Sun-Induced Changes in Stratum Corneum Function Are Gender and Dose Dependent in a Chinese Population

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Key Words

Stratum corneum • Hydration • Epidermal permeability barrier function • Gender • Stratum corneum resistance

Abstract

Previous studies have demonstrated that UVB radiation changes the epidermal permeability barrier and stratum corneum (SC) hydration. It is well known that sun exposure causes erythema, sunburn and melanoma. However, whether daily sun exposure alters SC integrity and epidermal permeability barrier function is largely unknown, especially in Chinese subjects. In the present study, we assess the SC integrity, SC hydration and epidermal permeability barrier function following various doses of sun exposure. A total of 258 subjects (124 males and 134 females) aged 18–50 years were enrolled. A multifunctional skin physiology monitor (Courage & Khazaka MPA5) was used to measure SC hydration and transepidermal water loss (TEWL) on the forearms. In males, basal TEWL was higher with higher doses of sun exposure than with lower doses and control, whereas in females, basal TEWL was higher with lower doses of sun exposure than with higher doses and control. In the group with higher doses of sun exposure, TEWL in females was significantly lower than that in males. The barrier recovery was faster in females than in males in both control and lower-dose

groups. In both males and females, barrier recovery was delayed with higher doses of sun exposure. In males, sun exposure did not alter SC hydration, while in females SC hydration was lower with lower doses of sun exposure as compared with control and higher doses of sun exposure. These results demonstrated that sun-induced changes in SC function and SC hydration vary with gender and the extent of sun exposure.

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Introduction

The alteration in cutaneous function induced by sun exposure is mainly attributed to ultraviolet (UV) radiation. Studies have demonstrated that UVB radiation causes a variety of changes in cutaneous function. For example, there is a higher incidence of acquired melanocytic naevi in sun-exposed sites [1, 2]. The incidence and number of melanocytic naevi are associated with the cumulative sun exposure [3–5]. Moreover, the risk of developing squamous cell carcinomas, skin malignant melanomas and actinic keratoses is strongly associated with lifetime sun exposure [6–10]. Chronic sun exposure is considered to be the major cause for non-melanoma skin cancers [11]. Most squamous cell carcinomas and basal

cell carcinomas are found on the sun-exposed body sites [12]. Furthermore, many dermatoses, such as solar urticaria, actinic dermatitis, rosacea and lupus erythematosus, are induced or exacerbated by sun exposure [13–15]. Finally, photo-aging is another common clinical problem induced by sun exposure. In addition to hyperpigmentation and sunburn, sun exposure induces formation of large wrinkles, increases skin surface roughness and reduces skin elasticity [16–19]. The number of wrinkles in humans is significantly related to total hours of sun exposure in life [20]. In animal models, UVB radiation suppresses the immune response to hepatitis B vaccination, tuberculosis and leishmanial infection [21–24] and cutaneous delayed hypersensitivity [22, 25, 26].

Likewise, with regard to stratum corneum (SC) biophysical properties, sun exposure causes dramatic changes. For instance, SC hydration is lower in sun-exposed sites in comparison with non-sun-exposed contralateral sites despite unchanged basal permeability barrier function [16]. Basal transepidermal water loss (TEWL) in human skin increases significantly following UVB radiations of 0.75 minimal erythema dose and is accompanied by decreased SC hydration and an increased melanin index [27]. Humans living in higher UV-exposed regions exhibit lower SC hydration [19, 28]. In photo-aged skin, barrier recovery is delayed as compared with chronologically aged skin, although the basal barrier function and SC integrity show no change [29]. In animal models, UVB radiation decreases SC water content [30–32]. Moreover, UVB radiation decreases epidermal permeability barrier function and disturbs the epidermal calcium gradient [33–36]. The changes in epidermal barrier function induced by UVB radiation are associated with radiation doses. While higher doses of UVB radiation perturb barrier function, lower doses (suberythral doses) accelerate barrier recovery [37]. However, the differences in SC biophysical properties such as barrier function and SC integrity among various doses of sun exposure have not yet been documented. In the present studies, we measure the SC integrity, SC hydration and epidermal permeability barrier function following various doses of sun exposure in males and females aged 15–50 years in a normal Chinese population.

Subjects and Methods

Subjects

A total of 258 volunteers with skin types III or IV (Fitzpatrick classification) aged 18–50 years (124 males and 134 females; mean age 27.90 ± 0.58 years) were enrolled in this study. According to

their daily direct sun exposure time in the last 5 days, the subjects were divided into: (a) a control group whose daily direct sun exposure time was less than 1 h and without direct sun exposure between 11.00 a.m. and 1.00 p.m.; (b) a group exposed to lower doses of sunlight whose daily direct sun exposure time was 1–2 h and without direct sun exposure between 11.00 a.m. and 1.00 p.m., and (c) a group exposed to higher doses of sunlight whose daily direct sun exposure time was 4–6 h and with direct sun exposure between 11.00 a.m. and 1.00 p.m. No skin care products were applied to measured sites 24 h prior to taking the measurement, and the measured sites were not washed with soaps or surfactants for at least 12 h prior to the study. There was no sign of sunburn on the measured sites.

Measurements

All measurements were randomly performed by 2 well-trained dermatologists. TEWL and SC capacitance were measured on the forearm (flexor site, 10 cm above wrist) with respective probes (TM300 and Corneometer CM825) attached to a Courage & Khazaka MPA5 system [38, 39]. For SC integrity assessment, TEWL was measured following each D-squame application for a total of 4 D-squames. For barrier recovery, barrier disruption was achieved by repeated D-squame applications for a total of 7 D-squames. TEWL was measured immediately and 3 h after the last D-squame application. All subjects rested for at least 30 min at $22\text{--}24^\circ\text{C}$, at a relative humidity of 45–47%, prior to measurement. This work was performed between June and August (summer time) at Dalian Skin Disease Hospital, which is at a latitude from $38^\circ 43'$ to $40^\circ 10'$ north. The study protocol was approved by the Human Research Committee of Dalian Skin Disease Hospital, PR China.

Statistics

Graphpad Prism 4 software was used for all statistical analyses. A one-way ANOVA, with Tukey's correction, was used to determine significant differences, when 3 or more groups were compared, while an unpaired t test with Welch's correction was used for comparisons between 2 groups. Data are expressed as means $\pm$ SEM.

Results

Alteration of Barrier Function Induced by Sun Exposure Is Associated with Gender and Sun Exposure Doses

We first assessed epidermal permeability barrier function following various doses of sun exposure in both males and females (table 1). In males, baseline TEWL was significantly higher in the group exposed to higher doses of sunlight in comparison with lower-dose and control subjects (fig. 1). In contrast, baseline TEWL in females was significantly higher in the group exposed to lower doses of sunlight as compared with higher-dose and control subjects (fig. 1). In addition, in females, TEWL in the group exposed to higher doses of sunlight was not differ-

Fig. 1. TEWL baseline following various doses of sun exposure. Basal TEWLs were compared by one-way ANOVA, with Tukey's correction, which was used to determine significant differences. Significant differences are shown in the figure. The number of subjects in each group is detailed in table 1.

ent from that in controls. There was no gender difference in baseline TEWL in both control and lower-dose groups. However, baseline TEWL in males was significantly higher than that in females in the group exposed to higher doses of sunlight (24.82 ± 1.68 and 12.62 ± 1.06 g/m²/h for males and females, respectively).

Since previous studies showed that UVB radiation alters barrier recovery in animal models [29, 37], we next evaluated barrier homeostasis with various doses of sun exposure. In both females and males, barrier recovery was significantly delayed in the groups with higher doses of sun exposure as compared with lower-dose and control groups (fig. 2). There was no difference in barrier recovery between control and lower-dose groups in both males and females (fig. 2). In both control and lower-dose groups, barrier recovery was significantly slower in males than in females (in controls, males 13.08 ± 13.21 vs. females $51.23 \pm 4.25\%$, $p < 0.01$; in the lower-dose group, males -16.53 ± 11.34 vs. females $53.03 \pm 6.38\%$, $p < 0.0001$). However, in the group exposed to higher doses of sunlight, there was no significant difference in barrier recovery between females and males.

SC Integrity Varies with Gender and Dose of Sun Exposure

As seen in figure 3a, in males, TEWL generally increased less in sun-exposed groups than in controls following the same number of D-squame application, especially in the higher-dose group. In females, TEWL increased significantly in the lower-dose group in com-

Fig. 2. Comparison of barrier recovery rates after different doses of sun exposure. The comparison of barrier recovery rates was analyzed by one-way ANOVA, with Tukey's correction. The number of subjects in each group is detailed in table 1, and significances are indicated in the figure.

Table 1. Characteristics of subjects

	Males		Females	
	n	mean age $\pm$ SEM years	n	mean age $\pm$ SEM years
Normal control	28	28.21 ± 1.27	45	32.04 ± 0.95
Lower dose	45	21.69 ± 0.40	50	30.74 ± 0.81
Higher dose	51	32.96 ± 1.00	39	19.82 ± 0.51
Total subjects	124		134	

parison with controls following 3 or 4 D-squame applications (fig. 3b). TEWL in both control and lower-dose groups also increased more in females than in males after the same number of D-squame application, whereas the percent increase in TEWL in females did not differ significantly from that in males in the higher-dose group (data not shown). These results demonstrated that changes in SC resistance to tape-stripping induced by sun exposure are also associated with gender and amount of sun exposure.

SC Hydration Varies with Gender and the Doses of Sun Exposure

We next measured SC hydration with various doses of sun exposure. In males, there was no difference in SC hydration among control, lower and higher doses of sun exposure (fig. 4). However, in females, SC hydration was

Fig. 3. Changes in SC integrity with gender and the doses of sun exposure: percent increase in TEWL following D-squame applications in males (a) and females (b). The number of subjects in each group is detailed in table 1. One-way ANOVA with Tukey's correction was used to determine the significant difference, and the significances are indicated in the figure.

significantly lower in the group exposed to lower doses of sunlight as compared with the control and higher-dose groups (fig. 4). SC hydration in females was significantly lower than that in males in both control and sun-exposed groups ($p < 0.05$ for control and $p < 0.0001$ for both lower- and higher-dose groups). These data indicated that the influence of sun exposure on SC hydration varies with gender and doses of sun exposure.

Discussion

Alteration in cutaneous function induced by UV radiation is determined at least in part by radiating doses [27, 36]. In contrast to the previous finding that basal TEWL in photo-aged skin is similar to that in non-photo-

Fig. 4. Changes in SC hydration with gender. Comparison of SC hydration in the groups exposed to various doses of sunlight was made in males and females. One-way ANOVA with Tukey's correction was used to determine the significant differences. The number of subjects in each group is detailed in table 1. The significance is indicated in the figure. AU = Arbitrary unit.

aged subjects aged 80–97 years [29], the present studies demonstrate that daily sun exposure does induce dose-dependent changes in basal TEWL, which is in agreement with previous findings [40]. The different results may be due to the subjects' ages. The subjects' ages in the present study range from 15 to 50 years. It has been shown that UVB radiation causes more intensive erythema in older subjects [41] and induces a more dramatic increase in TEWL in younger mice (27 weeks old) than in older ones, which shows a minimum increase (90 weeks old) [42]. Although suberythral UVB radiation accelerates barrier recovery in the animal model [37], in the present study no dramatic difference in barrier recovery was observed between control and lower doses of sun exposure. However, studies here show a significant delay in barrier recovery following higher doses of sun exposure. Previous studies showed that UVB radiation alters SC lipid structure and induces disorganized lamellar body and SC intercellular membrane bilayers in addition to disrupting barrier function [43, 44]. Moreover, UVB radiation increases SC pH, which, in turn, delays barrier recovery and increases epidermal desquamation [45, 46]. Furthermore, UVB radiation also decreases SC covalently bound ceramides and reduces epidermal differentiation proteins such as loricrin, transglutaminase type I, filaggrin and keratin K2e expression [47, 48]. Both SC lipids and differentiation are crucial for epidermal permeability [for a review, see 49, 50]. Finally, it has been shown that thymocytes play an important role in regulating permeability

barrier function including UV-induced barrier abrogation [36, 51]. Thus, alterations in SC lipid quality, differentiation protein expression and UVB-induced immune reaction could account for the delayed barrier recovery.

Interestingly, higher doses of sun exposure improve SC integrity (resistance to tape-stripping), especially in females, while lower doses of sun exposure cause either minimal or no changes in SC integrity. The mechanisms by which sun exposure improves SC integrity are not clear. As the permeability barrier mainly exists in the SC and the SC integrity in the present study was determined by measuring TEWL following each SC removal with D-squame, SC thickness could influence TEWL after each SC removal. Studies have demonstrated that repeated UVB radiation increases both epidermal and SC thickness [52–55]. Therefore, more SC layers were left with higher doses of sun exposure following the same number of D-squame application in comparison with a thinner SC in the control group. Then it is not surprising that the higher-dose group exhibited lower TEWL readings than controls following the same number of SC removal. Gender difference in SC integrity is also demonstrated in the

present study. SC integrity in females is significantly stronger than that in males in both control and lower-dose groups pointing to the negative impact of male sex hormones on barrier functions. In agreement with previous findings [38, 56], the present studies also show that SC hydration in males is higher than that in females, although sun exposure does not change SC hydration significantly as compared with controls.

In summary, the present study shows that sun exposure alters epidermal permeability barrier homeostasis and SC integrity. The extent of these changes varies with gender and the doses of sun exposure. These results suggest that improving SC function should be considered in future treatments for sun-induced skin damages.

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