

The Value of Combination Therapy for the Treatment of Rosacea

The treatment of rosacea continues to evolve as the dermatology community gains a better understanding of the drivers of this chronic disease.

Instead of a broad, overarching approach, clinicians are now able to incorporate specific therapeutic combinations that target individualized symptom profiles.

In this conversation, two experts in the management of rosacea share their insights into effective treatment strategies and ways to overcome common barriers to therapy.

James Del Rosso, DO: Rosacea is recognized as a common inflammatory skin disease that can be addressed with a variety of different treatment options. It has only been recently, however, that we've gained a better understanding of the pathophysiology of the disease, allowing us to combine treatment that correlates with some of its clinical manifestations.

Dr. Fromowitz, why do you think it's taken so long for our community to embrace combination treatment for rosacea?

Jeffrey Fromowitz, MD: When we think about the pathogenesis of acne—a condition for which we've used combination therapy for many years—there are a number of factors we are familiar with, including follicular hyperkeratinization, excess *Propionibacterium acnes*, inflammation, and increased sebum levels. With rosacea, we're learning that it's a

multimodal condition. It not only involves dysregulation of the immune system and general inflammation but also external drivers such as food, ultraviolet light, stress, exercise and Demodex colonization that may contribute to its development. Better understanding of the drivers of rosacea has helped us understand that combination therapy may be our best approach to treatment.

Dr. Del Rosso: The facial redness associated with rosacea may be due to a variety of different factors. Transepidermal water loss and what I call "rosacea dermatitis" can create some redness. There also may be vasodilation from persistent flushing episodes that leads to persistent facial erythema. Finally, some patients present with papulopustules surrounded by significant redness.

What this means is that we're slowly moving into an era in which we are able to utilize specific treatment combinations to target the different symptoms of rosacea.

Let's start our conversation with the treatment of persistent facial erythema. We have several current options, including alpha-2 agonists and intense pulsed light therapy. Which have you found to be the most successful in your practice?

Dr. Fromowitz: The first step in treating patients with rosacea is to improve their barrier function. My go-to agents include subantimi-

crobial-dose doxycycline, topical azelaic acid in the morning, and topical ivermectin in the evening. That combination tends to be effective in minimizing papules and pustules, as well as quieting down some of the inflammation and perilesional erythema that is often present.

Once the patient's skin has calmed down, that's when I will begin to address their background redness. I tend to lean more toward devices versus topical agents in patients with persistent, nondilation-induced background redness once their flaring has quieted down. I have found that these patients will often have a good response to a 595-nm pulsed dye or 532-nm potassium-titanyl-phosphate (KTP) laser. On the flip side, for patients with inducible erythema, alpha-2 agonists can be a great solution to prevent flushing and blushing during the daytime hours when patients are out and about.

Dr. Del Rosso: Subantimicrobial-dose doxycycline is often underutilized in the treatment of rosacea. We need to recognize that because we're not treating a bacterium, we don't necessarily need an antibiotic dose of doxycycline and can avoid potential antibiotic resistance, even with prolonged treatment, with a subantibiotic dose. I typically prescribe 40 mg once daily. I find that my patients are more adherent to a once-daily dose than 20 mg twice daily.

Dr. Fromowitz: I agree that the 40-mg dose is a good choice to provide the most predictable outcome for our rosacea patients while allowing us to be antibiotic-resistance stewards.

I have found that, if you are only able to choose one agent with which to treat rosacea patients, the evening dose of ivermectin tends to give us the best outcomes. Of course, the combination of subantimicrobial-dose doxycy-

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cline and ivermectin is even better, but that's not always an option for our patients.

Dr. Del Rosso: One thing to consider about topical ivermectin is that clinical studies have shown it is most effective in patients with papulopustular lesions.¹ Topical azelaic acid can also be an option for these patients. Integrating an alpha-2 agonist such as topical brimonidine, when possible, as part of a combination regimen also makes sense.

Dr. Fromowitz: There was a recent study looking at the combination use of brimonidine and ivermectin that did raise concerns about irritability issues with brimonidine. Rosacea patients treated with that combination, however, did see clinical improvement with good overall tolerability.²

What's important to emphasize is that the agents we use to treat rosacea need to be driven by the individual patient's signs and symptoms. We are at the point where we can tailor our therapies to individual patients based on their skin condition and response to therapies.

Dr. Del Rosso: Let's return to talking more about the use of pulsed dye laser in the treatment of rosacea. How often do you find you need to repeat the use of pulsed dye laser because of the return of dilated vasculature?

Dr. Fromowitz: That's a great question. Reuse of the pulsed dye laser tends to be driven in part by the baseline severity of a patient's erythema, but I find more often that it is driven by the patient's lack of attention to a follow-up care regimen. I have many rosacea patients whose skin becomes markedly improved with the use of pulsed dye laser, but when they leave my office, they tend to ignore the general skincare lessons we discussed during their previous visit. They start drinking or smoking again, take in a lot of caffeine, eat spicy foods, and forget about a general skincare regimen. Indulging in these behaviors often triggers the return of their rosacea symptoms. I have some patients like that who require monthly laser treatment.

But in a patient who demonstrates good adherence to our after-care instructions, once we complete an initial regimen of 3 pulsed-

dye treatments set a month apart to help their background redness and erythema, we'll typically schedule maintenance treatment once or twice a year, unless there is a need to address individual telangiectasias.

Dr. Del Rosso: It is extremely important to reinforce with our rosacea patients that if they partake in behaviors that intensify the condition, those behaviors will often overcome the efficacy of any treatment they are prescribed. Our current therapeutic options don't cure their underlying disease, so if patients don't control the known triggers of rosacea, they are going to flare. It's as simple as that. We need to continually remind our patients that they need to be our partners in care.

Are there any specific strategies you utilize to explain to your rosacea patients the importance of adherence to combination therapy regimens? I find that in my practice, despite our staff's best efforts, adherence is a real issue.

Dr. Fromowitz: Medication adherence is tricky for all of us. The more complicated the regimen, the less likely the patient is going to adhere to it. Again, we explain to the patient that there is no cure to their rosacea and this is a chronic condition they need to partner with us to manage. To keep their symptoms at bay will require making the right choices in terms of any prescription medications, general skincare routine, and device use. They need to know the importance of their role. I will often ask for my patients' buy-in before we start treatment, so at least they have verbalized their commitment to me.

Being a good listener is one of the keys to helping patients with adherence issues. Show them that you care, that you are hearing them when they tell you what is bothering them, and you acknowledge their issues. That can all positively impact their buy-in and general adherence level.

For the majority of my rosacea patients, I try to give them the simplest regimen possible that includes a bland cleanser, mild moisturizer, and well-tolerated sunscreen in addition to our active medication regimen. We re-educate on the importance of each component at every visit. My nurses are great at reviewing and reinforc-

ing key pieces of information with my patients.

Dr. Del Rosso: Those are all great recommendations. One more thing I want to bring up is that I used to have patients who would come in after 3 months and tell me they aren't using their medications because it's too expensive. So now I tell every patient with rosacea before they even leave my office that if for whatever reason they aren't able to get access to a medication, or if they are quoted a price that sounds unreasonable, let us know and we will work with them to get what they need.

It's a horrible feeling to work with a patient, figure out a plan, and then essentially lose 3 months because of financial issues. Access to medication is a major issue that is too often ignored, so we're doing what we can to let patients know upfront that we are here as a helpful resource.

Dr. Fromowitz: Access is the handicapper of innovation. It has become such a significant issue for us that we have one member of our staff whose primary responsibility is to serve as the point person for our patients with financial or other issues that inhibit their access to medication. Just like you, we tell our patients before they leave our office that if they can't get every medication we agree on in our plan of action, call the medical assistant on our team and we'll figure out a solution.

We don't want lost time or productivity for our patients. In the worst case scenario, patients will blame us for lack of access or insurance issues. They think we did something wrong, so they move on to another doctor and start the process all over again.

Dr. Del Rosso: Those are all great points. I hope we've been able to offer a variety of helpful pearls for the dermatology community today that will assist them in their treatment of rosacea patients.

References

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