

Treatment and Maintenance of Cutaneous Rosacea in Latino Skin Types With Prescription Medications and Non-Prescription Cleansers and Moisturizers as Adjuncts: A Review

Carmen Gloria Gonzalez MD,^a Anneke Andriessen PhD,^b Daniela Antelo MD PhD,^c Silmara Cestari MD,^d
Charles McKeever MD,^e Ana Laura Valencia Hernández MD^f

^aFellowship in Pediatric Dermatology, Feinberg School of Medicine Northwestern University, Chicago, IL

^bAndriessen Consultants and UMC St Radboud, Nijmegen, The Netherlands.

^cUniversidade do Estado do Rio de Janeiro (UERJ), Rio de Janeiro, Brazil;

Hospital Universitário Pedro Ernesto Member of Sociedade Brasileira de Dermatologia, Vila Isabel, Brazil

^dDepartment of Dermatology, Hospital Sirio Libanes, São Paulo do Potengi, Brazil

^eDepartment of Dermatology, University of Panama Medical School & Social Security Hospital, Panama City, Panama

^fUniversidad Autónoma de Mexico (UNAM) Affiliations CILAD, Academia Mexicana de Dermatologia, Mexico

ABSTRACT

Background: Rosacea is an inflammatory dermatosis with at least a ten percent prevalence reported among white adults. Rosacea occurs in nonwhite populations, but prevalence data are limited.

Methods: Five dermatologists from Latin America (the panel) met virtually after completing a survey of their prescription and adjunctive therapy practices when managing Latin American patients with rosacea. Panel members were chosen based on their dermatology expertise in treating a range of skin phototypes. Survey results were reviewed and discussed, along with a review of published guidelines for rosacea treatment.

Results: The panel addressed diagnostic challenges in richly pigmented skin individuals. Pathophysiology and treatment of rosacea were reviewed, with a primary focus on how to treat the skin barrier dysfunction in those affected, using prescription and over-the-counter measures.

Conclusions: Appropriate skincare is crucial for effective rosacea management. Cleansers and moisturizers with ingredients such as ceramides, hyaluronic acid, and niacinamide promote a healthy skin barrier, improving rosacea control.

J Drugs Dermatol. 2022;21(10):1111-1118. doi:10.36849/JDD.7010

INTRODUCTION

Rosacea is an inflammatory skin disorder with at least a 10% prevalence reported among White adults and limited data in people with skin of color.¹ However, the condition is not rare in people of Latin-American descent.^{1,2} The clinical presentation of rosacea in richly pigmented phototypes may be less visible and therefore overlooked. International guidelines for rosacea diagnosis and treatment will be reviewed, with emphasis on promoting a healthy skin barrier using skincare products as adjunctive therapy.

Rosacea Diagnosis

The first challenge in meeting the needs of patients with rosacea is a correct diagnosis. There is no consensus outlining rosacea diagnosis and treatment specific to people of Latin America. An international panel of dermatologists and ophthalmologists,

the global ROSacea Consensus panel (ROSCO), is recognized for its ongoing updates for the management of rosacea based on a phenotype rather than a subtype approach.^{3,4} A phenotype approach allows for rosacea treatment based on a patient's presenting disease features, thus fostering individualized care. The wisdom of a phenotypic approach to diagnosis and treatment is reflected in evidence-based systematic reviews of best practices for managing rosacea, which have incorporated a phenotypic approach to reviews of rosacea-specific research.⁵

Phenotype-Based Rosacea Classification

The findings of rosacea are not unique, which leads to underdiagnosis.⁶ The erythema and papulopustular lesions seen in rosacea can be mistaken for seborrheic dermatitis, acne vulgaris, flushing disorders, lupus erythematosus, dermatomyositis, contact dermatitis, or photodamaged skin.⁶

Rosacea is diagnosed clinically based on recognized major features. At least one major symptom is necessary for a correct diagnosis. Persistent facial erythema, episodic flushing, facial telangiectasias, and inflamed papules and pustules are major features. These characteristics typically involve the sebum-rich central face. Papules can be large and deep. Telangiectasias on the cheeks, chin, and forehead can be extensive.⁷ Minor symptoms perceived as uncomfortable skin sensations are experienced by most patients.⁷ Minor features can occur spontaneously but are often associated with flares of erythema. The skin is easily irritated with burning, itching, tingling, or painful prickly sensations. Facial skin is often dry and may feel rough, tight, and scaly. Edema, either transient or persistent, has been described. Despite a higher incidence of rosacea in women, a pathognomonic rosacea finding, phymatous skin, is seen in only a small percentage of patients, usually men. Phymatous changes manifest as facial skin thickening with fibrosis and sebaceous gland hyperplasia, most commonly affecting the nose.⁷

Rosacea Triggers

Dozens of triggers ranging from diet to emotions to environmental factors have been reported. In a survey conducted by the National Rosacea Society, more than a thousand respondents with rosacea identified the following as their most common triggers: Sun exposure (81% of respondents); emotional stress (79%); hot weather (75%); wind (57%); heavy exercise (56%); alcohol consumption (52%); and hot baths (51%).⁸

Rosacea and Quality of Life

Rosacea is a visible disorder. Since the face is affected, rosacea symptoms significantly impact the quality of life.^{9,10} The facial redness and pimply appearance cause embarrassment, low self-esteem, and social anxiety. A survey of more than 800⁹ patients with rosacea in the US and western Europe demonstrated the social isolation imposed by rosacea occurs more frequently than medical providers recognize. The stress and anxiety associated with an unsightly appearance aggravate facial flushing. An unattractive facial appearance is stigmatized by others, who may believe rosacea results from poor hygiene or other lifestyle choices.⁹

MATERIALS AND METHODS

To review international guidelines and address restoration of the skin barrier dysfunction in rosacea, a panel of five dermatologists from Latin American countries convened a virtual meeting on November 13, 2021. The objectives of the meeting were to gain a better understanding of the unique aspects of rosacea in people of Latin American descent and the nuances in treatment approaches for this population. The results of a pre-meeting survey highlighting the prescription and adjunctive therapy practices of the panel were reviewed.

The survey results were summarized and discussed, along with evidence-based recommendations for rosacea therapy.

RESULTS

Based on the medical literature and rosacea pathophysiology, the panel agreed on five statements to improve skin barrier function and patient outcomes.

Statement 1

Rosacea is an inflammatory skin disease with barrier impairment that involves the face. Symptoms of rosacea are bothersome and include stinging, burning, itching, and facial flushing.

Rosacea Pathophysiology

Genetic factors, innate immune disorders, neurovascular dysregulation, *Demodex* mites, environmental factors, and skin barrier destruction all contribute to the development of rosacea.^{6,18-20} High levels of cathelicidins, antimicrobial proteins stored in keratinocytes, and kallikrein 5 (a serine protease) are found in lesional skin. Kallikrein 5 cleaves cathelicidins into active peptides. Peptide fragments have immune-activating properties that promote angiogenesis and contribute to the production of proinflammatory cytokines. When injected into mice, fragments cause symptoms of rosacea, including erythema, vascular dilatation, flushing, and telangiectasias.^{20,21}

Skin flora may also play a role. Healthy skin contains diverse commensal organisms. Patients with rosacea have an increased burden of skin commensals, particularly *Staphylococcus epidermidis* and *Demodex folliculorum* though it is unclear whether skin flora dysbiosis is the cause of rosacea or if it is secondary to other rosacea-induced changes in the skin microenvironment. Some researchers suggest rosacea and demodicosis are different phenotypes of the same disease.^{22,23}

Statement 2

The clinical presentation of rosacea in diverse phototypes can vary; clinical features may be less conspicuous in individuals with deeper skin tones.

The Challenge of Recognizing Rosacea in Darker Skin

The panel discussed the range of skin phototypes in people of Latin American descent. This is a diverse population with rich histories and heterogeneous pigmentation. There is no "Latin" skin type. Rather, there are tens of millions of people of Amerindian (indigenous), European, African, Asian, and Arab heritage. The textbook patient with rosacea, often described as a White young woman with northern European ancestry, represents a minority skin phototype in people of Latin American descent.^{1,12} Worldwide, rosacea is not often reported in people with skin of color. Difficulty detecting typical rosacea features in dark skin leads to underdiagnosis.^{1,2,12} In people of color, women with rosacea outnumber affected men. Erythema, the most

widely reported symptom in white patients, can be assessed in darker skin, but persistent facial erythema is reported less frequently than papules and pustules.^{1,12} Other common rosacea features among people with darker skin include prior steroid use¹³ and demodicosis.¹⁴ A previous misdiagnosis of acne is common, and it is often the lack of response to acne treatment that leads to the correct diagnosis.¹² Darker skin is subject to post-inflammatory hyperpigmentation, which can mask erythema and telangiectasias.^{1,2} As reported by Alexis et al, delayed diagnosis has been reported in substantial numbers of people with skin of color, including Asian patients, African patients living in Europe, and richly pigmented-skinned patients living in North America.¹ Delayed diagnosis puts patients with richly pigmented skin at risk of having a progressive disease or receiving the wrong therapy that compounded the disease.^{1,2,12} There are few reports of the incidence of rosacea in Latin America.² In Colombia, a survey of 33 dermatologists identified rosacea, mostly papulopustular, in 2.85% of patients.¹⁵ The Brazilian Society of Dermatology has published a detailed consensus covering rosacea treatment without reporting that nation's rosacea prevalence.¹⁶

Climate variations can affect symptoms. Global reports indicate a correlation between rosacea, increased sun exposure, and hotter climates.^{1,17} The influence of weather on rosacea flares has been reported in Peru. During a 3-year observational study of patients seen for dermatologic complaints, the increased temperature caused by an "El Niño" appeared to increase the frequency and severity of rosacea.¹⁷

Statement 3

Erythema, telangiectasias, and a history of skin irritation such as burning and stinging with skincare products and other common triggers should raise the possibility of rosacea in all skin tones.

Central Facial Redness and Flushing

When queried about which rosacea phenotypes they see, the Latin American expert panel described a small percentage of patients with phymatous changes. Much more common was isolated mid-face erythema, followed by isolated pustules-papules, or a combination of the two. The panel reported using ROSCO criteria to help diagnose rosacea in richly pigmented skin individuals. In their experience, reliance on identifying triggers for central facial redness and flushing (eg, heat, alcohol, stress) improved the accuracy of a rosacea diagnosis, especially when skin pigment may mask a major clinical finding.

Rosacea Treatment

Prescription Treatment for Rosacea

When avoidance of triggers does not provide adequate improvement, medical treatment must be individualized based on disease severity, provoking factors, quality of life, and the patient's commitment to therapy. Medical management

strategies should be phenotype-based.^{6,7,11} Because rosacea has an adverse impact on quality of life, treatment should target symptoms most bothersome to the patient.^{4,7}

Treatment for Erythema

Guidelines recommend the erythematous phenotype be treated with topicals; however, the treatment of erythema in rosacea is challenging.^{5,7} Different medications have been used such as brimonidine and oxymetazoline, but, in most patients, erythema remains a persistent feature aggravated by trigger factors; therefore the use of lasers or intense pulse light have shown to be most effective.^{5,7,11} For persistent erythema and telangiectasias, there is evidence that laser and intense pulsed light therapy is effective.¹¹

Brazil is the only nation with published guidance for rosacea treatment in Latin America. The Brazilian consensus recommendations are similar to ROSCO recommendations with one notable exception: the use of botulinum toxin as treatment for erythema and flushing.¹⁶ This approach is supported by studies showing the neuromodulator function of botulinum toxin may positively improve erythematous rosacea symptoms by blunting neurovascular instability and reducing inflammation-related mast cell degranulation.²⁷⁻²⁹

Treatment for Papulopustular Rosacea

Systematic reviews^{5,6,11} of treatment for inflammatory papules and pustules have identified effective therapy with topical ivermectin, azelaic acid, and metronidazole. There are few head-to-head trials indicating one topical agent is superior to another, though there does appear to be higher quality evidence for the benefits of ivermectin.^{11,30} The addition of oral low-dose doxycycline, tetracycline, or minocycline will provide further skin anti-inflammatory effects if a topical agent alone is not adequate.¹¹ When considering the addition of an oral anti-inflammatory agent for individuals with richly pigmented skin, providers should keep in mind the higher risk of a minocycline-associated skin pigment change in people of color.³¹

Treatment for Persistent Disease

For severe inflammatory rosacea and phymatous changes, surgery or isotretinoin are effective.^{6,11,32} For persistent erythema and telangiectasias, or for fibrotic phymatous change, laser and intense pulsed light therapy can be considered.¹¹ However, a laser or light-based modality must be used carefully in individuals with richly pigmented skin.^{33,34}

The expert panel members individualize treatment based on their patient populations and expertise. The survey of their prescribing practices indicated panel members follow ROSCO guidelines for papulopustular and phymatous rosacea treatment. For erythematous lesions, they prefer topical ivermectin, topical metronidazole, and laser therapy to the

TABLE 1.**Summary of TEAEs Through Week 8 (Safety Population; Pooled Data)**

Expert Panelist	Erythematous Rosacea	Papulopustular Rosacea	Phymatous Rosacea	Combination Rosacea
1	ACM Rosacalm (contains ruscus extract)	Minocycline, azelaic acid	Adapalene 0.3%	Doxycycline plus topical ivermectin
2	Phytocorrective + topical ivermectin	Oral antibiotics	Isotretinoin	Topical ivermectin plus Phyto-corrective
3	No product specified	Doxycycline	Isotretinoin	Doxycycline
4	Topical metronidazole	Topical ivermectin	Isotretinoin	No product specified

use of topical α -adrenergic agonists. One expert preferred an over-the-counter topical cream that contains *Ruscus* extract, a botanical derivative thought to have α -adrenergic agonist properties.³⁵ A summary of the expert panel's primary treatment recommendations is found in (Table 1).

Skin Barrier Dysfunction in Rosacea

The panel focused on the role of the skin barrier in rosacea. Topical and oral therapies are directed at treating vasodilation, inflammation and inflammatory lesions, and imbalances of commensal skin flora. An underappreciated factor in persistent rosacea pathophysiology is the presence of a disrupted skin barrier.

Although rosacea occurs in sebaceous-rich skin areas, patients complain of dry, overly sensitive skin. Research indicates the skin barrier is dysfunctional in rosacea. The pH of lesional skin is high, with poor hydration and high transepidermal water loss (TEWL).^{36,37} In a recent detailed molecular analysis of the skin barrier,³⁸ gene expression and transcriptional analysis of papulopustular rosacea skin samples were compared with healthy sebaceous-rich skin. All major components of the skin barrier were severely altered in rosacea skin. To the authors' surprise, the barrier disruption was like that seen in atopic dermatitis (AD).³⁸ In AD, it has been proven that barrier disruption exists in normal-appearing skin. Skin barrier disruption in AD is the precursor to skin inflammation and the disease pathogenesis initiator.³⁹ Could barrier disruption be a primary cause of rosacea? The authors theorized that barrier alterations in different skin regions might initiate distinct types of immune-mediated responses. So, although skin permeability in AD and papulopustular rosacea are similar, different local immune mechanisms result in a major distinction between the two diseases.³⁸ It remains unknown whether skin barrier abnormalities lead to the disease of rosacea or whether they are secondary. Still, severe barrier alterations in the facial skin of patients with rosacea strongly support adding skin barrier restoring strategies into clinical practice.

Statement 4

Skin barrier function restoration and maintenance are essential.

Gentle cleansers and moisturizers containing ceramides, hyaluronic acid, and niacinamide promote a healthy skin barrier followed by improvement in rosacea signs and symptoms.

Barrier Repair Therapies for Rosacea

The panel reviewed evidence-based approaches for rosacea skincare, focusing on the goal of restoring a healthy skin barrier. Skincare includes cleansing, moisturizing, and use of sun protection and cosmetics. Because rosacea can be controlled but not cured, skincare should remain an integral part of one's lifestyle even when rosacea improves. The survey completed by the panel asked about the ingredients in non-prescription cleansers the panel considered to be the most important for their rosacea patients (Figure 1A) and those ingredients in cleansers that should be avoided (Figure 1B). Ingredients deemed most important in cleansers by the panel are ceramides and glycerin. Ingredients that should be avoided are salicylic acid, fragrance, and glycolic acid. Further ingredients to be avoided are retinol, menthol, sulfates, alcohol, and benzoyl peroxide. The panel answered a similar question about the ingredients in non-prescription moisturizers. Important ingredients in moisturizers, according to the panel, are hyaluronic acid, dexpanthenol, Vitamin E, niacinamide, dimethicone, glycerin, azelaic acid, chamomile, and alpha bisabolol (Figure 2A). Ingredients in moisturizers to be avoided are salicylic acid, alcohol, retinol, sodium laurate, menthol, fragrance, and lactic acid (Figure 2B).

Good skincare starts with an understanding of a patient's current skincare routine. Due to the redness and papulopustular lesions, patients may mistake their skin condition for acne and then self-treat with products that irritate their skin. Skincare practices can worsen rosacea, as reported in a survey by Huang et al.⁴⁰ More than 1200 Chinese people diagnosed with rosacea were queried regarding skincare habits. Frequent facial cleansing, facial mask use, and facial skin lightening treatments at salons are common practices among those surveyed. Use of facial cleansers more than twice daily, facial masks more than 4 times weekly, frequent salon visits, and skin makeup more than 6 times weekly were reported by those with rosacea.⁴⁰ The authors believed makeup did not cause rosacea but was used to disguise it. Although facial masks are widely used in China,

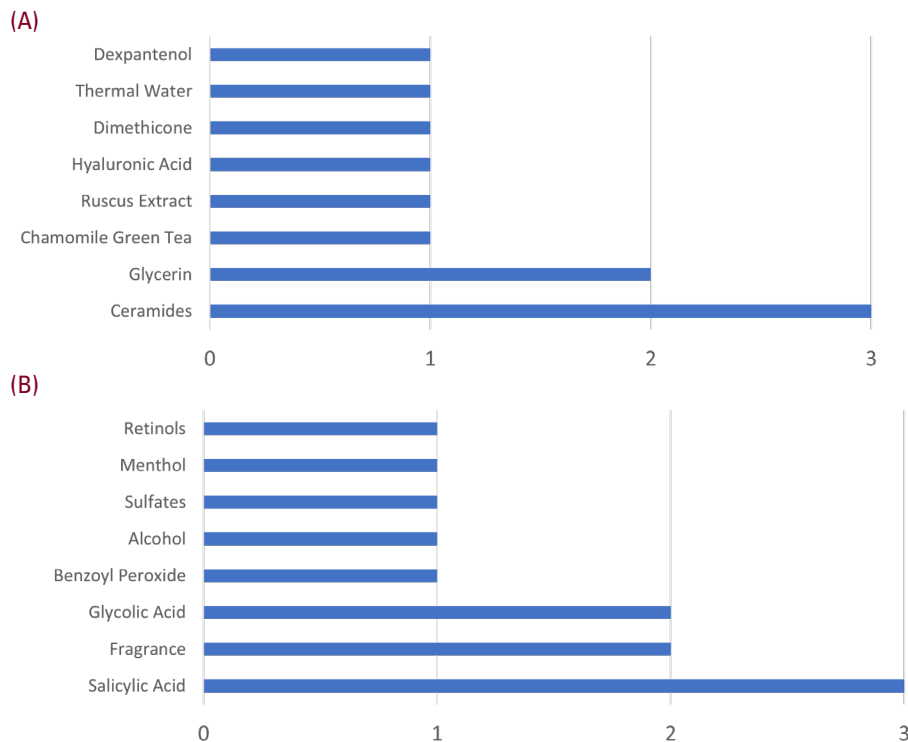
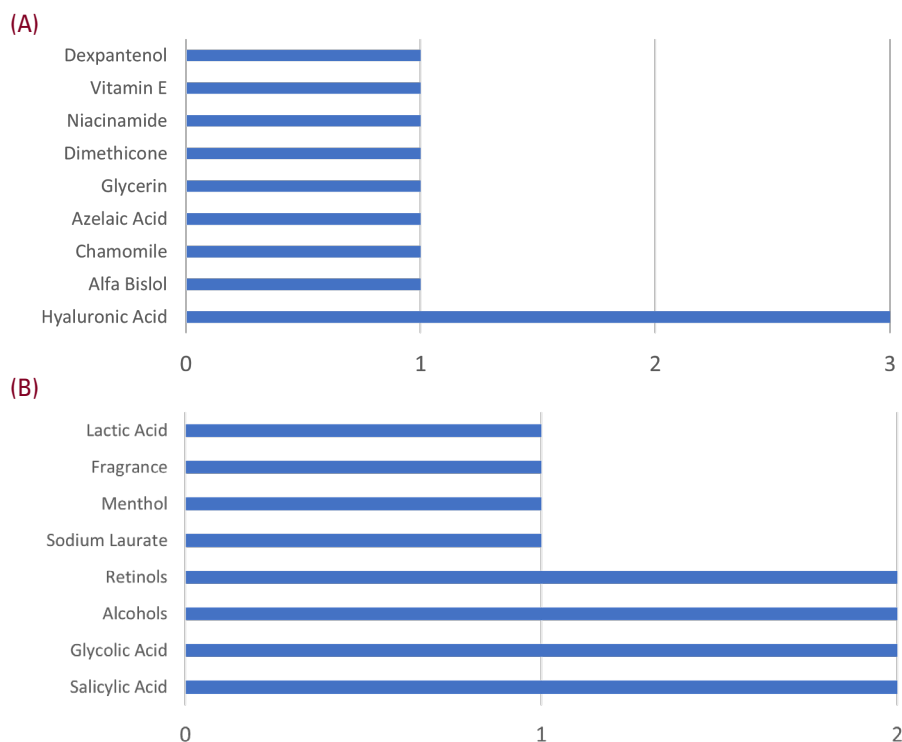
FIGURE 1. Pre-meeting survey (N=4): The ingredients in non-prescription cleansers you consider to be the most important for your rosacea patients are (A); The ingredients in non-prescription cleansers that should absolutely not be used for your rosacea patients are (B).**FIGURE 2.** Pre-meeting survey (N=4): The ingredients in non-prescription moisturizers you consider to be the most important for your rosacea patients are (A); The ingredients in non-prescription moisturizers that should absolutely not be used for your rosacea patients are (B).

TABLE 2.**Rosacea Educational Tips for Latin American Rosacea Patients and Their Healthcare Professionals**

1. Skin barrier function treatment is essential. Careful selection of cleansers + moisturizers containing ceramides, hyaluronic acid, and niacinamide promote a healthy skin barrier.
2. Use gentle skin cleansers only.
3. Use quality moisturizers frequently.
4. Daily sun protection with SPF \geq 50 is strongly advised.
5. Avoid known triggers and skin irritants.
6. Avoid skincare products with an elevated pH.
7. Avoid excessive cleansing and exfoliating.

mask ingredients may not be known. There are reports of masks containing nondisclosed high potency steroids.⁴¹ The survey found sunscreen use and moisturizing cleansers correlated with less risk of rosacea. The authors concluded excessive washing and masks disturbed the skin barrier, causing rosacea flares.⁴⁰ A separate study in adolescent patients with rosacea also observed that face washing more than twice daily increased the risk of developing rosacea.⁴²

The next step after gentle facial cleansing is the application of a moisturizer and sunscreen. Moisturizers suited for easily irritated, rosacea-prone skin are essential in skincare. The scientific worth of the wide selection of over-the-counter moisturizing skin products is not proven. Ceramide-containing skincare with multivesicular emulsion (MVE) technology has been studied in a variety of skin diseases, including rosacea. The advantage of MVE technology is it provides time-released delivery of ceramides for continuous benefits.⁴³ Ceramides may replenish deficient lipids in skin disorders characterized by stratum corneum impairment.⁴³ The prolonged efficacy of a ceramide-containing moisturizing study cream was shown in female subjects with dry, itchy skin.⁴⁴ A ceramide-containing study cream was applied to one lower leg, while the other leg served as a control. Cream use resulted in an immediate increase in skin hydration with reduced signs of dry skin and reduced skin discomfort. After 4 weeks of regular use, skin hydration was significantly improved. The stratum corneum demonstrated a significant increase in skin ceramides, cholesterol, and free fatty acids. Measurable improvements in skin hydration continued for 48 hours even after the moisturizer was discontinued.⁴⁴

Statement 5

Latin American patients with rosacea and their healthcare professionals should be educated on the importance of gentle skin cleansers; frequent use of quality moisturizers; careful selection of moisturizers and cleansers to maintain the functional and structural integrity of the skin; daily use of sun protection with SPF \geq 50; avoidance of known triggers and skin irritants; avoidance of skincare products with an elevated pH; and avoidance of excessive face washing and exfoliating.

Products that promote prolonged moisturizing benefits are ideal for patients with rosacea. Skin moisture loss can be higher at night.⁴⁵ Moisturizers formulated specifically for night use should optimize moisturization for the duration of sleep or longer. In a study of a night cream, participants with dry skin had improved skin hydration and reduced TEWL for up to 8 hours.⁴⁵ The same night cream was tried in patients with rosacea. The study cream proved to be an easily tolerated and effective moisturizer that improved hydration, cutaneous barrier function, and the visible appearance of sensitive rosacea skin.⁴⁵

Adding niacinamide (the amide of vitamin B3) to a moisturizer may provide additional benefits. Niacinamide has been shown to strengthen the epidermal barrier and reduce skin inflammation in several disorders, including rosacea.⁴⁶ A facial moisturizer containing niacinamide was applied on the arms and face of subjects with rosacea. Participants applied the study moisturizer on one arm and used a vehicle cream on the other arm as a control. Instrumental and subjective measurements demonstrated the test moisturizer improved stratum corneum barrier function in the treated arms. There was a parallel improvement in the facial signs of rosacea, leading to the conclusion that niacinamide is a safe and effective additive to moisturizers for those with rosacea.⁴⁷

High-quality moisturizers enhance absorption of topical rosacea prescription therapy. In a split-face study design, the inclusion of a moisturizer in a medical skincare regimen provided more rosacea improvement compared to the same medical regimen without a moisturizer.⁴⁸ There was a significant reduction in facial burning, tingling, and itching on the side of the face treated with the moisturizer. The authors attributed the reduction in irritant symptoms to stratum corneum improvement induced by the moisturizer.⁴⁸

The absorption kinetics of the order of application of topical prescription creams versus application of moisturizers were reported in a 2009 study.⁴⁹ Percutaneous penetration measurements on human skin showed that moisturizers might be applied before or after azelaic acid gel 15%, without affecting

the absorption profile of azelaic acid. An MVE ceramide moisturizing lotion enhanced penetration of azelaic acid when applied prior to the drug.⁴⁹

Sunscreen use is an essential part of rosacea maintenance. Surveys of rosacea patients report more than 80% are negatively impacted by sun exposure.⁸ A tinted sunscreen, designed to protect against UV damage while improving the skin's visible appearance, was studied in rosacea-prone skin.⁵⁰ In patients with normal skin, a single application improved moisturization of the upper epidermis that lasted for 8 hours. One day after use, TEWL was diminished, consistent with an enhanced barrier function. The tinted sunscreen also reduced skin dryness within 30 minutes of the first application. Skin dryness was measured after 3, 8, and 22 days of continuous use, with cumulative improvement relative to baseline. Facial redness improved due to a camouflage effect of tinting in the product. Consistent sunscreen use is essential in rosacea management. Patient satisfaction with a sunscreen product that improves the appearance and skin hydration is more likely to be used consistently.⁵⁰

CONCLUSION

Treatment of rosacea is challenging because multiple factors facilitate disease progression. There is no consistent rosacea treatment protocol for the region of Latin America. Although the expert panel follows ROSCO treatment guidelines, treatment can vary from country to country, depending on local expertise. Studies have demonstrated that disorders of the innate immune system, dysfunction of facial vascular regulation, neurogenic inflammation, elevated levels of *Demodex* mites, and skin barrier destruction are risk factors. Considering the hypersensitivity of the skin in rosacea patients, skin barrier disruption as a predisposing factor is attracting more attention. Carefully selected, consistent skincare can help mitigate damage to the skin barrier. Once rosacea improves with medical therapy, therapeutic moisturizers, cleansers, and sunscreen should be continued to maintain the integrity of the skin.

DISCLOSURES

The authors disclose receipt of an unrestricted educational grant from CeraVe International for support with the research of this work and also received consultancy fees for their work on this project.

REFERENCES

- Alexis AF, Callender VD, Baldwin HE, Desai SR, Rendon MI, Taylor SC. Global epidemiology and clinical spectrum of rosacea, highlighting skin of color: Review and clinical practice experience. *J Am Acad Dermatol*. 2019;80(6):1722-1729.e7. PMID: 30240779. doi: 10.1016/j.jaad.2018.08.049.
- Al-Dabagh A, Davis SA, McMichael AJ, Feldman SR. Rosacea in skin of color: not a rare diagnosis. *Dermatol Online J*. 2014;20(10):13030/qt1mv9r0ss. PMID: 25526008
- Tan J, Almeida LM, Bewley A, et al. Updating the diagnosis, classification, and assessment of rosacea: recommendations from the global ROSacea COnsensus (ROSCO) panel. *Br J Dermatol*. 2017;176(2):431-438. PMID: 27718519. doi: 10.1111/bjd.15122
- Schaller M, Almeida LM, Bewley A, et al. Rosacea treatment update: recommendations from the global ROSacea COnsensus (ROSCO) panel. *Br J Dermatol*. 2017;176(2):465-471. PMID: 27861741. doi: 10.1111/bjd.15173.
- van Zuuren EJ, Fedorowicz Z, Tan J, et al. Interventions for rosacea based on the phenotype approach: an updated systematic review including GRADE assessments. *Br J Dermatol*. 2019;181(1):65-79. PMID: 30585305. PMCID: PMC6850438. doi: 10.1111/bjd.17590.
- van Zuuren EJ. Rosacea. *N Engl J Med*. 2017;377(18):1754-1764. PMID: 29091565. doi: 10.1056/NEJMc1506630.
- Schaller M, Almeida LMC, Bewley A, et al. Recommendations for rosacea diagnosis, classification and management: update from the global ROSacea COnsensus 2019 panel. *Br J Dermatol*. 2020;182(5):1269-1276. PMID: 31392722. PMCID: PMC7317217. doi: 10.1111/bjd.18420.
- New survey pinpoints leading factors that trigger symptoms. National Rosacea Society. Published 2002. Accessed May 4, 2022. <https://www.rosacea.org/rosacea-review/2002/summer/new-survey-pinpoints-leading-factors-that-trigger-symptoms>.
- Halioua B, Cribier B, Frey M, Tan J. Feelings of stigmatization in patients with rosacea. *J Eur Acad Dermatol Venereol*. 2017;31(1):163-168. PMID: 27323701. doi: 10.1111/jdv.13748.
- Aksoy B, Altaykan-Hapa A, Egemen D, Karagöz F, Atakan N. The impact of rosacea on quality of life: effects of demographic and clinical characteristics and various treatment modalities. *Br J Dermatol*. 2010;163(4):719-25. PMID: 20545683. doi: 10.1111/j.1365-2133.2010.09894.x.
- van Zuuren EJ, Fedorowicz Z, Carter B, van der Linden MM, Charland I. Interventions for rosacea. *Cochrane Database Syst Rev*. 2015;4:CD003262. PMID: 25919144. PMCID: PMC6481562. doi: 10.1002/14651858.CD003262.pub5
- Florez-White M. Acne and Rosacea: Special considerations in the treatment of patients with Latin American ancestry. *J Drugs Dermatol*. 2019;18(3):s124-126. PMID: 30909359.
- Rathi SK, Kumrah L. Topical corticosteroid-induced rosacea-like dermatitis: a clinical study of 110 cases. *Indian J Dermatol Venereol Leprol*. 2011;77(1):42-6. PMID: 21220878. doi: 10.4103/0378-6323.74974.
- Rios-Yuil JM, Mercadillo-Perez P. Evaluation of *Demodex folliculorum* as a risk factor for the diagnosis of rosacea in skin biopsies. Mexico's General Hospital (1975-2010). *Indian J Dermatol*. 2013;58(2):157. PMID: 23716816; PMCID: PMC3657226. doi: 10.4103/0019-5154.108069
- Rueda LJ, Motta A, Pabón JG, et al. Epidemiology of rosacea in Colombia. *Int J Dermatol*. 2017;56(5):510-513. PMID: 28239916. doi: 10.1111/ijd.13491.
- Oliveira CMM, Almeida LMC, Bonamigo RR, Lima CWG, Bagatin E. Consensus on the therapeutic management of rosacea - Brazilian Society of Dermatology. *An Bras Dermatol*. 2020;95 (Suppl 1):53-69. PMID: 33172727; PMCID: PMC7772594. doi: 10.1016/j.abd.2020.08.001
- Gutierrez EL, Galarza C, Ramos W, Mendoza M, Smith ME, Ortega-Loayza AG. Influence of climatic factors on the medical attentions of dermatologic diseases in a hospital of Lima, Peru. *An Bras Dermatol*. 2010 Jul-Aug;85(4):461-8. PMID: 20944906. doi: 10.1590/s0365-05962010000400007
- Baldwin H, Alexis AF, Andriessen A, et al. Evidence of barrier deficiency in rosacea and the importance of integrating OTC skincare products into treatment regimens. *J Drugs Dermatol*. 2021;20(4):384-392. PMID: 33852244. doi: 10.36849/JDD.2021.5861
- Addor FA. Skin barrier in rosacea. *An Bras Dermatol*. 2016;91(1):59-63. PMID: 26982780. PMCID: PMC4782648. doi: 10.1590/abd1806-4841.20163541
- Ahn CS, Huang WW. Rosacea Pathogenesis. *Dermatol Clin*. 2018;36(2):81-86. PMID: 29499802. doi: 10.1016/j.det.2017.11.001
- Yamasaki K, Di Nardo A, Bardan A, et al. Increased serine protease activity and cathelicidin promotes skin inflammation in rosacea. *Nat Med*. 2007;13(8):975-80. PMID: 17676051. doi: 10.1038/nm1616
- Forton FMN, De Maertelaer V. Papulopustular rosacea and rosacea-like demodicosis: two phenotypes of the same disease? *J Eur Acad Dermatol Venereol*. 2018;32(6):1011-1016. PMID: 29478301. PMCID: PMC6001808. doi: 10.1111/jdv.14885
- Del Rosso JQ. Topical ivermectin: data supporting dual modes of action in rosacea. *J Clin Aesthet Dermatol*. 2017;10(9):39-42. PMID: 29515751; PMCID: PMC5749619.
- Kircik LH, DuBois J, Draelos ZD, et al. Pivotal trial of the efficacy and safety of oxymetazoline cream 1.0% for the treatment of persistent facial erythema associated with rosacea: findings from the first REVEAL Trial. *J Drugs Dermatol*. 2018;17(1):97-105. PMID: 29320594
- Del Rosso JQ. Topical α -agonist therapy for persistent facial erythema of rosacea and the addition of oxymetazoline to the treatment armamentarium: where are we now? *J Clin Aesthet Dermatol*. 2017;10(7):28-32. PMID: 29104721. PMCID: PMC5605221.
- Fowler J Jr, Jackson M, Moore A, Et al. Efficacy and safety of once-daily topical brimonidine tartrate gel 0.5% for the treatment of moderate to severe facial erythema of rosacea: results of two randomized, double-blind,

- and vehicle-controlled pivotal studies. *J Drugs Dermatol.* 2013;12:650-656. PMID: 23839181
27. Zhang H, Tang K, Wang Y, Fang R, Sun Q. Use of botulinum toxin in treating rosacea: a systematic review. *Clin Cosmet Investig Dermatol.* 2021;14:407-417. PMID: 33958886. PMCID: PMC8096341. doi:10.2147/CCID.S307013.
 28. Kim MJ, Kim JH, Cheon HI, et al. Assessment of skin physiology change and safety after intradermal injections with botulinum toxin: a randomized, double-blind, placebo-controlled, split-face pilot study in rosacea patients with facial erythema. *Dermatol Surg.* 2019;45(9):1155-1162. PMID: 30730346. doi: 10.1097/DSS.0000000000001819.
 29. Scala J, Vojvodic A, Vojvodic P, et al. Botulin toxin use in rosacea and facial flushing treatment. *Open Access Maced J Med Sci.* 2019;7(18):2985-2987. PMID: 31850105; PMCID: PMC6910814. doi: 10.3889/oamjms.2019.784
 30. Taieb A, Ortonne JP, Ruzicka T, et al. Ivermectin Phase III study group. Superiority of ivermectin 1% cream over metronidazole 0.75% cream in treating inflammatory lesions of rosacea: a randomized, investigator-blinded trial. *Br J Dermatol.* 2015;172(4):1103-10. PMID: 25228137. doi: 10.1111/bjd.13408.
 31. Cole PD, Hatf DA, Taylor S, Bullocks JM. Skin care in ethnic populations. *Semin Plast Surg.* 2009;23(3):168-72. PMID: 20676310; PMCID: PMC2884920. doi: 10.1055/s-0029-1224795
 32. Shidian E, Vicaut E, Chidiack H, et al. A randomized-controlled trial of oral low-dose isotretinoin for difficult-to-treat papulopustular rosacea. *J Invest Dermatol.* 2016;136(6):1124-1129. PMID: 26854486. doi: 10.1016/j.jid.2016.01.025.
 33. Battle EF Jr. Cosmetic laser treatments for skin of color: a focus on safety and efficacy. *J Drugs Dermatol.* 2011;10(1):35-8. PMID: 21197520.
 34. Alexis AF. Lasers and light-based therapies in ethnic skin: treatment options and recommendations for Fitzpatrick skin types V and VI. *Br J Dermatol.* 2013;169 Suppl 3:91-97. PMID: 24098905. doi: 10.1111/bjd.12526.
 35. Redman DA. *Ruscus aculeatus* (butcher's broom) as a potential treatment for orthostatic hypotension, with a case report. *J Altern Complement Med.* 2000;6(6):539-549. PMID: 11152059. doi: 10.1089/acm.2000.6.539.
 36. Darlenski R, Kazandjieva J, Tsankov N, Fluhr JW. Acute irritant threshold correlates with barrier function, skin hydration and contact hypersensitivity in atopic dermatitis and rosacea. *Exp Dermatol.* 2013;22(11):752-3. PMID: 24112695. doi: 10.1111/exd.12251.
 37. Ni Raghallaigh S, Powell FC. Epidermal hydration levels in patients with rosacea improve after minocycline therapy. *Br J Dermatol.* 2014;171(2):259-66. PMID: 24354646. doi: 10.1111/bjd.12770.
 38. Medgyesi B, Dajnoki Z, Béke G, et al. Rosacea Is Characterized by a Profoundly Diminished Skin Barrier. *J Invest Dermatol.* 2020;140(10):1938-1950.e5. PMID: 32199994. doi: 10.1016/j.jid.2020.02.025
 39. Tsakok T, Woolf R, Smith CH, Weidinger S, Flohr C. Atopic dermatitis: the skin barrier and beyond. *Br J Dermatol.* 2019;180(3):464-474. PMID: 29969827. doi: 10.1111/bjd.16934.
 40. Huang Yx, Li J, Zhao Zx, et al. Effects of skin care habits on the development of rosacea: A multi-center retrospective case-control survey in Chinese population. *PLoS ONE.* 2020;15(4): e0231078. PMID: 32339170. PMCID: PMC7185582. doi: 10.1371/journal.pone.0231078
 41. Xie H, Xiao X, Li J. Topical steroids in Chinese cosmetics. *JAMA Dermatol.* 2017;153(9):855-856. PMID: 28678994. doi: 10.1001/jamadermatol.2017.1615.
 42. Zhihoun Zuo Z, Wang B, Shen M, et al. Skincare habits, and rosacea in 3,439 Chinese adolescents: A university-based cross-sectional study. *Acta Derm Venereol.* 2020;100(6):adv00081. PMID: 32128599. doi: 10.2340/00015555-3442.
 43. Draelos ZD. The effect of ceramide-containing skin care products on eczema resolution duration. *Cutis.* 2008;81(1):87-91. PMID: 18306855.
 44. Draelos ZD, Baalbaki NH, Raab S, Colón G. The effect of a ceramide-containing product on stratum corneum lipid levels in dry legs. *J Drugs Dermatol.* 2020;19(4):372-376. PMID: 32272513. doi: 10.36849/JDD.2020.4796
 45. Santoro F, Teissedre S. A novel night moisturizer enhances cutaneous barrier function in dry skin and improves dermatological outcomes in rosacea-prone skin. *J Clin Aesthet Dermatol.* 2018;11(12):11-17. PMID: 30666273. PMCID: PMC6334838.
 46. Gehring W. Nicotinic acid/niacinamide and the skin. *J Cosmet Dermatol.* 2004;3(2):88-93. PMID: 17147561. doi: 10.1111/j.1473-2130.2004.00115.x.
 47. Draelos ZD, Ertel K, Berge C. Niacinamide-containing facial moisturizer improves skin barrier and benefits subjects with rosacea. *Cutis.* 2005;76(2):135-41. PMID: 16209160.
 48. Del Rosso JQ. The use of moisturizers as an integral component of topical therapy for rosacea: clinical results based on the Assessment of Skin Characteristics Study. *Cutis.* 2009;84(2):72-6. PMID: 19746764.
 49. Del Rosso JQ, Lehman PA, Raney SG. Impact of order of application of moisturizers on percutaneous absorption kinetics: evaluation of sequential application of moisturizer lotions and azelaic acid gel 15% using a human skin model. *Cutis.* 2009;83(3):119-124. PMID: 19363903.
 50. Baldwin H, Santoro F, Lachmann N, Teissedre S. A novel moisturizer with high sun protection factor improves cutaneous barrier function and the visible appearance of rosacea-prone skin. *J Cosmet Dermatol.* 2019;18(6):1686-1692. PMID: 30803131. PMCID: PMC6916358 doi: 10.1111/jocd.12889

AUTHOR CORRESPONDENCE

Anneke Andriessen PhD

E-mail:..... anneke.a@tiscali.nl