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Comparison of Transepidermal Water Loss Rates in Subjects with Skin Patch Test Positive versus Negative to Skin Care Products

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Abstract

Background.—Adverse cutaneous reactions to skin care products (SCP) are becoming increasingly common, and may be indicative of defective permeability barrier function.

Aim.—To determine the differences in transepidermal water loss rates (TEWL) between skin patch positive versus negative to skin care products in normal Chinese females.

Methods.—Skin patch test reactions to nine skin care products were assessed in 65 normal Chinese females. Correlations of cutaneous reactions to a panel of nine foreign and domestic SCP with permeability barrier function and stratum corneum (SC) hydration levels were analyzed.

Results.—Out of 65 subjects, 24 (37%) displayed positive reactions to one or more SCP. However, the occurrence of positive reactions to patch tests did not correlate with either transepidermal water loss rates or SC hydration levels.

Conclusions.—Though a substantial proportion of normal females display adverse reactions to SCP, this problem cannot be attributed to differences in the qualities of their epidermal permeability barriers, and therefore, these reactions more likely reflect the potential adverse events of the SCP themselves. However, further studies in large cohort of both males and females would be helpful to ascertain whether TEWL levels can predict cutaneous reactions to SCP.

Keywords

Skin care products; adverse reactions; skin barrier function; stratum corneum hydration

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Introduction

The incidence of adverse cutaneous reactions to skin care products (SCP) has been increasing steadily in recent years[1]. Indeed, skin care products are a major cause of irritant and allergic contact dermatitis[2,3]. It has been presumed that defects in the host's epidermal permeability barrier function could account for the development of adverse cutaneous reactions to SCP because: 1) disruption of epidermal permeability barrier provokes cutaneous inflammation and increases cutaneous inflammatory responses to external stimuli[4]; 2) improvements in epidermal permeability barrier prevent and/or alleviate contact dermatitis[5]; 3) higher transepidermal water loss (TEWL) rates correlate to skin susceptibility to irritation with sodium lauryl sulphate[6]. Yet, other studies showed that applications of formulations with putative barrier restorative properties did not prevent, but instead aggravated irritant-induced skin damage[7], suggesting that defective epidermal permeability barrier function may not always underlies adverse cutaneous reactions to SCP. Therefore, we assessed here whether abnormalities in permeability barrier function account for adverse cutaneous reactions to skin care products in normal humans. Our results demonstrate that abnormalities in epidermal function cannot account for adverse reactions to SCP, calling into question the inherent safety of many SCP.

Patients and Methods

Study Subjects:

Because the majority of people using skin care products are females in China, we only chose females in this study. A total of 65 normal females, aged 19 to 46 years old, were enrolled in this study during March, 2018 (Table 1). These volunteers denied a prior or current history of any inflammatory dermatoses, including atopic dermatitis, or self-perceived sensitive skin. All subjects were instructed to stop using topical skin care products, including soaps, on the forearm for at least 12 hours prior to testing. This human research protocol was approved by the Institutional Review Boards of Dermatology Hospital, Southern Medical University, China (GDDHLS-20180304). Study was carried out in accordance with the Helsinki principles. Informed consent was obtained from all volunteers prior to the study.

Assessment of Epidermal Functions: All subjects rested in a controlled environment (22–24oC, 45–55 % humidity) for 30 min prior to measurements. GPSkin Barrier® (GPOWER Inc, Seoul, South Korea) was used to assess TEWL rates and SC hydration levels on the flexor of the right forearm prior to patch tests8.

Skin Care Products and Patch Tests: All skin care products, which were claimed to benefit epidermal function, were purchased from local stores (Suppl. Tables 1&2). Blank patch test sheets (10 patches/sheet) were purchased from Hezhong Biotech (Sanming, Fujian, China). Each patch was covered evenly with small volume of one product, and one patch on each sheet left blank served as control. Because of the high humidity during the month of March in Guanzhou City, patch test on the sweat gland-enriched site, the back, a commonly used site, may cause false positive result. Thus, skin patch test was done on the forearm. Patch remained on the flexor of the right forearm for 48 hours. Reaction readings were taken 30min and 48 hours after removal of test patch. Based on the intensity of reactions, patch

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test reactions were graded as negative (−), no reaction; irritation, erythema; weak positive (+), slightly elevated pink or red plaques; strong positive (++), papulovesicles; and extreme reaction (+++), spreading redness, severe itching, and blisters or ulcers [9]. Allergic reactions were considered if lesions were with severe pruritus and undefined boundaries. Otherwise, irritant reactions would be considered.

Statistics:

GraphPad Prism 5 software was used for all statistical analyses. Mann Whitney, Fisher's exact test and Chi-square tests were used to determine significances. Data are expressed as mean ± SEM.

Results

Rates of positive reactions vary significantly with products

Among these 65 subjects, 16 (24.6%) developed irritant reactions to more than one products, while 8 subjects (12%) displayed irritant reactions to one product 48 hours after patch testing. Only one subject showed grade^{++} reactions to products No. 1 & 9. The rest of subjects exhibited grade^{+} irritant reactions, consistent with previous observations[10]. 48 hours after removal of patch, signs of irritant reactions disappeared in most subjects (Table 2). No allergic reactions were observed in any subject. As seen in Table 2, rates of irritant reactions to SCP varied significantly among individual products. Together, these results demonstrate that considerable proportion of young, otherwise normal Chinese females display irritant reactions to skin patch test of various skin care products.

Neither transepidermal water loss rates nor SC hydration levels differ significantly between patch test-positive and –negative subjects

Because defective permeability barrier enhances susceptibility of skin to external stimuli[4], we next determined whether cutaneous reactions to skin care products can be attributed to inherent abnormalities in epidermal function. As shown in Table 3, neither the basal TEWL rates nor SC hydration levels differed significantly between patch test-positive and -negative groups. Thus, neither permeability barrier function nor SC hydration levels predict the development of irritant reactions to skin care products in normal humans

Discussion

The incidence of adverse cutaneous reactions to skin care products is as high as 14% in certain region[11]. The pathomechanisms whereby skin care products induce adverse cutaneous reactions remain unknown. One theory is the involvement of cutaneous nervous system[12]. It was assumed that sensitive skin may have a higher density of nerve fibres, leading to increased sensitivity to external stimuli. In addition, transient receptor potential cation channels (TRP) express on both nerve fibres and keratinocytes. These receptors mediate sensation of pain, itch and burning upon exposure to stimuli in sensitive skin. Another widely assumed theory of how adverse cutaneous reactions develop is that pre-existing skin conditions with compromised permeability barrier results in enhanced penetration of substances into skin, or that skin sensitivity (such as sensitive skin) to external

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stimuli increases. This could be true in subjects with problematic skin conditions because subjects with certain dermatoses such as atopic dermatitis and sensitive skin predispose to the development adverse cutaneous events[13]. However, skin care products can also induce adverse cutaneous events in both normal mice[14] and humans[2, 15]. Therefore, we hypothesize here that harmful skin care products alone directly cause adverse cutaneous events, leading development of sensitive skin, compromised permeability barrier and/or aggravation of dermatoses.

It is generally accepted that defective permeability barrier play pathogenic role in the development of adverse cutaneous reactions to skin care products. Truly, subjects with other conditions with elevated TEWL rates exhibit low threshold to stimuli[16]. Thus, theoretically both TEWL rates can predict the probability of developing irritant reactions to skin care products. But we demonstrate here that rates of positive irritant reactions to patch test of skin care products did not correlate with TEWL rates in normal humans, strongly suggesting that skin care products per se dominate the development of irritant reactions, while pre-existing skin conditions determine the severity of irritant reactions.

It is worthwhile noting that these tested products are supposed to benefit skin, instead of damaging skin. About 37% of subjects displayed positive reactions to patch test. Such high rates of skin patch test could be ascribed to a) harmful ingredient(s) in the products and b) occlusion by the patch. Previous study showed that occlusion could increase stratum corneum hydration, which enhances penetration of substance into the skin, leading to the development of irritant and allergic contact dermatitis[17–19]. Thus, skin patch test is a sensitive approach to evaluate the safety of topical substances. Whether repeated daily applications of these skin care products to the skin can also cause such high rates of adverse cutaneous reactions remains to be determined. Nevertheless, the substantial high positive rates of patch test, including expensive products, raise further concerns about the safety of skin products. Although the reactions are minor irritant reactions, repeated long-term applications of these products will eventually lead to the impairment of epidermal function[14] and development of sensitive skin, needless to mention exacerbation of pre-existing skin disorders.

Though exact which ingredient(s) in these products cause positive irritant reactions are unknown, it is well known that a number of ingredients, commonly used in skin care products, particularly at high concentration, can cause irritant reactions. Examples of ingredients potentially causing irritation include α-hydroxy acids, propylene glycol, alcohol, fragrances[20]. Other ingredients such as stearic acid, ceteareth 20, PEG-40 castor oil and PEG-100 stearate, can also induce adverse cutaneous reactions, including inflammation, itching, hives, and even blistering of skin[21]. Of course, the possibility that adverse cutaneous reactions induced by newly formed compounds via chemical reactions of ingredients in formulation cannot be excluded. For example, reaction of thymol and the degradation products of triazine derivative can form a new allergen. Therefore, in addition to reduction in concentration of ingredients, minimization of the number of ingredients in formulation could reduce the risk of adverse cutaneous reactions.

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In summary, rates of positive reactions to patch test of skin care products are high even in normal humans. Although it is generally assumed that adverse cutaneous events induced by skin care/cosmetic products are attributed to pre-existing skin conditions, harmful ingredients in skin care products largely contribute to the development of adverse cutaneous reactions. However, further studies in large cohort of both males and females will be required to determine whether TEWL rates can predict adverse cutaneous events to SCP.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Demographic Characteristics of Subjects

	Age (N=65)
Minimum	19.00
25% Percentile	20.00
Median	20.00
75% Percentile	21.00
Maximum	46.00
Mean ± SEM	21.32 ± 0.51

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Table 2.

Rates of Skin Patch Test Reactions Vary Significantly with Products

Product No.	48 Hours		96 Hours	
	Positive No. (%)	Negative No. (%)	Positive No. (%)	Negative No. (%)
1	8 (12%)	57 (88%)	1 (2%)	64 (98%)
2	4 (6%)	61 (94%)	1 (2%)	64 (98%)
3	15 (23%)	50 (77%)	1 (2%)	64 (98%)
4	7 (11%)	58 (89%)	1 (2%)	64 (98%)
5	3 (5%)	62 (95%)	1 (2%)	64 (98%)
6	7 (11%)	58(89%)	1 (2%)	64 (98%)
7	4 (6%)	61(94%)	4 (6%)	61 (94%)
8	6 (9%)	59 (91%)	6 (9%)	59 (91%)
9	5 (8%)	60 (92%)	1 (2%)	64 (98%)

Chi-square test was used to determine the significances. p=0.0267 at 48 hours; p=0.0848 at 96 hours.

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Table 3.

Comparison of Epidermal Functions in Subjects with Patch Test Positive vs. Negative (MEAN ± SEM)

Epidermal Functions	Patch test positive (N=24)	Patch test negative (N=41)	Significance
TEWL ($g/m^2/hr$)	3.04 ± 0.51	3.80 ± 0.44	NS
Hydration (au)	31.16 ± 2.04	27.9 ± 1.78	NS

Mann Whitney test was used to determine the significances.