in subjects who were positive for the test at 3 min ($P = 0.01$), as at 5 min ($P = 0.03$). Concerning capacitance, values at three minutes were not statistically different but were significantly different at five minutes ($P = 0.002$). These data are summarized in Table 3 and Figure 3.

DISCUSSION

The term "sensitive skin" has been used by the general population and the cosmetic industry to describe an exaggerated and unpleasant reaction to common skin care products or environmental factors[2,12]. This syndrome is currently difficult to define and identify since its manifestations are notoriously subjective. Although it can be associated with other dermatoses[23,24], there is now enough evidence to consider it a true condition and not just a symptom of another disease[9,27,28]. Therefore, self-diagnosis is the preferred method to recognize sensitive skin[8]. Clinically, there are important implications such as the impact on the quality of life for these patients and their compliance to topical treatments[3,29]. In this study, we found that one third of subjects that declared themselves as having normal skin were positive to the LAST, indicating that self-diagnosis is not enough to identify the entire population affected by this condition.

In our study, we found a larger prevalence of sensitive skin than originally expected. We observed a higher prevalence of sensitive skin in women compared to men, but did not find differences in the frequency among age groups. Although some authors have reported similar rates of sensitive skin between men and women[2], most studies have shown that sensitive skin occurs more frequently in women[1,5,23,24]. On the other hand, the relationship between age and sensitive skin is still unclear; previous studies have described a lower prevalence with

Table 1 Demographic characteristics of the 246 subjects included in the study *n* (%)

Mean age in years (range)	31.8 (18-66)
Sex	
Male	78 (31.7)
Female	168 (68.3)
Skin phototype	
II	6 (2.4)
III	31 (12.6)
IV	87 (35.4)
V	122 (49.6)
Self-diagnosed sensitive skin	
Yes	89 (36.2)
No	157 (63.8)

Table 2 Prevalence of sensitive skin by self-diagnosis and response to lactic acid stinging test by age group, sex, and phototype (n = 246) (%)

	Self-diagnosis	Positive	Negative
Age groups (yr)			
< 20	16 (44.4)	18 (50.0)	18 (50.0)
21-30	32 (32.0)	49 (49.0)	51 (51.0)
31-40	17 (34.6)	31 (63.2)	18 (36.8)
41-50	15 (40.5)	21 (56.7)	16 (43.2)
> 50	9 (37.5)	9 (37.5)	15 (62.5)
Sex			
Male	18 (23.0)	27 (34.6)	51 (65.4)
Female	71 (42.2)	101 (60.1)[1]	67 (39.9)
Skin phototype			
II	6 (100)	6 (100)[1]	0 (0)
III	16 (51.6)	25 (80.7)[1]	6 (19.3)
IV	33 (37.9)	48 (55.2)	39 (44.8)
V	34 (27.8)	49 (40.2)	73 (59.8)[1]
Self-diagnosed sensitive skin			
Yes	-	71 (79.7)[1]	18 (20.3)
No	-	57 (36.3)	100 (63.7)[1]

[1] χ^2 test, $P < 0.05$ *vs* negative group.

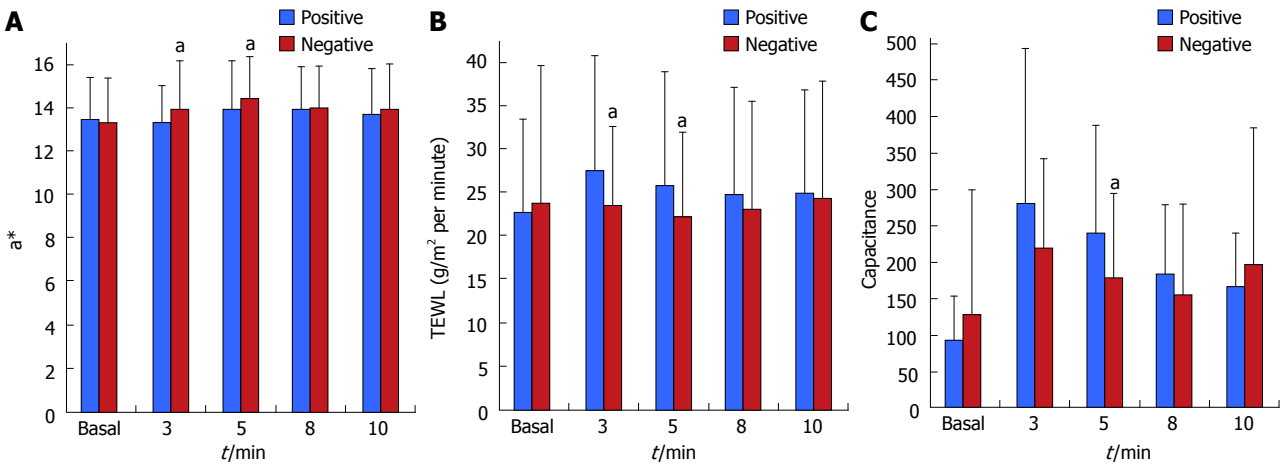

Figure 3 Differences in the skin biophysical response between those that were positive (*n* = 128) or negative (*n* = 118) to LAST. A: a* values, in arbitrary units; B: Transepidermal water loss, in g/m^2 per minute; C: Capacitance, in arbitrary units. Bars represent the mean and error bars represent the standard deviation. Mann-Whitney *U* test, $^aP < 0.05$ *vs* positive for the test.

Table 3 Biophysical measurements evaluated at onset and within 10 min after lactic acid stinging test

	a axis		TEWL		Capacitance	
	Positive	Negative	Positive	Negative	Positive	Negative
Basal	13.4 (11.6-15.2)	13.3 (11.4-15.2)	22.9 (12.5-33.3)	23.9 (8.3-39.5)	92 (30-154)	128 (42-298)
3 min	13.3 (11.7-14.6)	13.9 (11.8-16.0)[1]	27.5 (14.4-40.6)[1]	23.7 (14.9-32.5)	281 (70-492)	220 (98-342)
5 min	13.9 (11.7-16.1)	14.4 (12.6-16.2)[1]	26.0 (13.2-38.8)[1]	22.4 (13.0-31.8)	239 (92-386)[1]	179 (64-294)
8 min	14.0 (12.2-15.8)	14.0 (12.2-15.8)	24.9 (12.9-36.9)	23.1 (10.9-35.3)	182 (85-269)	156 (34-278)
10 min	13.7 (11.8-15.6)	14.0 (12.1-15.9)	25.1 (13.4-36.8)	24.4 (11.1-37.7)	168 (97-239)	196 (9-383)

Values are shown by positive and negative results to the test for the a value, transepidermal water loss (TEWL), and capacitance. TEWL was measured in g/m^2 per minute; *a* and capacitance are shown in arbitrary units. Numbers indicate mean and standard deviation in parenthesis. [1]Mann-Whitney *U* test, $P < 0.05$ *vs* negative group.

increasing age, but other studies have not delineated these differences[1,5,23]. A response was observed with the placebo application (0.9% saline solution), but it was of short duration and low score in the VAS. This placebo response could be attributed to the sensation that is felt after the skin is manipulated or put in contact with liquids.

We did not observe differences in the basal biophysical measurements between subjects with sensitive and normal skin; consequently these values could not predict skin sensitivity. However, in the first five minutes after the test, all patients with a positive response exhibited higher TEWL and capacitance levels compared to non-responders. These findings could be in accordance with the barrier function disruption theory, where the epidermal layer enhances access of a substance leading to its associated clinical response[6,10,30-32]. It is worth noting that nearly 10% of the subjects showed a delayed response to the test and responded after three minutes. This variation may support the presence of different mechanisms of irritation, such as an altered neurosensitive response, as proposed by other studies[14-16].

Although previous studies have reported an increase of the colorimetric *a** value, suggesting subclinical erythema[6,31], we did not observe this change. In contrast, we observed a higher *a** value in subjects negative to the test. These findings can be related to higher skin pigmentation of our population, in whom subtle changes in subclinical erythema can be difficult to identify through colorimetry compared to lighter skin phototypes[33]. It is also important to consider that the *a* value could have been altered by the serial measurements taken in this study; others have shown that reproducibility of erythema measured by colorimetry depends on controlling several mechanical and environmental factors[34].

An important finding was that subjects with lighter skin phototypes (II and III) had a higher prevalence of sensitive skin compared those with darker skin phototypes (V). Pigment increase has been associated with a lower surface pH and enhanced barrier function[35], which may indicate that subjects with darker pigmentation could be more resistant to lactic acid stimulation than subjects with lighter pigmentation. Regression analysis confirmed this relationship, suggesting that darker skin pigmentation may confer protection from sensitive skin. A lower prevalence of sensitivity in darker skin phototypes has also been reported in other studies[1,8,24].

Studies in Caucasians have described a higher prevalence of sensitive skin than observed in the Mexican population of this study[1,5,8,23,24]. There are no published studies that have investigated Latin-American populations,

although one study including Hispanic individuals living in the United States reported similar prevalence rates for this subgroup[1]. Differences in the self-diagnosis of our population sample may be related to inherent features of the population[35-38], as well as cultural differences, such as a low interest in using cosmetic products or reporting adverse reactions to them[23,37]. One limitation of this study is that we assessed the presence of sensitive skin by lactic acid sensitivity exclusively. As previous studies have shown, this sensitivity cannot predict the response to other irritants[7,17]. Therefore, our study may underestimate the prevalence of sensitivity to a wider number of irritants. Nevertheless, if we consider the LAST as a reference, our prevalence of sensitive skin is closer to that reported in many parts of the world[1,5,23].

In conclusion, this study shows that the prevalence of sensitive skin in a representative country of Latin-America, such as Mexico, is relatively high, but was not as high as the sensitivity reported among Caucasian populations. Darker skin phototypes may possess inherent features that confer them a certain resistance to topical irritants. These results show the importance of recognizing this condition as clinically significant in this part of the world. Patients of any ethnic background may exhibit intolerance to topical treatments, including pharmaceuticals, cosmeceuticals, and cosmetics. The proper objective identification of sensitive skin can improve poor compliance to topical treatments usually found in patients who have sensitive skin syndrome.

COMMENTS

Background

Sensitive skin is a syndrome characterized by personal experience of discomfort after the application of topical substances without any objective evidence of irritation. In Caucasians, its frequency has been described in up to 60% of females and 30% of males. There is no standard test to diagnose this syndrome, and so it is still considered a self-diagnosed entity.

Research frontiers

The prevalence of sensitive skin and its biophysical response have not been described in Latin-American populations. There are no previous studies of objective, diagnostic methods for this syndrome in this area of the world.

Innovations and breakthroughs

Self-diagnosis of sensitive skin in Mexico is less frequent than in other parts of the world. Using the lactic acid stinging test, we determined that its prevalence in Mexico is high, although not as high as that found in Europe and North America. Furthermore, individuals with darker skin showed a lower prevalence of this condition. Since this study was conducted in a relatively homogeneous population living under similar climate conditions, these differences among phototypes could be related to the inherent pigmentation of the skin.

Applications

The lactic acid stinging test is a simple, reproducible and non-expensive method for the diagnosis of sensitive skin. Subjects with lighter skin phototypes are at higher risk of having this syndrome. Identification of sensitive skin is important not only for the dermatologist, but also for the cosmetic and pharmacology industries, since these subjects can have a marked intolerance to topical treatments and poor treatment compliance within the medical context.

Terminology

The lactic acid stinging test is a diagnostic method where 10% lactic acid is applied on the nasolabial fold. Subjects with sensitive skin will indicate stinging or itching during the first three to five minutes with variable intensity. This response typically disappears 15 min after the application.

Peer review

The authors explored the prevalence and biophysical reaction of subjects with sensitive skin in a population from Mexico, through the application of the lactic acid stinging test. The results demonstrate a high prevalence of previously unknown sensitive skin and suggest that subjects with dark skin phototypes are less prone to this condition compared to subjects with lighter skin. This study is the first to explore the presence and behavior of sensitive skin in a Latin-American population. This work may also set a foundation for the investigation of pigment-associated physiological pathways that could explain the differences found among skin phototypes.

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