

Clinical Review:

Acne and Rosacea

Acne and Rosacea Review Part 2

Rosacea is a common dermatological disorder affecting approximately 10% of the population, with a disproportionate number of those patients being fair-skinned and of the female sex. It is typically divided into four subtypes characterized by symptoms such as flushing and persistent redness, papules, skin thickening, and nose enlargement, or ocular rosacea causing dry eye and corneal damage. This review will focus on topical management of rosacea subtypes that present with skin changes.¹ The pathophysiology of rosacea has not been fully elucidated, though changes in the immune, nervous, and vascular systems are often noted in patients. Some theories suggest that microbes often found on the skin including *Demodex* mites or *Staphylococcus epidermis* may play a precipitating role in the onset of rosacea.²

Common agents for topical treatment of rosacea include metronidazole, sodium sulfacetamide, sulfur/sodium sulfacetamide combinations, azelaic acid, ivermectin, topical retinoids, permethrin, topical calcineurin inhibitors, and cromolyn sodium. Other agents such as alpha-adrenergic receptor antagonists and nonselective beta-blockers are also occasionally used to manage flushing symptoms.

Metronidazole 0.75-1% is commonly used in the management of rosacea. It is beneficial in reducing reactive oxygen species production and has been demonstrated to reduce erythema, papules, and pustules. Though generally well tolerated, irritation and dermatitis are sometimes observed.¹ One study of patients treated with 0.75% or 1% metronidazole once or twice daily over 7 to 12 weeks noted a significant reduction in the number of papules and pustules during the treatment period with most effects observed within the first three weeks. The preparation was well tolerated with less than 2% of patients reporting stinging, dryness, burning, or itching. No systemic adverse effects were reported.³ Another study of metronidazole 0.75% gel applied twice daily noted that continued treatment was successful for the majority of patients in inducing and retaining remission.⁴

Sodium sulfacetamide, typically used at 10%, is another common treatment for rosacea. It is sometimes combined with sulfur 5% and commercially available preparations in foams are currently on the market.⁵ Sodium sulfacetamide works by inhibiting para-aminobenzoic acid thus inhibiting bacterial synthesis of folic acid and acting as a bacteriostatic agent.⁷ Sulfur also has antifungal and antibacterial activity that contribute to the benefit of combination products. However, sulfur has a distinct odor and is sometimes not included for this reason. One placebo-controlled trial spanning eight weeks found that sodium sulfacetamide and sulfur combination applied twice daily produced a significant decrease in inflammatory lesions and erythema as compared to placebo.⁶

Azelaic acid between 15-20% is also present in many rosacea compounds. Azelaic acid decreases inflammation by inhibiting the expression of two inflammatory markers that often play a role in the inflammatory cascade in rosacea.⁸ One study of 15% azelaic acid applied once daily for 15 weeks demonstrated significant improvement in the number of lesions and erythema in patients with mild to moderate rosacea.⁹ Other studies looking at twice-daily use of 15% gel also saw significant benefits as

compared to placebo.¹⁰ Adverse effects are generally local and include irritation, dryness, and transient stinging or burning.¹

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One of two anti-parasitic ingredients commonly seen for this indication is ivermectin 1%. Ivermectin kills *Demodex* mites that are sometimes implicated in precipitating rosacea, additionally, it appears to have some anti-inflammatory effects. Trials of ivermectin 1% have demonstrated significant benefits. One trial of ivermectin 1% applied topically once daily vs metronidazole 0.75% applied twice daily found ivermectin to be more effective at reducing and maintaining remission at 12 and 36 week time points.^{11,12} The second commonly used antiparasitic is permethrin 5%. More commonly known for the treatment of lice, fleas, and ticks, permethrin also has activity against *Demodex* mites. One study of permethrin 5% cream applied twice daily for two months compared to metronidazole 0.75% and a placebo arm found permethrin more efficacious than both at eliminating *Demodex* mites and equally effective as metronidazole at reducing erythema and papules.¹³

Tretinoin is another agent used for rosacea, though its mechanism here has not been fully elucidated. It has been hypothesized that tretinoin and other retinoids can reduce rosacea symptoms by reducing the effects of ultraviolet radiation which often exacerbates rosacea. One study of tretinoin 0.025% cream compared to 10mg/day oral isotretinoin found a significant reduction in the number of papules, pustules, and amount of erythema with both treatments. Oral isotretinoin produced more rapid benefits, but both groups were equal at 16 weeks.¹⁴ Another study of combined clindamycin phosphate 1.2% and tretinoin 0.025% gel found it efficacious for papulopustular and telangiectatic rosacea (fine blood vessels apparent on the surface of the skin).¹⁵ Other retinoids such as adapalene have also demonstrated benefit. One study of adapalene 0.1% vs metronidazole 0.75% found a statistically significant reduction in the number of inflammatory lesions in the adapalene group as compared to metronidazole group for 12 weeks with no difference being seen between the two groups in erythema or telangiectasia scores.¹⁶

Calcineurin inhibitors such as tacrolimus are sometimes used for particular types of rosacea. One study of tacrolimus ointment 0.075% twice daily found that it was beneficial for patients with steroid-induced rosacea.¹⁷ Another study of 0.1% ointment applied for 12 weeks found significantly improved erythema, but no decrease in the number of papulopustular lesions.¹⁸

Lastly, one emerging agent for the treatment of rosacea is cromolyn sodium. One placebo-controlled study spanning 8 weeks evaluated cromolyn sodium 4% applied twice daily and found that facial erythema was significantly decreased in the cromolyn group. It is proposed that this effect is due to decreased mast cells. Cromolyn sodium inhibits mediators of inflammation including the release of antigens from mast cells. This treatment is still emerging, but initial data is promising.¹⁹

Rosacea is a multimodal condition and symptoms can vary widely from patient to patient. Compounding pharmacists play an important role with combination treatments and medications tailored to what works for a specific patient and their skin. Head to the Fagron Academy site to check out our formula options for rosacea and to learn more about Cleoderm™, our new non-comedogenic cream base specifically designed for cosmeceutical care!

Sources:

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The matters discussed herein are for informational purposes only and not intended for the purpose of providing legal advice. You should consult your attorney in case of any questions as to when it is appropriate to compound or regarding any other particular issue discussed or referenced in this document.

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