

Devices and Topical Agents for Rosacea Management

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Practice Points

- Rosacea patients should be advised on appropriate skin care.
- Purpuric settings of the pulsed dye laser may be more effective in treating rosacea-associated erythema.
- Topical brimonidine tartrate can control facial erythema, but patients should be warned of the potential risk for rebound erythema.

Rosacea is a chronic inflammatory disease that predominantly affects facial skin in light-skinned individuals and can be divided into 4 subtypes. Patients can display signs of more than 1 subtype. Diffuse facial erythema is a common finding in rosacea patients and can lead to persistent erythema. Although there is no cure for rosacea, reduction of signs and symptoms can be achieved via various treatment modalities. This article reviews devices and topical agents currently available for the management of rosacea.

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Rosacea is a common chronic inflammatory disease that typically affects centropacial skin, particularly the convexities of the forehead, nose, cheeks, and chin. Occasionally, involvement of the scalp, neck, or upper trunk can occur.¹ Rosacea is more common in light-skinned individuals and has been called the “curse of the Celts,”² but it also

can affect Asian individuals and patients of African descent. Although rosacea affects women more frequently, men are more likely to develop severe disease with complications such as rhinophyma. Diagnosis is made on clinical grounds, and histologic confirmation rarely is necessary.

Despite its high incidence and recent advances, the pathogenesis of rosacea is still poorly understood. A combination of factors, such as aberrations in innate immunity,³ neurovascular dysregulation, dilated blood and lymphatic vessels, and a possible genetic predisposition seem to be involved.⁴ Presence of commensal *Demodex folliculorum* mites may be a contributing factor for papulopustular disease.

Patients can present with a range of clinical features, such as transient or persistent facial erythema, telangiectasia, papules, pustules, edema, thickening, plaque formation, and ocular manifestations. Associated burning and stinging also may occur. Rosacea-related erythema (eg, lesional and perilesional erythema) can be caused by inflammatory lesions or can present independent of lesions in the case of diffuse facial erythema. Due to the diversity of clinical signs and limited knowledge regarding its etiology, rosacea is best regarded as a syndrome and has been classified into 4 subtypes—erythematotelangiectatic, papulopustular, phymatous, and ocular—and 1 variant (granulomatous rosacea).⁵ The most common phymatous changes affect the nose, with hypertrophy and lymphedema of subcutaneous tissues. Other sites that can be affected are the ears, forehead, and chin. Ocular manifestations affect approximately

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50% of rosacea patients,⁶ ranging from conjunctivitis and blepharitis to keratitis and corneal ulceration, thereby requiring ophthalmologic assessment.

Because rosacea affects facial appearance, it can have a devastating impact on the patient's quality of life, leading to social isolation. Although there is no cure available for rosacea, lifestyle modification and treatment can reduce or control its features, which tend to exacerbate and remit. There are a number of possible triggers for rosacea that ideally should be avoided such as sun exposure, hot or cold weather, heavy exercise, emotional stress, and consumption of alcohol and spicy foods. It is essential to consider disease subtype as well as the signs and symptoms presenting in each individual patient when approaching therapy selection. Most well-established US Food and Drug Administration (FDA)-approved treatments of rosacea target the papulopustular aspect of disease, including the erythema associated with the lesions. These treatments include topical and systemic antibiotics and azelaic acid. Non-FDA-approved agents such as topical and systemic retinoids, topical calcineurin inhibitors, and topical benzoyl peroxide also are used, though there is limited evidence of their efficacy.⁷

Management options for diffuse facial erythema and telangiectasia, however, are limited. Standard rosacea treatments often are not efficacious in treating these aspects of the disease, thereby requiring an alternative approach. This article reviews devices and topical agents currently available for the management of rosacea.

Skin Care

The skin of rosacea patients often is sensitive and prone to irritation; therefore, a good skin care regimen is an integral part of disease management and should include a gentle cleanser, moisturizer, and sunscreen.⁸ Lipid-free liquid cleansers or synthetic detergent (syndet) cleansers with a neutral to slightly acidic pH (ie, similar to the pH of normal skin) are ideal.⁹ Following cleansing, the skin should be gently dried. It may be beneficial to wait up to 30 minutes before application of a moisturizer to avoid irritation. Hydrating moisturizers should be free of irritants or abrasives, allowing maintenance of stratum corneum pH in an acid range of 4 to 6. Green-tinted makeup can be a useful tool in covering areas of erythema.

Devices

A variety of devices targeting hemoglobin are reported to be effective for the management of erythema and telangiectasia in rosacea patients, including the 595-nm pulsed dye laser (PDL), the potassium titanyl

phosphate (KTP) laser, the 1064-nm Nd:YAG laser, and noncoherent intense pulsed light (IPL) sources.

The major chromophore in blood vessels is oxyhemoglobin, with 2 major absorption bands in the visible light spectrum at 542 and 577 nm. There also is notable albeit lesser absorption in the near-infrared range from 700 to 1100 nm.¹⁰ Following absorption by oxyhemoglobin, light energy is converted to thermal energy, which diffuses in the blood vessel causing photocoagulation, mechanical injury, and finally thrombosis.

Pulsed Dye Laser (585–595 nm)—Among the vascular lasers, the PDL has a long safety record. It was the first laser that used the concept of selective photothermolysis for treatment of vascular lesions.^{11,12} The first PDLs had a wavelength of 577 nm, while current PDLs have wavelengths of 585 or 595 nm with longer pulse durations and circular or oval spot sizes that are ideal for treatment of dermal vessels. The main disadvantage of PDLs is the development of posttreatment purpura. The longer pulse durations of KTP lasers avoid damage to cutaneous vasculature and eliminate the risk for bruising. Nonetheless, the wavelength of the PDL provides a greater depth of penetration due to its substantial absorption by cutaneous vasculature compared to the shorter wavelength of the KTP laser.

Although newer-generation PDLs still have the potential to cause purpura, various attempts have been made to minimize this risk, such as the use of longer pulse durations, multiple minipulses or “pulse-lets,”¹³ and multiple passes. Separate parameters may need to be used when treating linear vessels and diffuse erythema, with longer pulse durations required for larger vessels. The Figure shows a rosacea patient with facial telangiectasia before and after 1 treatment with a PDL.

According to Alam et al,¹⁴ purpuric settings were more efficacious in a comparison of variable-pulsed PDLs for facial telangiectasia. In 82% (9/11) of cases, greater reduction in telangiectasia density was noted on the side of the face that had been treated with purpuric settings versus the other side of the face.¹⁴ Purpuric settings are particularly effective in treating larger vessels, while finer telangiectatic vessels may respond to purpura-free settings.

In a study of 12 participants treated with a 595-nm PDL at a pulse duration of 6 ms and fluences from 7 to 9 J/cm², no lasting purpura was seen; however, while 9 participants achieved more than 25% improvement after a single treatment, only 2 participants achieved more than 75% improvement.¹⁵ Nonetheless, some patients may prefer this potentially less effective treatment method to avoid the socially embarrassing side effect of purpura.



Facial telangiectasia in a rosacea patient before (A) and after 1 treatment with a pulsed dye laser (B).

In a study of 12 rosacea patients, a 75% reduction in telangiectasia scores was noted after a mean of 3 treatments with the 585-nm PDL using 450- μ s pulse durations. Purpura occurred in all patients.¹⁶ In another study by Madan and Ferguson,¹⁷ 18 participants with nasal telangiectasia that had been resistant to the traditional round spot, 595-nm PDL and/or 532-nm KTP laser were treated with a 3 \times 10-mm elliptical spot, ultra-long pulse, 595-nm PDL with a 40-ms pulse duration and double passes. Complete clearance was seen in 10 (55.6%) participants and 8 (44.4%) showed more than 80% improvement. No purpura was associated with the treatment.¹⁷

Further studies comparing the efficacy of nonpurpuric and purpuric settings in the same patient would allow us to determine the most effective option for future treatment.

KTP Laser (532 nm)—Potassium titanyl phosphate lasers have the disadvantage of higher melanin absorption, which can lead to epidermal damage with postinflammatory hyperpigmentation. Their use is limited to lighter skin types. Because of its shorter wavelength, the KTP laser is best used to treat superficial telangiectasia. The absence of post-treatment purpura can make KTP lasers a popular alternative to PDLs.¹⁷ Uebelhoefer et al¹⁸ performed a split-face study in 15 participants to compare the 595-nm PDL and 532-nm KTP laser. Although both treatments were effective, the KTP laser achieved 62% clearance after the first treatment and 85% clearance 3 weeks after the third treatment compared to 49% and 75%, respectively, for the PDL. Interestingly, the degree of swelling and erythema posttreatment were greater on the KTP laser-treated side.¹⁸

Nd:YAG (1064 nm)—The wavelength of the Nd:YAG laser targets the lower absorption peak of oxyhemoglobin. In a study of 15 participants with facial telangiectasia who were treated with a 1064-nm Nd:YAG laser at day 0 and day 30 using a

3-mm spot size, a fluence of 120 to 170 J/cm², and 5- to 40-ms pulse durations, 73% (11/15) showed moderate to significant improvement at day 0 and day 30 and 80% improvement at 3 months' follow-up.¹⁹ In a split-face study of 14 patients, treatment with the 595-nm PDL with a fluence of 7.5 J/cm², pulse duration of 6 ms, and spot size of 10 mm was compared with the 1064-nm Nd:YAG laser with a fluence of 6 J/cm², pulse duration of 0.3 ms, and spot size of 8 mm.²⁰ Erythema improved by 6.4% from baseline on the side treated with the PDL. Although participants rated the Nd:YAG laser treatment as less painful, they were more satisfied with the results of the PDL treatment.²⁰ In another split-face study comparing the 595-nm PDL and 1064-nm Nd:YAG laser, greater improvement was reported with the Nd:YAG laser, though the results were not statistically significant.²¹

Intense Pulsed Light—While lasers use selective photothermolysis, IPL devices emit noncoherent light at a wavelength of 500 to 1200 nm. Cutoff filters allow for selective tissue damage depending on the absorption spectra of the tissue. Longer wavelengths are effective for the treatment of deeper vessels, while shorter wavelengths target more superficial vessels; however, the shorter wavelengths can interact with melanin and should be avoided in darker skin types. In a phase 3 open trial, 34 participants were treated with IPL with a 560-nm cutoff filter and fluences of 24 to 32 J/cm². The mean reduction of erythema following 4 treatments was 39% on the cheeks and 22% on the chin; side effects were minimal.²²

Photodynamic Therapy

Photodynamic therapy is an effective and widely used treatment method for a number of skin conditions. Following its success in the treatment of acne, it also has been used in the management of rosacea, though the exact mechanism of action remains unclear.

Photodynamic therapy involves topical application of a photosensitizing agent (eg, 5-aminolevulinic acid, methyl aminolevulinic acid [MAL]) followed by exposure to red or blue light. The photosensitizing agent accumulates semiselectively in abnormal skin tissue and is converted to protoporphyrin IX, which induces a toxic skin reaction through reactive oxygen radicals in the presence of visible light.²³ Photodynamic therapy generally is well tolerated. The primary side effects are pain, burning, and stinging.

In 3 of 4 (75%) patients treated with MAL and red light, rosacea clearance was noted after 2 to 3 sessions. Remission lasted for 3 months in 2 (66.7%) participants and for 9 months in 1 (33.3%) participant.²⁴ In another study, 17 patients were treated with MAL and red light. Results were good in 10 participants (58.8%), fair in 4 (23.5%), and poor in 3 (17.6%).²³

α -Adrenergic Receptor Agonists

Recently, the α -adrenergic receptor agonists brimonidine tartrate and oxymetazoline have been found to be effective in controlling diffuse facial erythema of rosacea, which is thought to arise from vasomotor instability and abnormal vasodilation of the superficial cutaneous vasculature. Brimonidine tartrate is a potent α_2 -agonist that is mainly used for treatment of open-angle glaucoma. In 2 phase 3 controlled studies, once-daily application of brimonidine tartrate gel 0.5% was found to be effective and safe in reducing the erythema of rosacea.²⁵ Brimonidine tartrate gel is the first FDA-approved treatment of facial erythema associated with rosacea. Possible side effects are erythema worse than baseline (4%), flushing (3%), and burning (2%).²⁶ Oxymetazoline is a potent α_1 - and partial α_2 -agonist that is available as a nasal decongestant. Oxymetazoline solution 0.05% used once daily has been shown in case reports to reduce rosacea-associated erythema for several hours.²⁷

Nicotinamide

Nicotinamide is the amide form of niacin, which has both anti-inflammatory properties and a stabilizing effect on epidermal barrier function.²⁸ Although topical application of nicotinamide has been used in the treatment of inflammatory dermatoses such as rosacea,^{28,29} niacin can lead to cutaneous vasodilation and thus flushing. It has been hypothesized to potentially enhance the effect of PDL if used as pretreatment for rosacea-associated erythema.³⁰

Conclusion

Rosacea can have a substantial impact on patient quality of life. Recent advances in treatment options and rapidly advancing knowledge of laser therapy are providing dermatologists with powerful tools for rosacea clearance. Lasers and IPL are effective treatments of the erythematotelangiectatic aspect of the disease, and careful selection of devices and treatment parameters can reduce unwanted side effects.

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