Acne Topical Therapy: Improving Outcomes

Four pearls for making today's acne therapies work for your patients.

BY JOSHUA ZEICHNER, MD

While drug development has brought a slew of new medications to the market for skin diseases like psoriasis and eczema, there have been no new chemical entities introduced to the acne market in a decade. New drugs currently in development that may come to the US acne market in the next few years include a new tetracycline-class antibiotic called sarecycline, a topical minocycline gel and foam, a topical sebum inhibitor called olumacostat glasaretil, and a new topical retinoid called trifarotene. Until we have new tools at our disposal, we must optimize the way we use currently available mediations. Following are four practical tips on best practices for treating acne with topical medications, based on available published data.

1. Hit acne hard from the beginning. Consensus guidelines recommend combining different medications with complementary mechanisms of action to address multiple pathogenic factors simultaneously. But what is the best way to combine agents? Should different drugs be used together from the onset? Given the potential for irritation, should one drug be started first then another added at a later date?

A 2007 study assessed different combination options in treating acne patients.[1] One hundred nine patients were enrolled in a 12-week study and randomized into one of three treatment arms. Patients applied a.) adapalene 0.1% gel alone for 12 weeks; b.) a fixed dose benzoyl peroxide 5% with clindamycin 1% gel (BPO/C) alone in the morning for four weeks, then added adapalene 0.1% for the last eight weeks; or c.) the combination of the BPO/C in the morning and adapalene in the evening for the full 12 weeks. Numerically, the combination of BPO/C resulted in a greater mean percent reduction in the total number of lesions as early as two weeks. By the week 12 visit, patients using the combination of BPO/C for the entire study demonstrated statistically significant improvements compared to the other arms. The patients who added adapalene to the BPO/C for the last eight weeks demonstrated numerically greater mean total lesion count reductions compared to the adapalene only arm.

Based on the data from this study, we can conclude that starting patients on combination therapy from the beginning is associated with improved outcomes.

2. Keep your regimen simple. "Keep it simple, silly" (KISS) can be applied to life and acne treatment. Even the most efficacious drug will only work if the patient is using it. The fewer times that a patient must apply a product, the fewer times that there will be a missed application. In the real world, even the most diligent patient will inevitably forget to apply every dose as prescribed. This effect is magnified when products must be used more than once per day.

A 2010 study evaluated both clinical outcomes and regimen adherence in acne patients using either once-daily or twice-daily dosing.[2] In the 12-week study, 26 patients with mild to moderate acne were randomized one-to-one to receive either a brand name fixed dose combination topical gel containing clindamycin phosphate 1.2% along with tretinoin 0.025% (CP/T) once daily or the generic monotherapies, one in the morning and the other in the evening. Endpoints of the study included clinical improvement of acne as well as regimen adherence; electronic monitoring caps measured whether subjects were actually using the products.

At week 12, the group using the once-daily fixed dose CP/T product achieved a 51 percent mean total lesion count reduction compared to only 32 percent in the twice-daily generic drug group. While some may argue this can be attributed to characteristics of the brand versus generic medications, there was a difference in adherence to the regimen, as well. The median adherence rate was 88 percent in the once-daily group, which decreased to 61 percent in the patients applying medications twice daily. We can imagine that adherence rates in the real world are significantly lower than that. Without frequent trips to the doctor, motivation from being in a study that may offer honorarium, and daily required logs, patients may be less motivated to apply prescribed regimen in a real-world setting.

Based on the data from this study, we can conclude that simpler regimens are advantageous compared to more complicated ones. Fixed-dose combination drugs offer the opportunity for

once-daily dosing and better outcomes for our patients.

3. Keep treating. Acne is not a 12-week disease. While acne trials have traditionally been designed with endpoints at 12 weeks, this is a relatively arbitrary endpoint; no true data establishes 12 weeks as the optimal time point at which to evaluate efficacy. Moreover, in the real world, acne lasts much longer than the 12 weeks. Patients may suffer from acne for years, either through adolescence or even into adulthood. To keep patients clear, it may be necessary to keep them on medications continuously.

Several studies have evaluated long-term use of topical acne drugs, and they show continued improvement in lesions beyond the 12-week endpoints of the initial clinical trials. In one 52-week, long-term study, both effectiveness and tolerability of fixed-dose combination adapalene 0.1% with benzoyl peroxide 2.5% gel (Ada/BPO) were assessed.[3] Four hundred eleven patients with moderate acne were enrolled in this open-label study. Improvements were observed as early as week 1, and patients continued to improve over the 12-month study period. Fully 327 patients remained in the study for its entirety, known as the per-protocol population, and were evaluated for percent reduction in acne lesions. At the month three visit, the same time point at which most acne trials end, mean percent reduction of total lesions was about 55 percent. As patients continued to treat the skin during the next nine months, percent reductions in total, inflammatory, and non-inflammatory lesion counts grew to 70.8 percent, 76 percent and 70 percent, respectively.

A long-term study looked at using fixed-dose combination clindamycin phosphate 1.2% with benzoyl peroxide 3.75% gel (CP/BPO) in adult women with acne.[4] Twenty patients aged 25-63 years old with moderate acne applied the medication once daily for an initial 12-week period. Patients who achieved at least a 50 percent reduction in total lesion count continued on to an additional 12-week extension. Eighteen of the 20 patients moved to the second study period. At week 12, the mean inflammatory and non-inflammatory lesion count reductions were 70.6 percent and 58.6 percent, respectively. Continued use of the medication resulted in inflammatory and non-inflammatory lesion count reduction reductions of 93.8 percent and 90 percent respectively at week 24.

Continued improvements past what is initially observed after 12 weeks have also been reported with topical dapsone. In a 52-week study evaluating use of topical dapsone 5% applied twice daily, mean percent reduction of total lesions of 38 percent at week 12 improved to 49 percent at week 52.[5]

4. Determine your maintenance regimen. Acne treatment may be viewed as an initial acute therapy phase followed by maintenance. A two-part study published in 2005 and 2006 evaluated initial treatment followed by maintenance therapy with topical adapalene gel.[6,7] For the studies, 467 patients with severe acne were treated with either adapalene gel, 0.1% once daily with doxycycline 100mg or vehicle gel with doxycycline. Patients who achieved at least a 50 percent improvement from baseline (n=253) moved over to the second study in which they were re-randomized to use either adapalene or vehicle gel once daily for 16 weeks maintenance therapy. By week 16, statistically significant worsening was observed in patients who were using vehicle gel compared to adapalene. Not prescribing a maintenance medication after initial clearance is associated with a relapse in acne.

Your choices for treating acne depend on severity, lesion type, and patient preference. The regimen that you may initially prescribe is often different from what you may prescribe for maintenance. Especially given the potential side effects of medications like oral antibiotics, appropriate choices must be made in maintenance drugs. In a 2006 study, 189 patients with moderate to severe acne were treated with a combination of minocycline 100mg twice daily along with tazarotene 0.1% gel.[8] At week 12, patients who achieved a 75 percent or greater improvement (n=110) moved into a 12-week maintenance phase and were randomized to receive tazarotene gel plus a placebo pill twice daily, vehicle gel plus 100mg minocycline twice daily, or tazarotene gel plus 100mg minocycline twice daily. After 12 weeks of maintenance treatment, there were no statistical differences in overall disease severity between the three regimens. Given this, we can conclude that maintenance topical tazarotene gel 0.1% monotherapy works as well as combination treatment with oral minocycline or use of minocycline alone in maintaining acne improvement. We can reduce overall antibiotic exposure in our patients by discontinuing them after initial improvement.

CONCLUSION

We must best use the tools at our disposal to optimize outcomes. Ways to achieve this include 1. combining complimentary acne treatment from the onset of treatment; 2. using fixed-dose combination drugs that offer simpler regimens for patients to adhere to; 3. educating patients on when improvements occur, and 4. properly selecting maintenance regimens. ■

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