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What Is “PFE”? It May Just Be Time You Found Out....

With all the literature and research we have on acne and rosacea, there are still many unanswered questions. Over time, as we uncover more information on both preexisting and newly recognized pathophysiologic pathways, modes of drug action, alternative therapies, caveats related to basic skin care, and the potential roles for physical modalities, we often find that specific information that we thought was fact, is later altered, expanded, or corrected. What is interesting, and sometimes perplexing to me personally, is how difficult it is for the clinical dermatology community at large to incorporate well-published concepts into everyday clinical practice. In this commentary, I address an example with rosacea that emphasizes the correlation of pathophysiology with clinical manifestations, and the importance of selecting treatment that targets the specific clinical manifestations of rosacea.

If persistent facial erythema (PFE) is the pivotal diagnostic feature of cutaneous rosacea, including in both the presence or absence of papulopustular lesions, why are the vast majority of medical therapy prescriptions within dermatology written for agents that specifically target papulopustular lesions and perilesional erythema?

This statement about topical prescribing data for rosacea is based on information I have had the opportunity to review from a research perspective. Two FDA-approved brand topical alpha-agonists (brimonidine 0.33% gel, oxymetazoline 1% cream) have been available for years, and specifically reduce PFE by constricting the chronically dilated superficial centrofacial vasculature.¹⁻³ Admittedly, their effects are transient, lasting several hours after application, thus warranting daily use. However, they successfully reduce PFE, which is the diffuse facial redness that intensifies during vasodilatory flares (flushing of rosacea) and persists between flares. In patients with papulopustular rosacea, perilesional erythema resolves as the papules and pustules resolve, leaving behind the diffuse redness of PFE that we so commonly see on the central areas of the cheeks, forehead, and chin. Nevertheless, the majority of prescriptions written for rosacea are for topical metronidazole, topical ivermectin, topical azelaic acid, and oral doxycycline.

If one considers that many cases of rosacea present only with PFE and do not have papulopustular lesions, the question I posed above becomes more perplexing. I think there are many facets to the “composite answer” to this question, which include cost considerations and access to medication, concerns regarding worsening of facial erythema due to the early adverse experiences with topical brimonidine affecting approximately 15% of patients (ie, rebound, paradoxical erythema), uncertainty with how to incorporate alpha-agonist therapy into rosacea management, and inconsistency of educational and promotional activities. However, I believe a major reason is that many clinicians have not fully grasped the concept of PFE of rosacea and the importance of addressing it in rosacea management. Despite spending a lot of time and effort researching, publishing, and discussing rosacea with colleagues, it took me years to grasp the concept of PFE in rosacea. I encourage my colleagues, if they do not yet fully understand or embrace the concept of PFE, to learn more about it, as I believe that will improve their clinical ability to manage rosacea. *Consider the role of PFE in essentially all patients with cutaneous rosacea.*⁴⁻⁶

The importance of moving beyond the “subtyping” of rosacea, evaluating the clinical manifestations that are present in a given patient, and addressing which of those manifestations are bothersome to the patient, has been discussed in the literature.⁵⁻⁸ This allows the clinician to recommend and select therapy that addresses each specific manifestation that is being treated. Ultimately, a combination of medical and physical approaches is warranted, either concomitantly or sequentially, to optimally manage rosacea. I credit my colleague, Dr. Julie Harper, for suggesting to me that the dermatology community at large needs a simple term like “PFE” to relate to. She ignited my desire to write this commentary.

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References

1. Fowler J Jr, Jackson M, Moore A, Jarratt M, Jones T, Meadows K, Steinhoff M, Rudisill D, Leoni M. Efficacy and safety of once-daily topical brimonidine tartrate gel 0.5% for the treatment of moderate to severe facial erythema of rosacea: results of two randomized, double-blind, and vehicle-controlled pivotal studies. *J Drugs Dermatol*. 2013;12(6):650-656.
2. Stein-Gold L, Kircik L, Draelos ZD, Werschler P, DuBois J, Lain E, Baumann L, Goldberg D, Kaufman J, Tanghetti E, Ahluwalia G, Alvandi N, Weng E, Berk D. Topical oxymetazoline cream 1.0% for persistent facial erythema associated with rosacea: pooled analysis of the two phase 3, 29-day, randomized, controlled REVEAL trials. *J Drugs Dermatol*. 2018;17(11):1201-1208.
3. Del Rosso JQ. Topical α -agonist therapy for persistent facial erythema of rosacea and the addition of oxymetazoline to the treatment armamentarium: where are we now? *J Clin Aesthet Dermatol*. 2017;10(7):28-32.
4. Tanghetti EA, Jackson JM, Belasco KT, Friedrichs A, Hougier F, Johnson SM, Kerdel FA, Palceski D, Hong HC, Hinek A, Cadena MJ. Optimizing the use of topical brimonidine in rosacea management: panel recommendations. *J Drugs Dermatol*. 2015;14(1):33-40.
5. Del Rosso JQ, Thiboutot D, Gallo R, Webster G, Tanghetti E, Eichenfield LF, Stein-Gold L, Berson D, Zaenglein A; American Acne & Rosacea Society. Consensus recommendations from the American Acne & Rosacea Society on the management of rosacea, part 5: a guide on the management of rosacea. *Cutis*. 2014;93(3):134-8.
6. Tan J, Berg M, Gallo RL, Del Rosso JQ. Applying the phenotype approach for rosacea to practice and research. *Br J Dermatol*. 2018;179(3):741-746.
7. Gallo RL, Granstein RD, Kang S, Mannis M, Steinhoff M, Tan J, Thiboutot D. Standard classification and pathophysiology of rosacea: The 2017 update by the National Rosacea Society Expert Committee. *J Am Acad Dermatol*. 2018;78(1):148-155.
8. Tan J, Almeida LM, Bewley A, Cribier B, Dlova NC, Gallo R, Kautz G, Mannis M, Oon HH, Rajagopalan M, Steinhoff M, Thiboutot D, Troielli P, Webster G, Wu Y, van Zuuren EJ, Schaller M. Updating the diagnosis, classification and assessment of rosacea: recommendations from the global ROSacea COnsensus (ROSCO) panel. *Br J Dermatol*. 2017;176(2):431-438.