Effective Combination Therapy for Moderate to Severe Acne

Evidence indicates that fairly short courses of oral antibiotic therapy when paired with a proven topical regimen can establish long-term efficacy.

BY LAWRENCE F. EICHENFIELD, MD

Dermatologists have access to a broad armamentarium for the treatment for adolescent acne. In treating more severe cases, oral antibiotics in addition to retinoids or retinoid combinations have proven particularly useful. However, questions continue to linger regarding the appropriate duration of therapy and how effective topical therapies can be after oral antibiotics have been discontinued. Fortunately, recent studies have clarified these issues and offered encouraging evaluations for effective combination regimens. One of these studies is the ACCESS trial, the results of which were published in recent months.

ACCESS DATA

With the evolution of topical combination therapies—which include retinoids and antimicrobials—a question behind the study was to what degree these agents improve acne when used along with oral antibiotics. How much better do our more severe patients get with topical combinations plus oral antibiotics, as compared to oral antibiotics alone? In addition, the ACCESS study sought to address what happens after the discontinuation of oral antibiotics when patients continue to use a combination retinoid/antimicrobial. Do they flare off of the oral antibiotics, or can the maintenance regimen of topicals maintain their improved acne?

The ACCESS study evaluated the combination agent adapalene 0.1% and benzoyl peroxide 2.5% (Epiduo, Galderma). The study was designed for patients with severe acne and was split into two parts. The first 12-week arm assessed the efficacy of adapalene 0.1% and benzoyl peroxide 2.5% (A/BPO) in a fixed dose used in combination with doxycycline 100mg once-daily, as compared to doxycycline alone (n=459).[1] In terms of total lesion counts, the combination group clearly fared better than doxycycline alone group as early as Week 2. Moreover, the A/BPO group saw statistical significant improvement in total inflammatory and non-inflammatory lesion counts by the end of 12 weeks.

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This part of the study showed the benefits of topical treatment with A/BPO with doxycycline, as compared to doxycycline alone, resulting in 64 percent reduction in lesion count—21 to 24 percent higher (depending on the type of lesion) in the combination group than with doxycycline alone. Additionally, digital fluorescent photography showed a marked reduction in *P. acnes* in the A/BPO group.

While these numbers are consistent with expectations based on clinical experience and previous data, the relatively high percentage (nearly 35 percent) of patients treated with the A/BPO combination that achieved clear or almost clear status was impressive, compared to less than 10 percent for doxycycline alone.

The second part of the study evaluated what occurs after stopping oral doxycycline, with and without contin-

ued use of A/BPO.[2] It is generally accepted that protracted use of oral antibiotics such as doxycycline should be avoided due to concerns of bacterial resistance. Tan, et al. combined data from the two previous controlled studies. Patients who had at least 50 percent improvement in their acne in part 1 of the study stopped doxycycline and were then randomized to received A/BPO or vehicle once-daily for 24 weeks. The highest rates of response were seen in patients who were on A/BPO plus doxycycline followed by A/BPO maintenance therapy. In this group, more than 50 percent of patients reached clear or almost clear status. In addition, in patients receiving A/BPO, total lesion counts decreased even after cessation of antibiotic therapy—down 76 percent by the end of the study. Patients receiving A/BPO also had an 85 percent satisfaction rate. Those in the vehicle group, by contrast, exhibited some regression and worsening of acne.

DISCUSSION

There are several takeaways from this study. For instance, it shows that a significant percentage of patients can be maintained with a retinoid/BPO combination after oral antibiotics, without a significant amount of flares. While a subset of individuals might flare off of oral antibiotic, this is probably not a significant portion of the population. Note that the ACCESS trial was performed in patients with severe acne, which may bode well for those with moderate acne.

This study argues that a topical combination product used with an oral antibiotic for several months yields good results, and that the continuation of a topical regimen consisting of a retinoid and antimicrobial such as A/BPO can result in continued acne control. This is an especially important message for our colleagues in pediatric medicine that may not have as much experience using oral antibiotics along with retinoid combinations in the management of acne. Overall, these studies should add to physicians' overall comfort level with appropriate use of oral antibiotics for fairly short durations, plus combination topical agents, both in terms of tolerability and efficacy.

Findings from the ACCESS trial fit well with recommendations of the American Acne and Rosacea Society Pediatric Acne Guidelines, which developed algorithms for the management of pre-adolescent and adolescent acne. The Guidelines stress that the use of oral antibiotics for moderate to severe acne is reasonable, but should be paired with the use of a BP-containing agent, either as a wash or in a combination treatment, to minimize the emergence of bacterial resistance. In addition, a retinoid should be used in essentially all regimens for moderate to severe acne; while some adolescents may want to use "a pill" alone without topical agents, this should be avoided. In general, after an adequate course of oral antibiotics used with topical retinoids or retinoid combination therapies, most all individuals should be transitioned to a topical regimen alone.

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This data may also prompt researchers and clinicians to ponder the possibilities of other combination approaches incorporating retinoids and antimicrobials. For example, there are several antimicrobial combinations with lower strength BPO plus clindamycin that might be useful in regimens of care with topical retinoids. The advantage of a lower strength BPO is that it potentially makes the formulation less irritating. Nevertheless, the particular combination employed in the ACCESS trial has shown a great deal of benefit itself and also benefits from the recent launch of pump delivery technologies. Unit dosing is generally much appreciated by patients, as it takes away a variability of under- or over-use of the agent, and it may improve adherence.

CONCLUSION

The ACCESS data confirm current guidelines advising use of topical retinoid combination regimens for moderate to severe acne. Additionally, these trials importantly reiterate that patients can likely continue to benefit from ongoing use of a topical retinoid/antimicrobial combination after the discontinuation of oral antibiotics. Moreover, the data provide good evidence that fairly short courses of oral antibiotic therapy when paired with a good topical regimen can establish long-term efficacious therapy for a majority of patients with acne. ■

Dr. Eichenfield has served as an investigator and past consultant for Galderma, Valient, GSK-Stiefel, and Medicis.

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