An Update on Topical Acne Treatments

Benzoyl peroxide alone and in combination remains a cornerstone of topical acne therapy. Recently presented data explore the efficacy and tolerability of novel formulations.

By Paul Winnington, Editorial Director

More than 80 years after it was formulated for use in topical acne treatment, benzoyl peroxide (BPO) remains a cornerstone of topical therapy. The agent has been the object of renewed attention recently, given that it provides efficacy against Propionibacterium acnes (P acnes) without inducing bacterial resistance and it has been associated with keratolytic, comedolytic, and anti-inflammatory activity in acne. BPO is also recognized for its versatility; it can be used alone or in combination with topical and/or systemic antibiotics and other topical acne treatments.1,2

Novel formulations containing BPO have come to market recently. Posters presented at the 28th Anniversary Fall Clinical Dermatology Conference, Las Vegas, NV (October 15-18) offered insights into new formulations featuring this commonly-used topical acne treatment.

Reported Findings

Use of antimicrobial washes has become standard for the management of trunk and back acne, but new data indicate a benefit for a novel benzoyl peroxide emollient foam formulation. A five-week open-label study of 20 healthy adult volunteers (19 were evaluable), compared P acnes reductions associated with BPO 5.3% emollient foam and those associated with BPO 8% wash (Leyden). Subjects applied the BPO foam to their backs daily during weeks 1 and 2, applied no products during week 3, and then applied BPO wash daily during weeks 4 and 5. Total P acnes counts were reduced by 1.8 log at the end of week 1 and by 2.1 log at the end of week 2, attributable to use of the BPO foam. Counts returned to baseline by the end of week 3 (washout). Use of BPO wash produced no reduction in P acnes counts even after two weeks. Because patients applied the foam under supervision at the study center but were not supervised during the period of PBO wash use, it is possible that misapplication or failure to apply the wash contributed to suboptimal performance.

Combination products featuring benzoyl peroxide and clindamycin have been used for some time, while a fixed combination formulation of benzoyl peroxide and adapalene is relatively new to the market. A short-term study compared the tolerability and irritancy in healthy adults of two fixed-dose combination gels (Grove, et al.). Forty-seven individuals completed the study in which subjects were randomly assigned to use either benzoyl peroxide 5%/clindamycin 1% gel or BPO 2.5%/adapalene 0.1% gel for two weeks. Subjects applied their assigned treatment to one half of the face; the contralateral side served as the control. Subjects were evaluated every weekday during the study period prior to application of the study medication. Primary measure was expert grader scores for tolerability, as indicated by erythema and dryness. Secondary measures included barrier integri-
ty as indicated by transepidermal water loss (TEWL), patient self-assessment of erythema and dryness, and adverse events.

Of the original 52 patients enrolled in the trial, one withdrew, one was lost to follow-up, and three were discontinued by the researchers due to irritation (one in the BPO/C group on day 1, and two in the BPO/A group on day 7). Expert grader ratings for dryness were not significantly different between BPO/C and controls throughout the study period, but ratings for BPO/A were higher than controls of BPO/C beginning day three and peaking at day 9. The difference was statistically significant. Patients’ self-assessments of dryness were also statistically significantly higher for BPO/A compared to BPO/C or controls, but the difference in scores was not as dramatic. Patient reports of burning associated with BPO/A rose at day 3 and fell by around day 9, while incidence of burning with BPO/C was similar to that for controls.

There was a statistically significant increase in TEWL associated with BPO/A compared to BPO/C or controls, beginning around day 3 and peaking at day 7. All treated and control sites exhibited a modest increase in erythema at day one; scores were similar for all evaluated sites throughout the course of the study. Researchers speculate that the facial cleanser applied to the full face of all subjects may have contributed to this erythematous effect.

A 12-week study (Zouboulis, et al.) compared the efficacy and tolerability of once-daily applica-

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**Pediatric Dermatology Updates**

A number of posters presented at the Fall Clinical Dermatology Conference addressed management of pediatric diseases.

Following are some highlights.

- In follow-up to a publication demonstrating the safety and efficacy of etanercept in pediatric patients, researchers presented sub-group analyses based on age, gender, and treatment history, demonstrating similar response to the biologic therapy across groups (Paller, et al.). The analyses revealed that, regardless of sub-group classification, consistently more etanercept-treated patients than controls achieved PASI 75 by week 12. Among treated patients, the percentages of patients achieving PASI 75 were similar when stratified by age (four to 11 or 12-17), gender, baseline BSA (≤ 20 percent or > 20 percent), baseline PASI (≤ 16.4 or > 16.4), baseline PGA (≤ 3 or > 3), baseline disease duration (< six years or ≥ six years), or history of previous systemic therapy or phototherapy. Anywhere from 52 to 64 percent of treated patients in any subgroup had achieved PASI 75 by week 12. Four serious adverse events occurred in three patients (benign ovarian mass and lobar pneumonia in two etanercept-treated patients and gastroenteritis and dehydration in an un-treated patient); six etanercept-treated patients discontinued the study due to AEs or infections.

- To provide additional data regarding the safety and efficacy of low-potency topical corticosteroids in the management of pediatric AD, two studies investigated the effects of hydrocortisone butyrate 0.1% lipocream (HCB). The first study was a double-blind randomized, controlled trial of HCB in patients from three months to less than 18 years of age with mild to moderate AD (Abramovits, et al.). At day 29, 63 percent of treated patients (HCB twice daily) achieved PGA score of 0 or 1 (treatment success), versus just 28 percent of controls. HCB therapy produced an 82.1% decrease in average BSA at day 29 compared to a 43.6 percent average decrease in BSA among controls. Treated patients were also significantly more likely to experience an improvement in pruritus scores by day 29. Incidence of side effects was similar in both groups, with no topical steroid related side effects reported in the treatment group.

- A four-week open label adrenal suppression study of HCB involved patients three months to less than six years of age and 12 to less than 18 years of age with moderate to severe AD (Abramovits, et al.). Five of 63 evaluable subjects (eight percent) had laboratory evidence of adrenal suppression at the end of the trial, but no patient had clinical signs or symptoms of suppression. Adrenal axis function returned to normal within four weeks of treatment discontinuation in three subjects and within eight weeks in one subject. One subject was lost to follow-up. The mean BSA involvement for treated patients decreased from 40.5 percent at baseline to 6.5 percent at day 29. No patient reported topical steroid related side effects.
tion of BPO/C to that of BPO/A in 382 subjects with mixed inflammatory and non-inflammatory acne lesions. There was no statistically significant difference in the overall reduction of inflammatory lesions (mean reduction of 76.8 percent for BPO/C and 72.2 percent for BPO/A) or non-inflammatory lesions (mean reduction of 62.2 percent for BPO/C and 61.5 percent for BPO/A) between the two groups over the course of the study, although BPO/C had provided a statistically significantly greater decrease in inflammatory lesions at week 4. Nonetheless, week 12 Investigator’s Static Global Assessment (ISGA) of success was statistically significantly higher in the BPO/C group compared to BPO/A (31 percent versus 22 percent). Physician- and patient-rated scores for erythema, dryness, peeling, pruritus, and burning/stinging were generally higher in the BPO/A arm throughout the duration of the study.

A third study involving benzoyl peroxide 5%/clindamycin 1% gel compared its antimicrobial effects to those of clindamycin 1.2%/tretinoin 0.025% gel (C/T) in 54 subjects with mixed inflammatory and non-inflammatory acne lesions (Jackson, et al.). Subjects were randomized to use either treatment once daily for 16 weeks. While both treatments led to reductions in P. acnes counts, reductions were greater in the BPO/C group throughout the study (median percent reduction was 94.5 percent for BPO/C versus 16.8 percent for C/T at week 2; 99.7 percent versus 73.3 percent at week 16). Of interest, only subjects treated with BPO/C demonstrated decreases in clindamycin- or erythromycin-resistant P. acnes. By week 16, reductions in inflammatory and non-inflammatory lesion counts, Investigator Global Assessment scores, and Overall Disease Severity scores were similar in both groups. However, inflammatory and total lesion counts were greater with BPO/C at week 4.

Data were also presented for a different BPO/C fixed combination gel, suggesting that clindamycin phosphate 1.2%/benzoyl peroxide 2.5% gel improves skin hydration and barrier function compared to other fixed combination products (Jorizzo, et al.). Twenty subjects were enrolled in the study, which compared once-daily BPO 5%/C 1% and twice-daily BPO 5%/C 1% to once-daily BPO 2.5%/C 1.2%. Subjects were randomly assigned in a double-blind fashion to apply products to four different test fields on the forearm (two fields per arm). Skin hydration, measured by TEWL, was maintained by BPO 2.5%/C 1.2%, while the twice-daily fixed combination formulation produced a statistically significant decrease in skin hydration.

Erythema and irritation were measured as markers of barrier disruption. Compared to untreated control sites, the clindamycin phosphate 1.2%/benzoyl peroxide 2.5% formulation produced no notable irritation or erythema. The lower-concentration formulation was better tolerated than either of the other active treatments.

BPO 2.5%/C 1.2% is the only fixed combination product indicated for once-daily application to treat inflammatory and non-inflammatory acne lesions; one BPO 5%/C 1% formulation is indicated for twice-daily application to treat both types of acne lesions, and the other is indicated for once-daily use for inflammatory acne lesions.

Finally, one poster reviewed data for solubilized BPO in the topical treatment of acne (Seidler EM, et al.). A meta-analysis of 23 randomized controlled trials assessing the efficacy of solubilized BPO 5% ± salicylic acid 2% (sBPO±SA), BPO 5%, clindamycin 1-1.2% (CL), or combination BPO/CL suggested that sBPO±SA is at least as effective in reducing inflammatory and non-inflammatory lesion counts as other studied products. At weeks 2 to 4, sBPO±SA provided a statistically greater reduction in inflammatory and non-inflammatory lesion counts. Only two evaluable studies of sBPO±SA extended to 10-12 weeks, limiting the reliability of data comparisons, but these showed similar efficacy of sBPO to BPO/CL.