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Case Review: Rethinking Benzoyl Peroxide in Rosacea

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Dr. Bhatia:
Effective treatment of rosacea can decrease severity, prevent scarring, and improve self-esteem as well as quality of life. However, many clinicians do not understand the importance of diagnosing and treating rosacea early and effectively. What role does benzoyl peroxide play in the treatment algorithm for pustular rosacea?

This is CME on ReachMD, and I’m Dr. Neal Bhatia.

Dr. Sugarman:
And I’m Jeff Sugarman.

Dr. Bhatia:
Well, Jeff, good to be with you, as always. Dr. Sugarman, to start the discussion, would you please give us an overview of rosacea? A very broad question, but a good one I know you can answer.

Dr. Sugarman:
Thanks Neal. Sure. Rosacea is a chronic inflammatory condition that predominantly affects the central face, so the cheeks, chin, nose, and forehead. Usually starts between 30 and 50 years of age, but it really can occur at any age. And some affected individuals have recurrent episodes of flushing, persistent redness, and telangiectasia. So that’s so-called erythematotelangiectatic rosacea or ETR because it’s too hard to say the full name. Other people have more inflammatory papules and pustules. We call that papulopustular or inflammatory rosacea. And it turns out that many affected individuals actually have both ETR and inflammatory lesions coinciding.

One feature of rosacea that many people don’t fully appreciate is that a lot of people with rosacea also have ocular features, and that could include dryness, foreign body sensations, conjunctivitis, etc. And a few, mostly men, have phymatous changes on the nose, so-called rhinophyma. And historically, we’ve used these subtypes – ETR, inflammatory, ocular, and phymatous – to categorize our rosacea patients. But more recently, there’s been an updated phenotype-based schema that is being utilized. And I’ll just mention that briefly. There are 2 features that are independently diagnostic for rosacea, and that’s persistent centrofacial redness with periodic intensification by triggers and phymatous changes. And in the absence of those diagnostic criteria, there are major features that can establish a diagnosis, and those are flushing, which is transient, central redness; inflammatory papules and pustules; telangiectasia; and ocular manifestations. And last, there are also minor features that can present with or without those other features, and those include burning, stinging, dryness, and edema.

I’ll finish the introduction by just mentioning triggers because they’re important and your patients will ask you about triggers for rosacea.

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So triggers are factors that increase inappropriate inflammatory pathways, and that includes dysregulation of the innate and adaptive immune system as well as neurocutaneous mechanisms. In my opinion, the sun is really the major trigger for rosacea, but microbes play a very important role, and that includes demodex and other commensal organisms. And finally, once the rosacea phenotype is established, anything that increases blood flow to the facial skin can exacerbate symptoms. So that would be hot foods, spicy foods, exercise, etc.

Dr. Bhatia:
It's good you mentioned the triggers because it's the one prescription that we cannot write is the avoidance of triggers. And even more so just, again, the different presentations. Not just in darker skin types but also in men, you can see some activity on the neck, some areas around different parts of the face, and of course the ocular rosacea component to that is very important, because if we're not asking the right questions, the diagnosis can often elude us. So I think it's really a good overview, what you gave us. Even more so, again, the signs and symptoms. We don't think of itch as often as we do flushing and burning, but, you know, rosacea skin is just very hypersensitive as a whole, and that's where the right vehicles and the right topical combinations are very, very important for tolerability as well as maximizing adherence, which we'll get into in a little bit, as well.

Dr. Sugarman:
Well, now that we understand the condition, we really need to know how to treat our patients. Dr. Bhatia, can you walk us through some of the current treatment options for pustular rosacea?

Dr. Bhatia:
I think hitting the diagnosis first is pivotal because the potential to label these patients as possibly having acne or folliculitis or some other overlap of demodex-related dermatosis can happen. But pustular rosacea is not as uncommon as we give it credit for. But again, in many respects, rosacea under the hood is still rosacea, and we have to think about all the major components that led us to all of these flares, whether it be the cathelicidin pathways, the vanilloid receptors, the neutrophil roles, all of those are potential targets for therapy. And again, a pustular presentation can often lead the average clinician, whether it be an experienced dermatologist or anywhere in between, to immediately look for antibiotics. And antibiotics at the right dose are very pivotal. You know, the right subantimicrobial dose, for example, is really all you need for rosacea since there's no pathogen like there is with acne or an infection. The other part to that is the risk of small intestinal bacterial overgrowth that can go along with those antibiotic doses, and that can lead to some other issues as well as resistance on a global scale.

So really the maximal, you know, effort for topicals should really be in play for a good cleansing and moisturizing program that's compatible with whatever topical therapy that's a prescription, whether it be a gel, foam, or a wash, allowing the wash to at least sit for several minutes and then rinse. And then of course some new cream-based therapies with benzoyl peroxide, which we'll talk about in a little bit. All of these have to have good adherence, good tolerability, and, I think, ease of use.

Dr. Sugarman:
Oh, yeah, I completely agree. I think one thing that often strikes me when I get referrals from other physicians, you know, for treatment-resistant rosacea, is that they haven't really done the job of categorizing the phenotype. They might be treating just the redness and telangiectasias with antibiotics, for example, not realizing that the antibiotics really aren't going to help you with the inflammatory lesions of papules and pustules, and you really need either a vasoconstrictor or laser for the erythema and telangiectasia. So there's a reason why those patients aren't improving because they're really not on the right rosacea therapy.

Dr. Bhatia:
We want to customize treatment for age, gender, you know, occupation, and everything else that goes in between, but again, there's also a lot of stereotypes that patients may have from what they've been exposed to. And, you know, now we've been hearing a lot about benzoyl peroxide as a new treatment for rosacea, which, you know, historically has been an acne drug. There's still a lot of questioning why would benzoyl peroxide fit?

Now, Dr. Sugarman, you and I have both been involved with the development of the benzoyl peroxide cascade for, you know, where it's fit into both acne and rosacea. Let's hear your overview about the newer formulation and what it might mean for the management of rosacea.

Dr. Sugarman:
We've known for a long time that benzoyl peroxide could be very helpful for rosacea, but its use has really been limited by its irritancy potential, and it's really microencapsulation technology that's solved this problem. So in the microencapsulation technology, a silica shell wraps the benzoyl peroxide crystals and really serves as a barrier between benzoyl peroxide crystals and the skin, and that leads to less irritation. The skin lipids will migrate through that silica shell and promote solubilization of the benzoyl peroxide. And then that dissolved benzoyl peroxide would migrate through the sebaceous follicles in a more controlled release. And that'll promote efficacy for rosacea

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while minimizing the potential for irritation. And taking this through clinical trials, I'll just review the two phase 3, double-blinded, randomized, controlled trials for microencapsulated benzoyl peroxide.

So this is once-a-day dosing, 12 weeks of treatment, over 700 subjects. The results were compelling. And these are subjects that had moderate or severe rosacea at baseline and had to be clear or almost clear at 12 weeks to be considered a success. Nearly half of the subjects in the benzoyl peroxide-treated groups were treatment successes compared to only 16% to 26% in the vehicle groups, and that's a highly statistically significant result.

Similarly, the inflammatory lesion counts also improved in a statistically significant way compared to the vehicle, approaching a 70% reduction. But the most striking results, in my opinion, were the tolerability results. The tolerability in the benzoyl peroxide groups was remarkably similar to the vehicle group, and so really surprising that the tolerability would be that good.

Dr. Bhatia:
Yeah, I think you hit on some really major points there, especially the way that the active ingredient is preserved in the silica shells and how they interface between the oil and water, you know, brings everything together and makes for easy release. You know, that really, really is a testimony to the new technology that is going to maximize tolerability but also, again, the delivery to the amount of surface area that's involved. And I'm glad you covered some of the study data because, again, 700 patients or more, that's a good powered study, but also, you know, what we're learning from is, again, the tolerability equal to vehicle really says a lot because that means that we're not going to have the difficulties of what we used to have with poorly grade or even over-the-counter [OTC] benzoyl peroxide. And one of the things I think we'll face that we can use tolerability to our advantage is when generic substitution or even OTC substitution of this prescription comes into play and we'll have the data that says, look, we know what happens when benzoyl peroxide is in a substandard vehicle and what that does to compliance as well as disease outcomes.

Dr. Sugarman:
So let's put that knowledge into practice with a hypothetical patient, and let's just say we have a 33-year-old Caucasian female who has had about 2 or 3 years of central facial papules and pustules. People are starting to ask her about it at work, she's embarrassed about it, and she comes to you wanting to know what she can do to have a clearer face.

Dr. Bhatia:
I think, you know, the options for this patient would be readily available, especially a little bit more papular flare, we would probably want to get into anti-inflammatory dose or modified dose doxycycline. Probably want to think about what her cleansing and moisturizing habits are, especially anything medicated like with sulfacetamide. But where benzoyl peroxide would fit would probably be a great mainstay for her if she's perhaps used ivermectin cream in the past or if she's used metronidazole cream or gel, anything in that similar fashion. And then of course, azelaic acid, you know, there's always a useful tool, especially in darker skin or for whenever there's an overlap of acne or post-inflammatory change, but also for this kind of rosacea alone.

I think the way that we could recognize the place of benzoyl peroxide is what the patient's experience has been, but also sharing with them what the study numbers, what the tolerability numbers are, and even more so if there are any samples. This is a patient I would probably just give them the sample while they're sitting in the exam room and say, all right, put this on and tell me how it feels, because if they're presenting with their rosacea in full force and they can accept it as tolerable during a hypersensitive flare, that would be very telling to say, okay, well, this would be a compliance algorithm for the long run. So I think those would be some really useful ways of countering some of the discussion, as well as getting into the triggers and some of the other components of long-term outcomes and managing redness like we mentioned before.

Dr. Sugarman:
Yeah, those are really excellent points; I completely agree. I have a lot of patients who don't want antibiotics, and I think starting with a topical regimen for a lot of people is much more palatable, so I think benzoyl peroxide would fit in really well. Some people are going to need orals also, temporarily, and I think it's important not to discontinue the topicals because I like to leave people on their topicals after their oral course has completed so they can have some sort of maintenance therapy.

Dr. Bhatia:
Really, a lot of it is tolerability and what they're willing to accept, and I think we have a lot of opportunities ahead of us with benzoyl peroxide coming up.

Well, Jeff, this has been great, and as always, we know how to put our heads together and come up with some ideas. But before we wrap up, do you have any take-home messages for the audience?

Dr. Sugarman:
My take-home message is this: There's really been a paradigm shift in thinking about using benzoyl peroxide in rosacea, and it's really

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technology that's driving this. Microencapsulation has allowed the use of benzoyl peroxide to be exploited in the management of rosacea without compromising tolerability in these very sensitive skin patients.

Dr. Bhatia:
Yeah, I couldn't agree with you more, especially, you know, you think about tolerability of vehicle on a really hypersensitive face where you don't want to feel any kind of grittiness, any kind of burning or stinging from the active ingredients. This is where preservation of something like benzoyl peroxide, which will have good efficacy on the disease process, being put into a tolerable vehicle, which could, again, be something that could be the mainstay for some of these patients. So I think this is a real good time coming up for them, and I think we'll have a lot of opportunities.

So from here, I'll say thanks to Dr. Sugarman and thanks to everyone for tuning in, and we'll see you next time.

Dr. Sugarman:
Thanks, Neal.

Announcer:
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