REVIEW ARTICLE

Regional Challenges and Opportunities with Rosacea Management in the Middle East

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ABSTRACT

Rosacea is a chronic inflammatory skin disorder most commonly noted in people of northern European origin. However, while data on the prevalence of rosacea in the Middle East are scarce, individuals of various ethnic groups, including darker-skinned types, are afflicted. A panel of Middle East dermatology experts convened to review current practices in the management of rosacea in the Middle East region. This article aims to address unmet needs, and discuss regional considerations and latest treatment options that could lead to improved outcome in patients affected by this skin disease in the region.

KEY WORDS: Rosacea, inflammatory, erythema, Middle East, exacerbating factors, trigger

INTRODUCTION

Rosacea is a chronic inflammatory skin disease characterized by flushing, erythema, papules, pustules, and telangiectasia. Its manifestations are physical, predominantly affecting the face, but it can lead to psychological problems such as depression, anxiety, low self-esteem, and social stigma.[1,2]

In May 2017, a group of dermatologists from the Middle East, led by an international expert in the field of rosacea, met in Abu Dhabi, UAE to discuss rosacea management in the region. The goal was to allow the panel of experts, who also authored this paper, to understand current diagnosis and treatment practices across the region, identify unmet needs, and address regional specificity. The picture of rosacea prevalence in the Middle East is unclear because of a lack of epidemiological studies. Limited disease awareness and a significant proportion of the population with dark skin phototype might result in patients with rosacea being undiagnosed or misdiagnosed. For those who receive treatment, the impact of the disease on their quality of life might be underestimated by their physician. The authors also highlighted that achieving marked improvement of persistent and recurrent facial erythema is a key challenge in these patients. When managing rosacea, proper consideration should be given to region-specific lifestyle habits, educational

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needs, and available treatment options.

Epidemiology and pathophysiology

As with the Middle East, there is still very little known about the epidemiology of rosacea worldwide. Methodological differences seem partially to explain the wide-ranging prevalence statistics from around the world, estimated to be from less than 1% to 22% of the adult population.[3] The relatively fragmentary prevalence data available show that it predominates in women and disproportionately affects fair-skinned individuals of northern European origin between 20 and 50 years of age.[3,4] People with darker skin types are also afflicted by rosacea, although the true prevalence in this population has not been established, and may go undiagnosed due to their different skin pigmentation.[5] A study by Al-Hoqail[6] that looked at common dermatological conditions of patients attending dermatological consultations in Saudi Arabia found an overall prevalence of 1.59% for rosacea. In 2000, Tomb and Nassar[7] published observational data from a hospital in Lebanon where rosacea was present in 5% of subjects.

A better understanding of the mechanisms responsible for rosacea can help further the development of targeted and effective treatment. Its pathogenesis is complex and involves dysregulation in cutaneous neurovascular control as well as innate and probably adaptive immunity. Blushing, the sine qua non of rosacea, is a neurally mediated function. The activation of neuronal transient receptor potential ion channels mediates blood flow and inflammation.[8,9] Vasodilation is more pronounced and more persistent in individuals with rosacea and can be triggered by a variety of stimuli such as food, medication, high environmental temperatures, emotional stress, and exercise. Inflammation damages the skin barrier, which can result in enhanced irritability and a cycle of flares of disease.[10] Recent observations also suggest involvement of an altered innate immune response. Individuals with the disease express abnormally high levels of epidermal cathelicidins, an antimicrobial peptide and immunomodulator with both vasoactive and inflammatory effects.[11] Furthermore, this abnormal immune response in rosacea may induce elevated levels of kallikrein[5], a trypsin-like serine protease responsible for the cleavage and activation of cathelicidins.[12]

Diagnosis and Management

The classification of the National Rosacea Society (NRS), which groups the most common presentations in four main subtypes (erythematotelangiectatic, papulopustular, phymatous, ocular), remains the primary reference for Middle Eastern dermatologists when evaluating individuals with rosacea (Table 1).[13] Their diagnosis relies

Table 1 National Rosacea Society subtype classification of rosacea

Subtype	Characteristics
I. Erythemato-telangiectatic	Flushing and persistent central facial erythema with or without telangiectasia.
II. Papulopustular	Persistent central facial erythema with transient, central facial papules or pustules or both.
III. Phymatous	Thickening skin, irregular surface nodularities and enlargement. May occur on the nose, chin, forehead, cheeks, or ears.
IV. Ocular	Foreign body sensation in the eye, burning or stinging, dryness, itching, ocular photosensitivity, blurred vision, telangiectasia of the sclera or other parts of the eye, or periorbital edema.

Adapted from *Standard classification of rosacea: Report of the National Rosacea Society Expert Committee on the Classification and Staging of Rosacea*[13]

on findings from careful review of the patient history and thorough clinical examination. The selected treatment approach is driven by subtype classification, severity of symptoms, and treatment availability, which varies by country.

Erythematotelangiectatic rosacea (ETR)

ETR is treated using vascular lasers, intense pulse light (IPL) and electrocoagulation. Systemic vasoconstrictors, more specifically beta-blockers, have been reported to successfully treat refractory flushing and persistent erythema of rosacea but are not commonly used by dermatologists in the region (except in Lebanon where clonidine has been part of rosacea management).[14,15] Depending on country-specific availability, a new FDA-approved topical alpha-adrenergic agonist, brimonidine, has become part of the treatments for ETR. Brimonidine causes vasoconstriction of facial blood vessels, which are abnormally dilated in rosacea, and has proven effective in rapidly reducing facial erythema.[16-19] Topical metronidazole formulations are also prescribed. Studies have shown modest efficacy in treating erythema of rosacea.[20,21]

Papulopustular Rosacea (PPR)

In the region, combination therapy with topical and systemic agents is the most common treatment for PPR. Topical azelaic acid, ivermectin, and metronidazole are generally considered as first-line treatment. Benzoyl peroxide and crotamiton may also be prescribed.[22] Ivermectin, a FDA-approved and newly registered treatment in the Middle East, is a macrocyclic lactone derivative with anti-inflammatory and anti-parasitic properties. In two randomized, double-blind, vehicle-controlled pivotal studies of patients with moderate to severe PPR, ivermectin significantly reduced the number of inflammatory lesions and provided superior and continuous improvement as measured by the Investigator's Global Assessment (IGA) of rosacea severity.[23] Our group of experts has limited experience with ivermectin as it was only recently launched onto Middle Eastern markets.

Frequently, topical agents are combined with subantimicrobial doses of oral doxycycline. Studies demonstrated equivalent efficacy of anti-inflammatory vs. antimicrobial doses of this second-generation tetracycline.[24,25] Isotretinoin is also prescribed for severe cases of PPR given its documented efficacy in these patients - although its use in women should be closely supervised given its teratogenicity.[26]

Phymatous Rosacea (PR) and Ocular Rosacea (OR)

Mild to moderate cases of PR can be treated pharmacologically but more severe or advanced cases require surgical intervention or ablative laser therapy. Typically, a combination of topical retinoids and oral doxycycline is prescribed in the early stage of the manifestations. Through its anti-inflammatory effect, isotretinoin has been shown to delay or halt the development of rhinophyma.[25,27,28]

In our region, the majority of management strategies for OR aim at relieving ocular discomfort and preventing symptoms progression. This is achieved through lid hygiene, the use of topical immunomodulators applied to the eyelid, and artificial tears. More serious affectations are usually treated systemically with low-dose oral doxycycline.[22] Severe cases of OR are referred to an ophthalmologist to prevent complications.

Recently, the global ROSacea COnsensus (ROSCO) panel proposed an update of the diagnosis, classification, and assessment of rosacea to be based on phenotypes rather than subtypes.[29] This recommendation stems from the reality of overlapping rosacea features across subtypes, often requiring combined therapy. The international expert panel recommended an approach for diagnosis and classification of rosacea based on the presenting features, optimizing individualized rosacea management and enabling physicians to take a more sign/symptom-led approach to addressing patient needs. Our experts' discussion on current practice patterns in the Middle East suggests an increasing trend toward this approach. Regardless of the rosacea subtype, there is consensus amongst the group of experts that environmental and lifestyle triggers should be identified and eliminated, a defective skin barrier should be repaired through appropriate skin care, and sun damage should be prevented.

Regional considerations for Middle East populations

In discussion, the panel of experts identified key opportunities to improve the management of rosacea in the region. Epidemiological studies on rosacea in the Middle East are lacking and needed. Accurate understanding of the disease prevalence could help to raise awareness with patients and physicians, as well as support the development of regional healthcare policies and practice guidelines. The group estimates that a significant number of patients with rosacea are misdiagnosed - leading to inappropriate treatment and poor outcome. Given the increasingly diverse population of Middle Eastern countries, the evaluation of patients who present with morphological features akin to rosacea should take into consideration their skin phototype. Rosacea has been reported in people with dark skin.[30,31] However the clinical presentation may differ from that of fair-skinned individuals and a low index of suspicion can make it difficult to diagnose. Physicians should ask patients with darker skin types about subtle skin changes. The panel of experts suggest the development of a region-specific modified subtype classification that would better reflect Middle East populations.

Educational needs about rosacea abound in the region. Physicians should be trained on appropriately diagnosing and managing the disease. The psychological impact of rosacea and the reduced quality of life (QoL) associated with it are well documented but often overlooked.[32] They should be acknowledged and understood by healthcare practitioners. Effective treatment of rosacea symptoms has been shown to positively correlate with patient QoL.[33] The rosacea-specific quality of life score (ROSaQoL) was developed to provide a quantitative measure of the disease burden and help physician assess patient-reported treatment impact over time.[34]

Educating patients about the disease is essential to help them manage expectations. Rosacea is a chronic inflammatory skin condition that cannot be cured but can be treated effectively.[35,36] Patient counseling regarding the long-term nature of rosacea treatment and the results that can be expected from the various therapeutic approaches is paramount.[21] Patients should be encouraged to take an active role in managing their condition by learning about triggering or exacerbating factors, using sunscreen, and monitoring their symptoms. The panel of experts suggest that online resources should be made available

to answer rosacea questions of Middle Eastern patients.

It is understood that first-line treatment of rosacea includes avoidance of potential triggers.[21,22] Those are individually variable and what might cause an exacerbation in one patient may have no effect on another. Based on their observations, the panel of experts noted exacerbating factors with stronger predominance in the Middle East.

Heat

The basic climate in the Middle East is warm with temperatures reaching scorching levels during the summer months. Heat has long been recognized as rosacea trigger.[32,35-37] During a National Rosacea Society survey of 431 patients with rosacea, 80% of respondents said hot weather and sun exposure aggravated their condition.[37] A study by Metzler-Wilson et al.[38] showed that patients with rosacea have heightened sympathetic nerve activity when exposed to heat and stress, contributing to rosacea symptomatology. Patients with rosacea who live in the Middle East should minimize time spent outdoors on hot days and use adequate skin protection.

Food

Foods are common triggers of rosacea. Pickled, fermented, spicy, and thermally hot foods and beverages are known to exacerbate the disease in some individuals.[21] The Middle East is home to a diverse population eating a wide range of diets, such as Western, Middle Eastern, Indian, and Asian. The panel of experts suggested the development of a list of dietary triggers that reflects the nutrition patterns of the region.

Alcohol and cigarettes

Alcohol is consumed in some parts of the Middle East and has been reported by patients with rosacea as trigger of flare-ups. Anecdotally, red wine, which contains histamine as byproduct of bacterial fermentation, is most often identified as the culprit.[39,40] While alcohol seems to contribute to rosacea symptoms exacerbation, the epidemiologic association between alcohol and the disease is unclear. A large epidemiological study and dermatology database analysis previously showed marginal to no association between alcohol and the risk of rosacea.[41,42] However a more recent cohort study of 82,737 women found that alcohol intake is associated with an increased risk of developing rosacea in this population. White wine and liquor were the types of alcoholic beverages with the strongest association.[43]

Cigarette and waterpipe smoking has reached epidemic level in the Middle East, where about half of the male population smokes daily, and growing use of waterpipe tobacco among youth is well documented.[44,45] In a study of 60,042 rosacea cases, the risk of developing rosacea was significantly reduced among current smokers.[42] Potential explanations include cigarette's effect on vasodilation and microcirculation, resulting in altered blood flow and perfusion.[46,47] Additionally, nicotine has been shown to have anti-inflammatory properties in the skin.[48-50] The experts agreed that these findings should not prevent smoking cessation efforts in rosacea patients.

Steroid-induced rosacea

In our discussion, we noted that we often encounter patients with steroid-induced rosacea following the use of skin bleaching products - a popular trend in the Middle East. Severe local and systemic consequences of skin-lightening cosmetics containing corticosteroids have been reported.[51] In other instances, topical corticosteroids are used for their powerful and immediate

effect. Educating patients about the misuse of these topical agents and their adverse effects is paramount.

CONCLUSION

This article has summarized the discussion of a panel of dermatology experts on the management of rosacea in the Middle East. Disease prevalence, both worldwide and in the region, is unclear, and regional epidemiological studies are needed. In general, current practice patterns across the region are aligned with the National Rosacea Society subtype classification and recommendations, but the group noted a trend toward a symptom-led approach aimed at a more individualized treatment. In order to address the multiple features of rosacea, combined therapy, topical and systemic, is often prescribed. Topical treatments that were recently launched onto the Middle East market (ivermectin and brimonidine) are promising for the effective management of rosacea. Our panel noted the importance of addressing region-specific determinants such as the educational needs of patients and physicians, and common triggering or exacerbating factors.

DISCLOSURES

Dr Guy Webster consults for Allergan, Galderma, and Cutanea. Drs Meshal Alghareeb, Fahad Almutawa, Amal Elardi, Salah Al Rubaie, and Roland Tomb have no disclosure.

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