Clinical Experience Utilizing Topical Combination of Benzoyl Peroxide 5%/Clindamycin 1% and Retinoids

The use of a fixed combination clindamycin/benzoyl peroxide formulation in conjunction with topical retinoids addresses multiple elements of the pathophysiology of acne.

By Joseph B. Bikowski, MD

Use of combinations of different classes of topical products—frequently antimicrobials and retinoids—is common in the management of acne vulgaris. This article provides background on the benefits of different classes of anti-acne medications and reviews data supporting their use in combination to complement three case reports of patients treated with benzoyl peroxide 5%/clindamycin phosphate 1% gel in combination with a retinoid. Clinical improvement is noted by photographic and physician assessments at baseline and follow-up visits.

Introduction

Acne has a multifactorial pathogenesis including sebaceous gland hyperplasia, follicular hyperkeratinization, microbial proliferation, immune reactions, and inflammation.[1] There is a variety of agents available for the treatment of acne, including topical and systemic retinoids and antibiotics, and antibacterials, such as benzoyl peroxide (BPO). Decades of clinical experience have shown unequivocally that acne responds best to a combination of agents that act upon different areas of pathophysiology, and drug development has increasingly focused on formulating combination products that can more effectively address multiple pathogenetic targets.

Benzoyl peroxide 5%clindamycin phosphate 1% (BPO/CP, Duac® Topical Gel, Stiefel Laboratories, Inc.) is such a product. This once-daily, fixed-combination moisturizing gel has demonstrated significantly improved efficacy and tolerability compared with its individual components.[2,3] Consensus guidelines recommend the use of a retinoid either alone or in combination with BPO and/or a topical antibiotic for mild-to-moderate inflammatory acne, and for most comedonal acne, except for very severe disease.[4,5] The combination of BPO/CP and a topical retinoid provides optimal synergism of agents. While each of these agents has some degree of anti-inflammatory activity, and both antibiotics and BPO decrease *Propionibacterium acnes* (P. acnes) proliferation, retinoids are the only anti-acne agents that normalize keratinization.[1,5,6] By using these agents together, the benefits of each overlap, thereby maximizing efficacy.

Data Supporting BPO/CP Gel Plus Topical Retinoids

The rapid efficacy of this combination was demonstrated in a study comparing tazarotene 0.1% cream (Tazorac, Allergan) once daily and either vehicle gel or BPO/CP gel in 121 subjects with moderate-to-severe acne.[7] Starting at week four, the combination of actives achieved a significantly greater ($P \geq 0.01$) and

Photos courtesy of Joseph Bikowski, MD

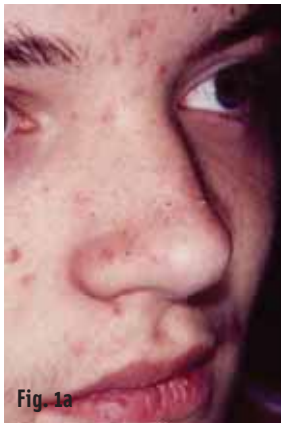
Fig. 1a

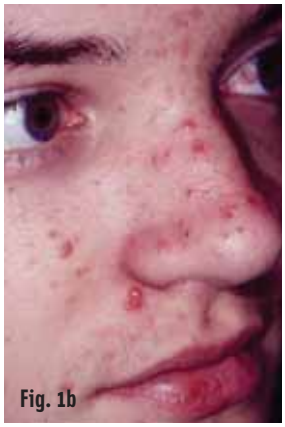
Fig. 1b

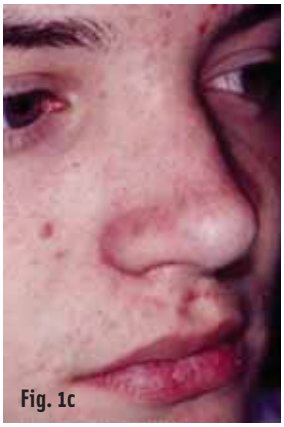
Fig. 1c


Fig. 2a


Fig. 2b

more rapid median reduction in comedones than tazarotene monotherapy (34 percent versus 18 percent and 70 percent versus 60 percent at week 12), and there was a significantly greater reduction in inflammatory lesions in patients with mean baseline papule/pustule counts of ≥25. In addition, the combination of tazarotene and BPO/CP gel was at least as well tolerated as tazarotene alone.

The combination of BPO/CP gel and a retinoid is also useful for moderate-to-severe acne. In a 12-week, randomized, investigator-blind trial in 353 patients with moderate-to-severe acne, the comparative efficacy of BPO/CP gel with tretinoin microsphere gel (TMG, Retin-A Micro, Ortho Dermatologics) 0.04% and 0.1%, and adapalene 0.1% (ADA, Differin, Galderma) was assessed.[8] Results showed 44 percent of the BPO/CP + tretinoin MG 0.04% group and 47 percent of the BPO/CP + tretinoin MG 0.1% had decreased by at least two grades of global disease severity at week 12, and BPO/CP + tretinoin MG 0.04% was significantly superior to BPO/CP + adapalene in mean percent reduction in inflammatory lesions from baseline (P = .0045). Adverse events in each group were few and mild, and lower than is typically observed in retinoid monotherapy studies.

These represent a fraction of the plethora of data supporting the combination of a topical retinoid and BPO/CP gel, and these data support what I have observed in practice. These agents are eminently flexible: they can be started together at the initiation of acne therapy or added to one another in any sequence to best tailor therapy to the individual patient's needs.

Case Report 1

A 16-year-old male had a one-year history of moderately severe grades 1, 2 and 3 acne vulgaris on the forehead, nose, cheeks, chin and central third of his face (Fig. 1a). He had been using over-the-counter (OTC) medications for one year and had not seen a dermatologist for his acne previously. I prescribed tazarotene cream 0.1% once daily at night on the entire face and instructed him to use a non-irritating, noncomedogenic cleansing and moisturizing regimen.

After six weeks of treatment the patient improved overall but still had multiple open and closed comedones on the nasal bridge and forehead, as well as persistent inflammatory lesions and comedones on the forehead, cheeks, nose, and chin (Fig. 1b), and one inflammatory nodule on the left side of his nose. I extracted six lesions without difficulty. I instructed him to continue the same treatment regimen; if he was not markedly improved after six more weeks of therapy I would add a systemic antibiotic.

After six more weeks of tazarotene treatment, I observed a 50 to 75 percent decrease in inflammatory lesions and open and closed comedones on the forehead, cheeks, chin, and nose, which was nearly 100 percent clear (Fig. 1c). There was no need for a systemic antibiotic. I instructed him to add BPO/CP gel to his evening regimen, continue the same cleansing and moisturizing regimen, and return in two months.

Case Report 2

The patient was a 14-year old female with a two-year

Photos courtesy of Joseph Bikowski, MD

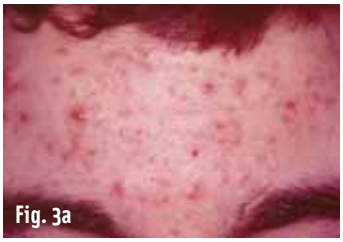
Fig. 3a

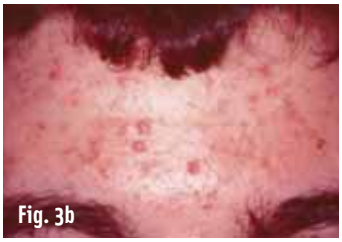
Fig. 3b

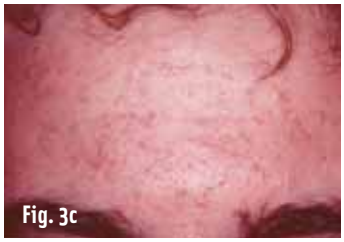
Fig. 3c

history of facial acne (Fig. 2a). In the past she had been treated by her primary care physician but did not recall which medications had been prescribed. Recently, she had been using OTC acne products, but with unsatisfactory effect. I prescribed BPO/CP gel to apply on her entire face in the morning, and adapalene 0.1% gel in the evening, and I instructed her to use a non-irritating, noncomedogenic cleanser and moisturizer twice daily. After six weeks of treatment, the patient showed dramatic improvement with only post inflammatory erythema on the forehead, cheeks and chin (Fig. 2b). I instructed the patient to continue with this regimen and follow up again in six weeks.

Case Report 3

This 14-year old male patient presented with a one-year history of acne, which he had treated unsuccessfully with a popular OTC acne kit. Upon examination, the patient had inflammatory papules and pustules and open and closed comedones of the forehead and chin and scattered on the left cheek (Fig. 3a). I prescribed BPO/CP gel once daily in the morning and clindamycin phosphate 1.2% tretinoin 0.025% gel (CP/TR, Ziana® Topical Gel, Medicis) at night. I instructed him to use a non-irritating, noncomedogenic cleansing and moisturizing regimen.

After one month of treatment, the patient had at least 30 percent improvement with a decrease in inflammatory lesions on the forehead, nose, cheeks, and chin (Fig. 3b). After four more weeks on this regimen, he experienced at least a 50 percent decrease in lesions on the forehead, nose, cheeks and chin, with only some postinflammatory erythema (Fig. 3c). After an additional five weeks (13 weeks total) of treatment, the patient showed dramatic improvement with the combination of BPO/CP and CP/TR. At that time he was essentially clear on the forehead, nose, cheeks and chin. I instructed him to continue using this regimen and return for follow-up in two months.

Conclusions

Concomitant use of topical BPO, antibiotics, and a retinoid is an ideal approach for the treatment of acne, because the combination of these agents addresses multiple pathogenetic processes and provides faster results and improved tolerability. In these cases, patients with mild-to-moderately severe acne vulgaris achieved meaningful therapeutic benefit from different combinations of these agents, which further validates existing clinical and trial data supporting the efficacy of combination therapy with BPO, an antibiotic and a retinoid. Furthermore, there is general agreement that when inflammation is an important component, concomitant use of a fixed combination agent such as BPO/CP and a retinoid is best; this was reconfirmed with these case reports. Other benefits of the fixed-combination BPO/CP gel include flexible, once-daily dosing and compatibility with other therapies, each of which ensures an easy-to-use regimen for the patient, which likely could improve patients' therapeutic adherence. ■

Dr. Bikowski has served on the advisory board, served as a consultant, received honoraria, and/or served on the speaker's bureau for Allergan, Barrier, CollaGenex, Coria, Galderma, Intendis, Medicis, OrthoNeutrogena, PharmaDerm, Quinnova, Ranbaxy, Sanofi-Aventis, SkinMedica, Stiefel, UCB, and Warner Chilcott.

1. Gollnick H. Current concepts of the pathogenesis of acne: implications for drug treatment. Drugs. 2003;63:1579-1596.

2. Lookingbill DP, et al. Treatment of acne with a combination clindamycin/benzoyl peroxide gel compared with clindamycin gel, benzoyl peroxide gel and vehicle gel: combined results of two double-blind investigations. J Am Acad Dermatol. 1997;37:590-595.

3. Tschen EH, Katz HI, Jones TM, et al. A combination benzoyl peroxide and clindamycin topical gel compared with benzoyl peroxide, clindamycin phosphate, and vehicle in the treatment of acne vulgaris. Cutis. 2001;67:165-169.

4. Gollnick H, Cunliffe W, Berson D, et al. Management of acne. A report from a Global Alliance to Improve Outcomes in Acne. J Am Acad Dermatol. 2003;49:S1-S38.

5. Thiboutot D, et al. New insights into the management of acne: An update from the Global Alliance to Improve Outcomes in Acne Group. J Am Acad Dermatol. 2009;60:S1-S50.

6. Kligman AM. The growing importance of topical retinoids in clinical dermatology: a retrospective and prospective analysis. J Am Acad Dermatol. 1998;39:S2-S7.

7. Tanghetti E, et al. Tazarotene versus tazarotene plus clindamycin/benzoyl peroxide in the treatment of acne vulgaris: a multi-center, double-blind, randomized, parallel group trial. J Drugs Dermatol. 2006;5:256-261.

8. Kircik L. Community-based trial results of combination clindamycin 1%-benzoyl peroxide 5% topical gel plus tretinoin microsphere gel 0.04% or 0.1% or adapalene gel 0.1% in the treatment of moderate to severe acne. Cutis. 2007;80:10-14.