UNDERSTANDING THE COMPLEXITIES OF THE STRATUM CORNEUM: FORMATION, STRUCTURAL COMPONENTS, MAINTENANCE AND ADDITIVE EFFECTS OF ENDOGENOUS AND EXOGENOUS FACTORS

Release Date: October 1, 2016
Termination Date: September 30, 2017
Estimated Time to Complete This CME Activity: 1 hour
Medium or Combination of Media Used: Written article
Method of Physical Participation: Journal article, Journal post-test, web-based post-test, and evaluation
Hardware/Software Requirements: High speed internet connection, any web browser

Statement of Need
There is a gap in the medical knowledge of dermatology healthcare practitioners on the integral role of the stratum corneum and importance of maintaining a healthy skin barrier. There is need for expanded awareness and understanding of the need for proper maintenance of the stratum corneum throughout the average lifespan. Gaps exist in the understanding of the complex structure and function of the stratum corneum and the various intrinsic and extrinsic challenges affecting normal skin barrier function. Gaps exist in the understanding of endogenous and exogenous factors that affect stratum corneum integrity and its role in the management of inflammatory conditions including atopic dermatitis, acne, rosacea, and psoriasis.

Educational Objectives
The overall educational goal of this year-long initiative is to provide the dermatology healthcare practitioners with the latest clinical, scientific, and evidence-based information on advances in the understanding of the structure and function of the stratum corneum and insights into maintaining its integrity and function and role in the management of various cutaneous diseases and disorders.

Upon completion of the CME activity, learners should be able to:

- Describe the role of the stratum corneum in maintaining skin barrier function
- Summarize the major structural components of the stratum corneum and its function in maintaining the skin barrier
- Categorize various endogenous and exogenous factors that adversely affect normal stratum corneum function
- List the structural components of the stratum corneum and related to their physiologic functions
- Review the role of ethnicity and genetics in the structure, physiology and function of skin in persons with diverse skin types
- Categorize various endogenous and exogenous factors that adversely affect stratum corneum function in various disease states
- Summarize characteristics of stratum corneum impairments in inflammatory diseases
- Create effective therapeutic regimens for inflammatory diseases including acne

Target Audience
This activity is intended for dermatologists, residents, and fellows in dermatology, and physician assistants and nurses and to provide the dermatology healthcare practitioners with the latest clinical, scientific, and evidence-based information on advances in the understanding of the structure and function of the stratum corneum and insights into maintaining its integrity and function and role in the management of various cutaneous diseases and disorders.

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Stratum Corneum Abnormalities and Disease-Affected Skin: Strategies for Successful Outcomes in Inflammatory Acne

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ABSTRACT

Stratum corneum (SC) abnormalities are associated with disease-affected skin conditions such as inflammatory acne. Current topical acne treatment options including benzoyl peroxide and retinoids can worsen the barrier dysfunctions by increasing transepidermal water loss, depleting SC vitamin E levels, and relatively decreasing SC thickness. However, strategies exist to employ these treatments in a more effective manner and lessen barrier function disruption including use of less irritating vehicles or concomitant application of moisturizers. Patients also play a role in the outcome of their skin barrier function based on their compliance and administration technique. By increasing patient compliance and proper application of treatments, patient skin barrier function can improve. Additionally, future treatments are on the horizon that may customize acne therapy at a molecular level.


INTRODUCTION

Acne is associated with inherent abnormalities in epidermal barrier, which may contribute to the process of comedogenesis and inflammation. Such dysfunctions occur in both the surface and follicular stratum corneum, and many current therapies used to treat acne vulgaris (AV) can cause further barrier dysfunction. Further, patient activities may worsen their stratum corneum (SC) impairment.1

Stratum Corneum Abnormalities

Acne vulgaris (AV) is associated with impaired water barrier function. In a cross sectional study comprising 36 patients with AV and 29 controls, Yamamoto et al. sought to identify the mechanism behind AV comedogenesis and its relationship with atypical follicular keratinization. The study determined an interrelationship between sebum secretion rate, lipid barrier function, and water barrier function of the stratum corneum (SC). It found that patients with moderate acne experienced sebum secretion and transepidermal water loss (TEWL) at increased rates when compared to the control population. Additionally, moderate acne patients had less hydration than the control group, and both moderate and mild acne patients had significantly less ceramides and percent free sphingosine than the control group. The study concluded that SC barrier dysfunction in AV is accompanied by hyperkeratosis of the follicular epithelium, and impaired skin barrier function in patients with facial acne is marked by a reduction of ceramides, which may be responsible for comedone formation.2

The weather also has an impact on AV SC abnormalities. In a year-long longitudinal study including adolescent male patients ages 13-18 in central New Jersey (7 with acne and 10 controls), Meyer et al. investigated potential seasonal differences in facial skin of acne patients.3 Average temperatures during this year were 18°F in January and 85°F in July. They looked at monthly evaluations of patients’ sebum production, TEWL, skin moisture, and bacterial population. Sebum production was increased in acne patients compared to controls (P<0.019) and displayed a seasonal variation with lowest production in winter. TEWL was higher in acne patients than in controls across the board and also showed a seasonal variation with an increase in colder weather (P=0.001). Skin moisture was higher in both groups in warmer weather (P≤0.016). Patients with acne had a higher recovery of both anaerobic and aerobic bacteria (P≤0.015), and fluorescence studies suggest P. acnes was increased in patients with acne. The study substantiated the differences in barrier function between patients with and without acne and displayed evidence for seasonality of this dysfunction.3

Role of Acne Therapy on Barrier Dysfunction

Topical acne therapies can have a negative impact on the skin barrier with the potential to increase dysfunction. Increased TEWL has been reported with benzoyl peroxide, tretinoin, and tazarotene. Appropriate vehicle choice and Improvements in vehicle technology have mitigated some of these problems. For example, creams versus gels, aqueous gels, microsphere formulations, micronization of actives, and the addition of humectants and emollients.5,6

Benzoyl peroxide (BP) is a concentration-dependent irritant and is mildly keratolytic in nature. However, there is a paucity of data identifying the specific epidermal effects caused by BP. It is shown to increase TEWL by 1.8-fold and deplete stratum
Role of Patients in Barrier Repair

Patients can play a vital role in skin barrier repair, depending on the product used as well as patient adherence and correct application of the product. The Sonic skin care brush was created in response to the innately user-dependent and inconsistent cleansing of the skin, which can lead to inadequate or excessive cleansing. Such cleansing can compromise the skin barrier, cause chronic skin conditions, and reduce medication use. The brush was intended to provide consistent cleansing techniques while avoiding over-manipulation by utilizing a dental cleansing technique. The brush claims to apply oscillatory flexing which works with the skin’s natural elasticity, with the goal of loosening and detaching the inelastic comedones from the infundibular wall.11

Ortblad et al. investigated the efficacy and tolerance of the Sonic skin care brush and 2% salicylic acid (SA) cleanser. The study involved 50 patients, ages 18-60, with mild to moderate AV who had been utilizing acne medications for greater than 6 months. Patients continued on their pre-study medications but added cleansing twice daily. After 2 weeks of product use, there was no significant difference in TEWL, corneometry, or erythema compared to pre-study figures. Similarly, after 12 weeks, there was no significant difference in these values, and patient questionnaires found that 80% of patients considered the brush gentle, 88% felt hydrated, 60% experienced less oil, and 80-89% noted decrease in acne. The study concluded that this cleansing regimen was both safe and effective for daily application to acneic skin.8

Acne cosmetics can occur when products such as cosmetics chronically occlude follicles. Common offenders include isopropyl myristate, propylene glycol-2, lanolins, &C red dyes, and tropical oils. Labeling of products can be misleading to patients such as use of the phrases oil-free, dermatologist tested, hypoallergenic, and non-comedogenic. Particularly problematic cosmetics include eye creams which can result in peri orbital milia, lip products which can cause perioral comedones, and hair-care products particularly after exercise. Despite potential for acneiform reactions to cosmetic products, they continue to offer benefits. Cosmetics can serve to camouflage, contour, and conceal, improving patient quality of life.13

Acknowledging that certain dermatoses can significantly impact a patient’s quality of life (QOL), Boehncke et al. investigated whether decorative cosmetics could improve QOL in this patient population. The study involved 23 patients with disfiguring facial conditions including acne (8) and rosacea (9). Patients were taught to use cosmetics by professionals. The dermatology quality of life questionnaire was performed at baseline and two weeks after the start of study, finding statistically significant increase in QOL in all patients.14 As a follow-up to Boehncke’s study, Hayashi et al. investigated whether use of cosmetics in acne patients interfered with acne treatment and if their QOL changed. Eighteen patients with acne were taught to use acnedesigned cosmetics for 2 to 4 weeks while continuing their acne treatment. The study revealed that both patients’ acne and QOL improved with application of cosmetics.15

Strategies for Successful Outcomes

Several strategies exist that may potentially aid in successful outcomes for inflammatory acne such as helping to prevent cutaneous irritation associated with topical agents (BP, retinoids) and reversing patient-initiated barrier dysfunction. Feldman and Chen performed an Internet-based survey of 200 subjects 15- to 40-years old who used clindamycin-BP (5%) in the past 6 months. The survey found that side effects from treatment caused sub-optimal use including spot application, use only during flares, infrequent use, and discontinuation. Thirty-one percent of patients called the doctor’s office to complain; 23% felt that their physician did not understand the side effect potential; 21% experienced a loss of confidence in their doctor with 11% feeling less likely to see their doctor again; and 41% used moisturizer to combat dryness/redness.16

Moisturizing can improve outcomes in treatment with retinoids. Tanghetti et al. found that when lotion was applied 20 minutes before applying tazarotene 1% Cr, patients experienced a reduction in signs and symptoms of retinoid dermatitis without apparent loss of efficacy.17 Similarly, Draelos et al. found that...
when moisturizer was applied 2 weeks before and during treatment with tretinoin 0.025% cream used for photoaging and an increase in TEWL was prevented. Further, Munehiro et al. studied 18 male Japanese patients with AV being treated with adapalene and clindamycin phosphate gels. Moisturizers were applied to one side of the patient's face, and lesion counts were measured at weeks 0, 2, and 4. The study found that moisturizer use did not impact the efficacy of medications and that patients experienced less irritation and greater satisfaction.  

Patients can reduce barrier dysfunction by improving their cleansing techniques. Physicians should encourage patients to avoid use of irritating behaviors such as washcloths, scrubs, toners, and microdermabrasion and to use mild non-soaps, cool water, and gentle drying. 

Concomitant use of anti-inflammatory botanicals have also been evaluated in acne regimens with an eye to either increasing efficacy, decreasing irritancy, or both. Draelos et al. performed a double-blinded 12-week study of 80 patients, ages 12 and older. Patients were randomized to either an established OTC regimen with BP/SA or a new BP/SA kit with botanical extracts. Global assessment, tolerability, characteristics of acne lesions (erythema, lesion height, diameter of inflammation, and pus), and subject assessment were performed at weeks 2, 4, and 12, and digital photographs were also taken at these intervals. Botanical plus drug outperformed drug alone in speed at weeks 2 and 4 and in lesion count at week 4. Parity between regimens was achieved at week 12.  

Role of Antibiotics/Prebiotics  

Antibiotics used in acne treatment are employed to target *P. acnes* thought to play a role in the pathogenesis of acne. *P. acnes* is the major human skin bacterium and the dominant bacterium in pilosebaceous unit in both acne and healthy patients. It plays an important role in maintaining skin health through its hydrolysis of triglycerides into free fatty acids. This action contributes to the acidic pH of skin, allowing it to outcompete pathogens such as *S. aureus* and *S. pyogenes*, inhibiting invasion. Tomida et al. performed a genome analysis of *P. acnes* and revealed its diversity with several phylogenetic subtypes of *P. acnes* in existence which have genes that encode for various products that can play essential roles in health and virulence. Subtypes IA, IB, II, and III have been identified. IA has been associated with acne and IB and II with skin health. This begs the question do antibiotics do more harm than good? Tomida et al. propose the future goal of customizing acne therapy at the molecular level.  

Prebiotics are chemicals that induce the growth or activity of microorganisms that contribute to the well-being of their host. For example, moisturizers may act as prebiotics to improve the activity or composition of the skin microbiota.  

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that prebiotics alter the microbiota in atopic dermatitis and psoriasis in a study which employed twice daily application of a moisturizer containing niacinamide and thermal spring water high in Selenium/Xanthomonas species. It is possible that moisturizing (as a prebiotic) alone can alter the skin microbiome and bring about healthier skin. Whether or not this will be applicable in acne remains to be seen.  

SUMMARY  

There is an inherent barrier defect in acneic skin which is severity dependent. The role this dysfunction plays in disease and whether repairing the barrier improves disease remains unclear. Topical medications often worsen the defect, especially in the first 2 weeks; however, this initial worsening may be inherent in or inseparable from the efficacy of the product. Often the deleterious effects can be mitigated by quality moisturization. Patients often utilize unhelpful and damaging OTC products and techniques. No acne visit is complete without discussing skin care, with the goal of repairing the deficient barrier, preventing further barrier defect, strengthening compliance, and ultimately improving acne.  

DISCLOSURES  

Dr. Jordan and Dr. Baldwin have no conflicts of interest, financial or otherwise, to disclose.  

REFERENCES  


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1. Patients with acne vulgaris experience decrease in transepidermal water loss:
   a. True
   b. False

2. Patients with acne vulgaris experience a reduction of ceramides in the stratum corneum:
   a. True
   b. False

3. Which of the following can further disrupt barrier function in patients with acne vulgaris?
   a. Retinoids
   b. BPO
   c. Cosmetics
   d. Prebiotics
   e. All of the above
   f. a, b, and c

4. *P. acnes* has one subtype:
   a. True
   b. False

5. The Sonic skin care brush is safe and effective for daily application to acneic skin:
   a. True
   b. False
Evaluation Form

Stratum Corneum Abnormalities and Disease-Affected Skin: Strategies for Successful Outcomes in Inflammatory Acne

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